UC Riverside

UC Riverside Electronic Theses and Dissertations

Title

Resting as Knowing: a Lagged Structure Analysis of Resting State fMRI with Application to Mind Wandering During Oral Reading

Permalink

https://escholarship.org/uc/item/9d0583jd

Author

Jahner, Erik Erwin

Publication Date

2017

Supplemental Material

https://escholarship.org/uc/item/9d0583jd#supplemental

Copyright Information

Peer reviewed|Thesis/dissertation

UNIVERSITY OF CALIFORNIA
RIVERSIDE

Resting as Knowing:
a Lagged Structure Analysis of Resting State fMRI
with Application to Mind Wandering During Oral Reading

A Dissertation submitted in partial satisfaction
of the requirements for the degree of

Doctor of Philosophy

in

Education

by

Erik Erwin Jahner

December 2017

Dissertation Committee:
      Dr. Lee Swanson, Chairperson
      Dr. Katherine Stavropoulos
      Dr. Mary Helen Immordino-Yang
      Dr. Rollanda O'Conner

The Dissertation of Erik Erwin Jahner name is approved:

_____

_____

_____
                                                    Committee Chairperson

University of California, Riverside

Acknowledgements

I am grateful for the opportunity to work with a number of accomplished scholars who graciously offered their valuable time. My colleagues at the Brain and Creativity Institute at University of Southern California were helpful in challenging me and assisting in the development of the technical and cognitive-emotional skills necessary to complete this dissertation. In particular, Dr. Xiao Fei Yang helped me on numerous occasions with theory and technical skills and Rodrigo Riveros and Rebecca Gotlieb helped me build the necessary confidence and gave me invaluable feedback during the process. Dr. Bosco Tijan, whose life was taken earlier this year, also supported my development in fMRI analysis encouraging my use of new tools and critiquing methods.

I would also like to thank the members of my committee. As my personal and professional mentor, Dr. Mary Helen Immordino-Yang taught me what it means to be a scientist. Dr. Rollanda O'Connor's assistance with tedious editing was also greatly appreciated along with her encouragement to explore. Dr. Katherine Stavropoulos helped me reflect on the role of neuroscience in education and helped me limit the scope of this project and prepare me for a life in academia.

I would finally, like to thank my parents, Ruth and Egon Jahner, who offered me the financial and personal support without which this would not have been possible.

Dedication

This dissertation is dedicated to my life partner Etien Mendoza as this intellectual endeavor was a joint experience. At every stage of my thinking he offered invaluable intellectual support as we thought through the philosophies presented here. But above all, the dissertation process involves an emotional transformation and resilience during which my partner supported my development and repeatedly grounded me during particularly difficult moments and moments of unbounded enthusiasm. Working with Etien on this project was a great pleasure, and I know he enjoyed participating in this shared creation of knowledge; this accomplishment is equally his. This is only the beginning of the knowledge and experiences we will create. Together we collect, build, appreciate, and begin to see.

ABSTRACT OF THE DISSERTATION

Resting as Knowing:
a Lagged Structure Analysis of Resting State fMRI
with Application to Mind Wandering During Oral Reading

by

Erik Erwin Jahner

Doctor of Philosophy, Graduate Program in Education
University of California, Riverside, December 2017
Dr. Lee Swanson, Chairperson

The human brain is an ongoing dynamic system not activated by experience but nudged from intrinsic activity into new network configurations during perception and learning. Ongoing neural activity during rest is assumed to reflect these intrinsic dynamics in a relatively closed system state. Traditionally, inter-regional connectivity in this system is measured by obtaining time-locked correlations in BOLD activity using fMRI. It is well documented, however, that neural activity unfolds across time and is not isolatent to some reference point.

This exploratory study is a theoretical analysis of how a lagged analysis of resting state dynamics in fMRI could represent persistent representations of knowledge in the neocortex. A novel procedure using both surface based maps and independent component analysis (ICA) is applied to a small group of 54 adolescents. The ICA methods appear to reveal lagged structures with different information than traditional

resting state analysis. The group level results are symmetrical between hemispheres and may represent high level perceptual systems.

The components obtained from this exploration are then used to attempt understand how these knowledge systems in neocortex frame mind-wandering frequency when reading aloud in a subset of 38 individuals. The results did not correlate with any known neural systems related to mind wandering, but the methods here are unique. One of the identified components shows significant difference in the lag structure of the occipital cortex as a function of mind wandering frequency during oral reading. This demonstrates that it may be worth exploring the timing in visual system to understand why individuals mind wander when reading aloud. Reverse inference is used to interpret results and suggest future approaches.

Table of Contents

List of Figures

List of Tables

Introduction

The ultimate goal of this document is to explore an fMRI approach to identify persistent neural representations of knowledge for readied skilled engagement with the environment. In this approach, knowledge is not a set of actions to be "activated" by context nor is it limited to qualitative experiences, but is ongoing system dynamics always ready and available to be nudged into heightened states of activation and simultaneously reliable and novel configurations. Importantly, this approach does not examine these traces in action, but instead asks the question of what system representations might be when not in action. We will end with an examination of how these persistent representations may enable mind wandering in an oral reading activity.

Knowledge cannot just disappear when not in use. Knowledge must have a "persistent" representation to change a future "behavior or behavior potentiality" and for this potentiality to exist there must be some trace in the learner which can give weight to continued skill development even when that cognitive apparatus is not directly engaged (Shuell, 1986). Therefore, these sought representations are persistent in that they last beyond the immediate context of skill application and persist in the latent dynamics of neural activity. Part 1 of this document will establish the metatheoretical and neurological motivations for this exploration and how they inform an analytic neurosceintific methodology. In Part 2, we will apply this methodology to a group of adolescents and examine what may be group level representations of these system dynamics in this population. Finally, in Part 3, we will use the group neural representations of knowledge systems extracted in Part 2 to explore what might give rise to the specific behavior of

mind wandering while reading aloud. But, before we begin, a basic overview clarifying the focus and neurological methods and their application will be presented.

While persistent representations exist in artifacts outside the individual in written, artistic, and other social tools, one place to examine these persistent representations is in the brain. Experience is written into the brain making it an artifact, albeit a living one, of persistent representations of knowledge. This approach is built on specific epistemological assumptions requiring the reader to recognize the brain as the location of knowledge, and it will therefore require an explication of the mind-brain relationship. Knowledge is not floating out in the ether in a Platonic sense (White, 1976), nor, it will be argued, is it a separable mysterious emergent level of cognition (Bunge, 1980) as an agent causing changes on the brain; knowledge is embodied and encultured and thus it leaves a print on concrete artifacts of the biological.

One common way to observe knowledge would be to observe brain dynamics as they interact with the world. This would be a context dependent view of knowledge where knowledge is continually reconstructed with engagement with the external world. This approach is not denied here, but if rigidly adhered to also misses a key aspect of knowledge: knowledge must persist beyond experience. It may not be complete until it is engaged, but some representation, even if it is incomplete must exist in the learner.

Here, knowledge will be examined in the awake but externally disengaged participant through magnetic resonance images (MRI). Wrapped in the humming magnets of the MRI, relatively motionless, awake but staring onto a blank screen, an individual is relatively disengaged from the world. With the important exception of personal history,

the individual's body and embodied neurology become a relatively closed system when compared to the exposure to external events of daily life. In this situation we may observe more easily the representations we seek as the system is not strongly biased by external task demands. So, do we see a reduction in activity? Without active engagement with the world, does the brain shut down?

Based on pop-culture representation of neurobiology one may be forgiven for believing that the brain adjusts its global activity when presented with external tasks as opposed to resting. However, only very negligible differences in metabolic processes of the brain are observed in changes between internally and externally focused attention states (Raichle, et al., 2001; Raichle & Gusnard, 2002). Neural activity does not depend on energetic input from the environment to drive activity, nor does the environment "flip a switch" to "turn-on" skilled engagement in neural regions that are currently "off". All neurons are in a constant state of activity, and this constant state of activity is essential for environment engagement; neural activity is not simply stopped nor is it dramatically reduced when individuals are disengaged with external processes. This dynamic ongoing activity is rooted in constant fluctuations in anatomical, electrical, and chemical dynamics in the brain. As will be discussed, while stochasticity plays a central role in learning, the resulting patterns are not random and they are governed by previous bidirectional influences which leave persistent representations in the hardwiring of the brain that we can indirectly observe. The brain is an active living system and the eddies in the system dynamics help us unveil the neural components of cognition and perhaps can even help us understand the relation between cognitive events.

It is the goal in this document to understand how these system dynamics can be observed and interpreted. Functional magnetic resonance imaging (fMRI) of resting individual across time will be the primary method of exploration here. It is theorized that this resting state fMRI (rs-fMRI) data can be analyzed in such a way as to reveal these latent dynamics representing persistent neural representations of knowledge for readied skilled engagement with the environment. In essence, the resting state scans are used to reveal modularity of thought (Fodor, 1983), but the modules of thought are not the traditional machines to be activates when needed; they are ongoing dynamics (Sporns, & Betzel, 2016). Identifying these systems may help us understand reasons that the mind wanders in specific circumstances.

Overview of rs-fMRI analysis

Before diving into the metatheoretical and neurological foundations establishing why these methods are appropriate, let me briefly introduce the neurological methods that we will be working towards throughout this document. While many neurological methods could be used to examine these persistent representations discussed here, I shall focus on the use of rs-fMRI to uncover these neural dynamics. However, fMRI is useful only through an understanding of what it might represent about the system components. By itself, it is only an indirect measure of magnetic resonance in tissues.

While the fMRI signal is not completely understood, it relates to the oxygenation of blood supplying the nutrients for neuronal maintenance and development; the fMRI signal reveals system dynamics, albeit at a very gross high level. This results in some weakness in the MRI methodology. First, the fMRI does not directly record neural

activity but is thought to be a record of changes in blood oxygenation level affected by neural activity (Ogawa, Lee, Kay, & Tank, 1990). Secondly, the fMRI operates at a recoding scale much larger than the components it purports to measure. To give some idea of scale, the cerebral cortex (a thin layer covering the brain <4 mm thick) accounts for about 80% of the brain's weight and 20% of its neurons (Raichle, 2006). This neocortical region of 16 billion neurons is the region where the current analysis will be limited. In a single mm^2 of surface area in the cortex, we have approximately between 100,000 and 150,000 cells and of these cells ~95,000 are neurons (Carlo, & Stevens, 2013). For each neuron we have approximately 10,000 synapses and about 1 cm of myelinated axons (Schüz, & Palm, 1989). The methods described here attempt to maximize this resolution giving us just under 1 million neurons per data point. Secondly, the fMRI methods used here sample the data only every 2 seconds as compared to neural transmission which travels between 1 and 100 meters per second. At these scales is it worth it to examine neural data and is it useful to even discuss the neural level of representation?

A useful analogy is a similar attempt to understand human society through the observation of the city lights of earth from space. As Charles Gallestel (2017) points out, observing a visual map of the world at night can tell us actually quite a bit about the connections between countries: lights coming from North Korea pale in comparison to its more developed southern counterpart reflecting the regions connectivity. Similarly, we can see the impact of historical events. Even after decades of normalization between East and West Germany, the city night lights still reflect their historical division. But although

city lights cannot tell us detail about a culture, there is still much to be gleaned about the relationship between regions. In a similar, vein we are going to be examining fMRI to attempt to revel the history and connections between brain regions; connections reflect learned experiences and developmental predispositions. But more specifically, we will examine how temporal dynamics of fMRI signal during rest reveal some of these properties.

It is ideal to observe the ongoing system dynamics of the cortex when an organism simply rests (but does not sleep) for a period of time in the scanner. In recent years there has been a growth in the number of studies used to interpret this "default" mode of brain activity (Raichle et al., 2001). A casual search in PsychInfo (2007-2017) demonstrates demonstrates the rapid increase in recent years of research on "resting state" in neural dynamics: this can be seen in figure 1 limited to peer reviewed articles. This research is not the subject of fringe groups but is the core of analysis conducted by large international brain consortiums examining thousands of subjects such as in the Human Connectome Project (Van Essen et al., 2013). Analysis of this type of data is still only in its infancy, and methodological and philosophical problems are still being addressed, but the findings have been reported and robust. This analysis of default mode activity is thought to reflect the building blocks of cognition (Sporns, 2010), or as Luczak (2009) describes, resting state activity may reveal the "vocabulary" or "repertoire" of dynamic states available for skills such as perception and higher level cognitive processing.
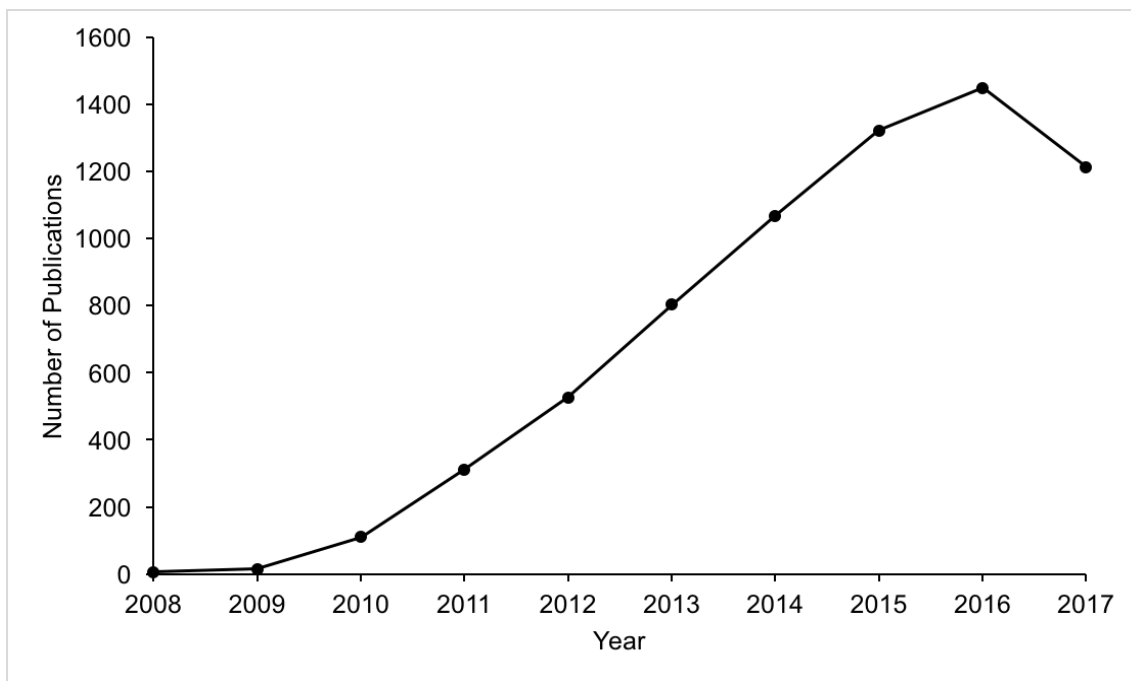
Figure 1. Number of publications in PSYCHinfo which relate to fMRI and resting state.

Waves of thought. In general, data sets for this type of study involve several minutes of functional magnetic resonance images recorded while participants are not actively engaged in any outward task (historically this resting condition was a faulty control condition (Biswal, 2012). Following image capture and preprocessing to remove systematic noise, the fMRI images of the neocortex can be divided into regions and each region's blood oxygen level dependence (BOLD) level changes over time can be represented graphically by a waveform 2. In this figure we can se a typical fMRI slice through the brain of one of the participants from the present study. The intensity of each colored square (or voxel) represents a comparative signal strength. The intensity of each voxel changes over time and this is represented as frames in the fMRI sequence. These types of waveforms are the observed signal in our analysis.

Using these waveforms we make estimates of connectivity between regions. Comparing the waveforms from different regions, two analysis methods could be applied to uncover this interregional functional connectivity. These two analytical methods reveal potentially different emergent levels in the data: one involving time locked interactions and the other examining interactions delayed across time. Returning to figure 2, we could ask if region A and B are more correlated and thus more "connected" than region B and C. Neural connectivity in resting state fMRI data has traditionally been estimated by estimating these interregional correlations over time (Sporns, & Betzel, 2016).

However, this assumes that synchronous activation between brain regions are the optimal indicators of connectivity. This does not take into account propagation of activity across the cortex through time. In figure 3, we can see, through visual inspection, that the

time series for region A and B are identical and C differs. In the standard correlation approach, C is deemed unrelated or minimally connected to A or B. Conversely, if we temporally "lag" time series C until it reaches maximum correlation with A and B we notice all three wave forms are nearly identical (Mitra, Snyder, & Hacker, 2014). The first approach emphasizes the magnitude of the connection as reveled though proposed shared synchronous activity; the second emphasizes the probable order and relative timing of that activity across the neocortex. Regions which are very tightly modular in a lagged fashion would eliminated in the standard correlation approach if we did not lag the series and thus interpreted as low connectivity between regions. We know that large neural systems do not work in a time-locked matter; and one intrinsic feature of the brain is sequential activation of regions which has been observed on the time scale of hundreds of milliseconds to minutes (Loveless, & Sanford, 1973).
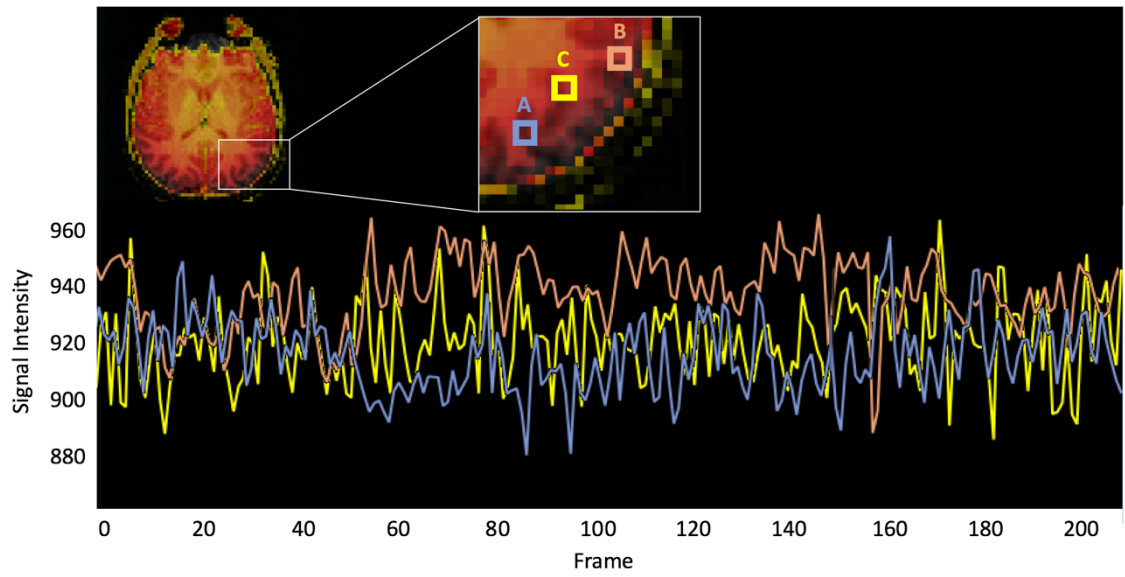
Figure 2. Intensity Waveforms. The intensity at each point A,B,C on the cortex can be represented as a sequence of activations over time (frames).
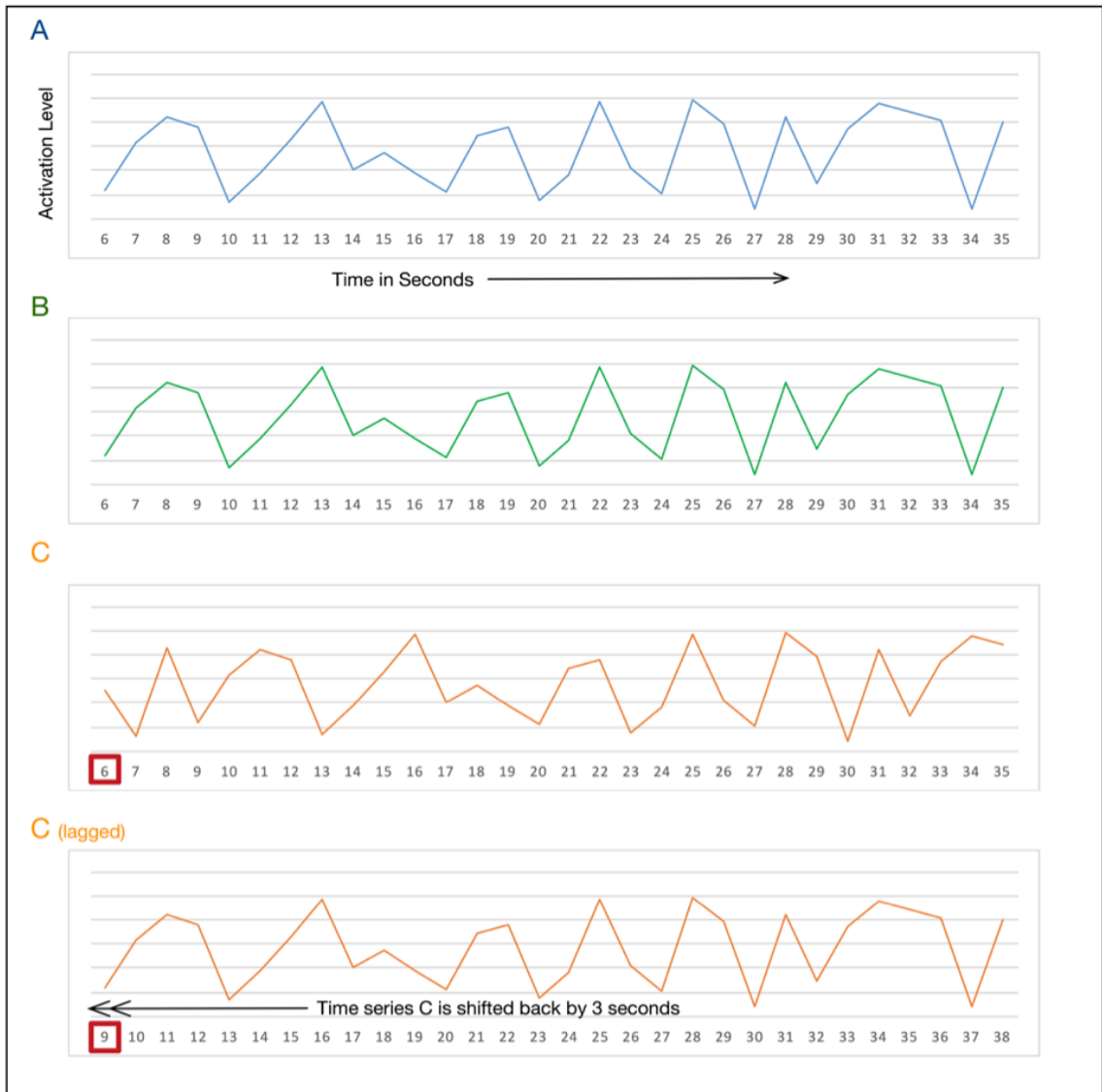
Figure 3. Wave Correlations. These toy time series representing three neural regions illustrate two models of connectivity. In the correlation model A and B more strongly correlated but C is not. If, however, we allow C to shoot in time we notice that it too is correlated. In other words, C is likely active before A and B. (These models illustrate a point and perfect correlation is never truly found in neural data)

Data decomposition. An examination of these lagged time series involves an analysis of matrices which, using methods described later, exceed more than 350 million comparisons per participant. For interpretation and regression against behaviors this data set must be decomposed into interpretable components and simplified. The mere size of the data limits the possible comparisons due to current limits on computational power; specific analytic methods are appropriate for data sets of this size and their interpretation involves some explication. Attempts to simplify and find meaning in this data set will be the core of the analysis completed in Part 2.

From neural systems to behavior. Finally, these persistent representations of knowledge found in resting state create a system structure that is responsible for certain behavioral outputs. A very standard approach observed in resting state data is to examine correlates with mind wandering (Smallwood, & Schooler, 2015) as this is a process observed during resting state. Research in mind wandering has demonstrated that there are many types of mind wandering and it is very context dependent (Smallwood, 2013). Therefore, we shall seek to explain both mind wandering in the context of oral reading as well as the behavioral features which accompany it in a specific population. This detailed description of the context is meant to frame the findings we will observe as we regress mind wandering against the discovered lag network representations seeking to understand how mind wandering is seated in neural systems of thought.

Examination of the resting brain has been a rapidly growing and a fruitful area of neural methodology and although the methods used here are still young, it is hoped that through this exploration, suggestions will be made for future approaches. The limitations

are great but are also a great place to continue improving methods. It is hoped that this exploration can be coupled with future experimental investigations to help us unearth persistent neural representations of readiness for skillful engagement and stored knowledge.

Let's begin by diving deep into the philosophical and historical foundations that motivated the current exploration of fMRI image sequences during rest. An epistemological analysis is of central concern if we are to discuss mind in brain. If we are going to discuss neural activity as knowledge, pains must be taken to define our subject of study. This will be followed with a multilevel neurological justification of these neural dynamics from cells to cognition with specific attention to fMRI. Part 1 establishes the metatheory that motivates an interest in the methodologies which will be explored in Part 2.

PART 1: Knowledge in the Brain

Knowledge

Before asking about neural representations of knowledge we need to address the deceptively simple question of how we are going to define "knowledge?" This paper assumes that an individual has "knowledge" of the world that affects their behavior and behavior potentialities. This knowledge is assumed to be dynamic and skillful, represented simultaneously at both behavioral and neurological levels. When talking about knowledge, memory, and skill, I am purposefully not making a distinction. All neurological representations are living things that are not static but dynamic, i.e., they change over time. These representations can vary in the sense of "dynamic skills" from perceptual skills to episodic memories and complex systems of skills such as how to engage in self regulation or be the leader of a nation (Fischer & Bidell, 2006; Fischer & Yan, 2002). As we will discuss, perception itself is a form of knowledge (Fischer & Bidell, 2006; Rock, 1985). Knowledge can be represented explicitly in the outward behavior of individuals or as implicit behavior not directly accessible to consciousness (Polanyi, 2009), or less commonly knowledge may also be represented in the persistent internal states of an organism and the behaviors of neurological systems. But, we can never measure knowledge directly, it must be measured through the behaviors of organisms, or the behaviors of biological systems within organisms. It is worth emphasizing that all measures of knowledge are indicators not direct measures.

One common way to examine knowledge is through behavioral tests, surveys, observations, reflections, and interviews; often we confuse these as direct measures of

knowledge, but they are approximates that indicate knowledge; they are assumed to correlate with internal representations of knowledge. In other words, all these measures examine the behavioral output of a knowledge system, not the knowledge construct directly.

Similarly, we might be able to examine the knowledge construct through changes in an organism's biology. While this initially may seem less useful, it is not a novel idea. The first well known scientific evaluation of knowledge in this was in the historical work of classical conditioning experiments coming out of Ivan Pavlov's research lab (Pavlov, 1927). Changes in the knowledge system of an organism were approximated by measuring saliva. As the pairing of the unconditioned stimulus to the unconditioned response increased, it had a direct effect on the amount of saliva produced in Pavlov's dogs. Alternative biological indicators are blood pressure changes, galvanic skin responses, pupil dilation, the blink response and more (Germana, 1968). Basically, some unconditioned response frequency is changed through experience and is conditioned to change its response rate in reference to a new conditioned stimulus. Change in the amount of saliva is an indicator that the internal knowledge state of the organism has changed; it is evidence they have learned something. This is also a type of connectionism building a connection between stimulus and response (Hebb, 1949).

While the other biological indicators are often accessible measures of learning, we do not often think of brain states, as behaviors which can be measured. But, indeed the brain itself has a measurable response to changes in its environment. With learning, the brain "behaves" differently. Brain activity and structure is a similar indicator of changes

in knowledge states of an organism. Knowledge in the form of memories or skills is not only correlated with changes in external behavior, it is correlated with changes in brain. When skills are highly practiced and entrenched, they lead to observable differences in neural activity constrained by structural relations set up through previous experience (Tambini, Ketz, & Davachi, 2010).

While in a behaviorist tradition, only changes in responses to environmental stimulus is measurable, more modern approaches assume that these changes are a result of changes to the intervening variable of the mind itself. The thesis I hope to convince you of though this section is that this knowledge is not only accessible in the environment where the skill was learned, but experiences leads to persistent dynamic changes in the brain; and, while BOLD responses can be evaluated as indicator variables they indicate brain activity which is the intervening variable of knowledge.

Mind-Body Problem

Today, it is uncontroversial to think of knowledge as represented in the mind of the individual, but if we are going to explore the neurology of knowledge we need to first spend some time examining the relationship between mind and brain. While knowledge is unquestionably represented in mind, whether mind is represented in brain is an important metatheoretical question that must be addressed as a foundation for what shall be discussed. Mind is not equivalent to behavior, nor is it equivalent to neurons. I shall now spend some time explicating aspects of this relationship. While a definitive answer to this question is clearly beyond the scope of the current paper, some metatheoretical assumptions made in this paper must be explained first as they are the grounding of this

research in this cognitive neuroscience of persistent representations of knowledge. Through the remainder of this chapter, I will attempt to outline this theoretical stance and leads the reader from cartesian dichotomies to an emergent complex systems view of the embodied and encultured mind in brain upon which the current research is built. This discussion will bring meaning to the neurological measures which will be proposed.

What role does the mind play in the brain if it plays a role at all? This may seem like a dangerous place to begin, but understanding the role of the mind in neural dynamics is central to the cognitive neuroscience of education. As we shall see later in research of mind wandering it is equally important to critique the role of the mind as an agent in thinking if we are going to examine mind wandering, so understanding the perspective that mind is not an active agent on brain is central to any discussion of mind wandering.

Based on my experiences working with and listening to educators, psychologists, and neuroscientists, no assumptions can be made about where one stands on the mind-body problem. In fact, one often does not understand where they stand on the problem. It is not uncommon to hear at scholarly conferences how if one changes their thinking they can then change the wiring on their brain, or to hear that one's thinking is caused by a particular configuration of neural wiring. These types of comments are casually common by even plenary speakers at American Educational Research Association, Cognitive Neuroscience Society, International Mind Brain Education Society, Society for the Neurobiology of Language, and Society for Neuroscience annual or biannual meeting. Research methodology cannot stand on its own without a metatheoretical approach

describing how it is to be interpreted (Witherington, January 2014). And since we are looking for evidence of knowledge typically relegated to the mind through an analysis of neural activity, we must first outline what it means to look for mind in brain.

Dualisms. The seventeenth century philosopher Rene Descartes shall act as our familiar foil to start this narrative because he clearly separated the mind from the body in what has become known as cartesian substance dualism. In his approach, the ethereal mind reaches into our physical world via the brain's pineal gland[1] pulling and pumping the sprits of the body: the disembodied soul acting as a puppeteer and observer acting on the passive machines of the physical world. "The mechanism of our body is so constructed that simply by this gland's being moved in any way by the soul or by any other cause, it drives the surrounding spirits toward the pores of the brain, which direct them through the nerves to the muscles; and in this way the gland makes the spirits move the libs" (Descartes,1989). This is often referred to as substance dualism, where the mind and the body are made of different substances. While this colorful science fiction has been rightly rejected by modern science, the notion that the mind operates at a higher autonomous level directing the actions of the body is still very much accepted in some approaches to the psychology of learning. In these vertical approaches, the mind may be bound within the body, but it still holds an executive position where it drives (or at least plays an important role in) cognitive development through acting on the biology and the environment. In these approaches the mind drives the brain in a causal relationship.

---

[1] The pineal gland was assumed to be the seat of the soul because he wrongfully thought there was only one in the brain.

However, this is still an unacceptable dualism. So, it is from this approach that we begin, in reaction, to examine mind and brain in monisms. But, as we shall see, some attempts at monisms simply recapitulates earlier dualism under a new disguise.

Monisms. One way to address the problems of dualism is to simply ignore or dismiss the parts we do not understand. Centuries earlier, Plato and his contemporaries proposed idealism which eliminated the biology of mind as worthy of study (White,1976; Bunge, 1980). All that existed was of the mind's creation. Similarly there is the philosophy where all matter and mind are resultant manifestations of energies (Bunge, 1980). These approaches are easily dismissed for their lack of clear grounding in scientific principles and being steeped in mysticism suggesting that the mind creates reality and all reality is thought. However two other types monisms must be addressed which are more accepted but equally problematic: all knowledge is behavior, all knowledge is brain.

Early, attempts to empiricize studies of knowledge led to research in the area of human behavior, John Watson and B. F. Skinner transformed the individual into probability machines of behavioral output. While Watson decries the existence of mind at all (Watson, 1930), B.F. Skinner's approaches to education viewed scientific exploration of the mind as a "fiction" or "illusion" ignoring any influence on the biological body or behavior (Skinner, 1974). It is simply denied the intervening variable as unnecessary to understanding knowledge. In their view, environment acted on behavior and determined behavior by changing behavior potentialities, the mind had little role, if any, in knowledge formation. Mind became epiphenomenal. The field of behaviorism completely

ignored the internal representations of mind or even the brain as viable material for the study of learning.

While more empirically sound than Cartesian dualism or idealism, behaviorism simply ignored part of the problem. It left an open question of where the stored representation is and what its nature was, assuming that knowledge formation was simply the creation of deterministic influences from the environment. Behaviorism did not solve the theoretical hard problems, it chose to ignore them. Perhaps rightly so, all science must reduce, simplify, or model the problem temporarily in order to address it. This limiting of scope is, of course, one of the hallmarks of scientific research, however, complete dismissal is not necessary, as analysis methods can accept that we are only examining part of system without denying the existence of other parts.

Clearly these approaches will give us no traction in searching for persistent knowledge in neurology and we have moved historically beyond this simplistic thinking. They did not search for knowledge representations; they only examined their behavioral output. They studied indicators of learning.

From the other direction some neurologists worked on theories grounding in materialism beginning with the idea that all that exists is brain.

Reductive materialism: mind does not equal brain. Similar to the behaviorism perspective, some have suggested that mind does not exist and that all that exists is the neurophysiology (Bunge, 1980). Since we are searching for knowledge in the neurology this approach has no use in the current analysis. But, what if we assume that mind is equal to the material?

While I will be reductive, I am not being ontologically reductive in the sense that all events including biological entities can be reduced into the component parts (Jones, 2000). From this reductive ontological materialism approach, the mind is "nothing more" than cells, chemical reactions, and physics; by understanding these components we can understand how mind or knowledge emerges. This approach does not eliminate mind but assumes that the brain is equal to the mind, if we understand brain, we will understand mind. It holds that "every mental state (event or process) is a state (event or process) of the central nervous system or part of it" (Bunge, 1980, p. 6). In other words, the mind is organized like a computer. By understanding the components we can understand the function by simply adding up the components; a set of logical functions respond to external events and predictably interact to produce a behavior. Essentially, this approach says that understanding cells is not only necessary but also sufficient to explain the mind. This approach would suggest that neural or molecular representations are equal to knowledge.

But, something is sorely missing in this approach, no one would realistically say that music is a collection of ones and zeroes because that is how a computer represents it; there is something more to music than this. This approach would ignore the perceptual experience dismissing it as an illusion it would also ignore the system of relations between neurons as something different and more than the components. A collection of neurons is not knowledge.

To begin with, qualia are our experience of the world which while determined by neurological representations, they cannot be described by them. Simple example comes

21

from the perception of color which does not exist in the world but is constructed by the mind, however it is restricted by the biology. There is no blueness, or redness in the physical world, the physical representation of the color has no physical equivalent (Kay & McDaniel, 1978). Color is light represented in science as wave frequency; we do not see light waves. However, differences in the experience of color between individuals with different receptor types illustrates that color is a subjective experience of perception and not an objective property of the world (Bimler, Kirkland, & Jameson, 2004). We can clearly say that color is not equal to wavelength, because color is viewed differently based not only on your experience but also the distribution of rods and cones. There is a shared world, but not a shared perception. Our unique experiences and biology constrain our perception. Extreme examples can be seen in analysis of neural circuitry of synesthetes who differ in their neural architecture and thus perceive the world differently from a cross over in sense circuits: they see graphemes in different colors (Hubbard, Arman, Ramachandran, & Boynton, 2005). Or similarly, the perceptual apparatus of dyslexia (Serniclaes, Van Heghe, Mousty, Carré, & Sprenger-Charolles,2004) and autism (Mottron, Dawson, Soulieres, Hubert, & Burack, 2006) changes their perception and variation in their skilled interaction with the world. Through these studies we can see that the physical is necessary to understand the qualitative experience, but the qualitative experience is more than the sum of the physical components. We cannot work in a bottom up fashion to generate the qualitative experience, we must integrate the qualitative experience in our exploration. To explain the biological brain without the qualitative experience misses essential properties of the brain itself; however this also shows that

qualia are grounded the biology. All qualia can be partially observed in the biology which enable it. A description of complete knowledge would include these extended representations, but qualia cannot change without changing the neural foundations of it simultaneously.

Furthermore, the reductive materialism approach asserts that the whole is equal to the sum of its parts. Beyond the qualitative experience, this is also a clear fallacy. As Mario Bunge (1980) points out "to say that the composition of a human society is a bunch of humans is to say that a society is nothing more than a set of its members" (p. 8), or put another way, a hurricane is no more than water and wind. This is clearly also not the case, the brain, like human society or weather patterns, is a system of components not just the components themselves. It is therefore clear that thinking of the set of neurons as equal to mind is not a useful approach.

To both reject dualism and to embrace a holistic monism, new philosophies and ways of thinking had to be devised.

A new monism: Phenomenology. While ontological reduction and monistic idealism rejected the body, and behaviorism and eliminative materialism rejected the mind, the reacknowledgment of the importance of the perceived experience in development was tackled in philosophy, particularly in the philosophy of phenomenology. A consensus began to emerge that the experience of the perceptual phenomena itself was worthy of scientific study, something lost in behaviorism and reductive materialism. But to be a subject of empirical study, the phenomena had to be tied down to the physical world and this was elegantly done through the work of Maurice

Merleau-Ponty (1996). As a pivotal figure in phenomenology, Merleau-Ponty discussed how examining the experience as a unit of analysis was essential to the scientific study of the mind. However, he went further than other phenomenologists, by saying that this experience was also grounded in the material world, in the biology of the body itself and through contiguous connection part of the brain.

This approach is central to thinking about knowledge as persistent in the biology of brain. It includes in the knowledge phenomena, the sensory experience whether directly or indirectly experienced. Using this philosophy as grounding, we will go further and move beyond our traditionally defined body into abstract emotion, concrete tool use, and cognitive tool use as parts of this persistent knowledge framework, finally integrating the non experienced or tacit knowledge as it was envisioned by Merleau-Ponty's contemporary Michael Polanyi. As we shall see in the following paragraphs these phenomenologies of mind cumulatively give us a foothold in the biological allowing us to perceive a unity of mind and body.

More than I see. A crucial point that phenomenologists made was that perception as an element was persistent and real outside the physical representation of the perceived and only in the perceptual apparatus of the observer. Using the classic example of the Müller-Lyer Lines (figure4), Merleau-Ponty (1996) pointed out that the illusion as a persistent entity did exist. An illusion is not something that does not exist, it exists simultaneously both in the mind and physically in the body. In this example outward directed arrows on edges appears to compress the length of the line when compared to the same line with inward facing arrows at the edges. While one could always measure the

lines and show that they were the same length, perception always overpowered empirical knowledge and the illusion persisted. Therefore the illusion must be somehow grounded in our perceptual apparatus. Illusions must not come from the world, but from our internal knowledge.

Additionally, this quality of experience was extended to the edges of visual field. The world does not cease to exist beyond our visual perception. The edges of the visual field are in fact not perceivable because the mind continues to represent the external world beyond the visual field. Knowledge of the world persists beyond our sensory apparatus. What is not observed through the eyes still exists in perception, although it is outside of attention, and is real in the sense that it is experienced; we experience ourselves in the world not trapped in our visual field. The state of the organism represented in the brain affects what is seen or perceived. Merleau-Ponty gets into the mind through perceptual experience.

Here we begin to understand what persistent representation in mind or brain may mean. Skills and memories exist and directly influence our perception. Classically, this represents the top down component of classic cognition theories (Mechelli, Price, Friston, & Ishai, 2004). To ground this idea further in biology, Merleau-Ponty brought our attention to the phantom limb phenomena.

The body inside. Having been a physician in the war, Merleau-Ponty was familiar with the phenomena of phantom limb. In the absence of an amputated limb, a patient still perceived the limb. Thus similar to the line illusion the representation, the experience persisted beyond its external representation. While a man with a missing arm could

clearly see that the arm was not there, he nonetheless perceived it to still be a part of his body and to feel pain. Perceptions were persistent beyond direct experience. The body, was mapped onto the brain. When the limb ceased to exist, its neural representation in the brain remained. Representations of body and world persist past direct experience.

While Merleau-Ponty is primarily concerned with conscious experience, we shall briefly dwell on the phantom limb phenomena because it gets to the core of persistent representations of knowledge. Experience maps the body onto the brain where representations of experience persist. This phenomenon has been explored in depth by V. S. Ramachandran and his colleagues (Ramachandran, Rogers-Ramachandran, & Cobb, 1995). The new body needed to be remapped onto the brain. While phantom legs were compensated for due to their continued use, the phantom arm remained a problem and only through repeated training of the perceptual apparatus was the missing limb mapped onto the cortex (Ramachandran, Stewart, & Rogers-Ramachandran, 1992). It is only after repeated attempts to use the limb are met with inconsistent feedback that the sensory and motor cortices remap this region (Yang et al.,1994). The mental representation of self as body is clearly grounded in the neural networks of the brain.

The world inside. But, this representation is importantly not limited to gross body anatomy, the senses are similarly maps of the world. We know that information enters through the various sensory organs, it is transduced into neural signal and somehow represented on the cortex. We actually have a strong understanding of this transduction process and the senses happen to be mapped onto the brain for the most part, in a topographically consistent way. The sense of hearing is mapped in a tonotopic map where

similar frequencies are represented near each other (Wessinger, Buonocore, Kussmaul, & Mangun, 1997; Formisano et al., 2003; Evans, Ross, & Whitfield, 1965), the visual system is mapped across the occipital lobe in a way that preserves relative size and space from the visual fields and retinotopic organization of rods and cones on the eye (Gardner, Merriam, Movshon, & Heeger, 2008); the motor, proprioceptive, and touch senses are mapped across the sensory cortex in a way that preserves the map of the body in a familiar homunculus with representation area correlating with the degree of sensory or motor specificity in the body region (Penfield & Boldrey, 1937; Metman, Bellevich, Jones, Barber, & Streletz, 1993). Thus the brain has ways off representing the outside world. The outside world persists in the brain. But the brain is not simply a cartographer, these maps are then associated with each other in association cortex allowing us to perceive complex relationships and emotional action sequences (Damasio et al., 2000).

While easy to see the physical environment is mapped into the brain, what about the narrative aspects of self, the emotional grounding of self. Hanna and Antonio Damasio and their colleagues (Damasio et al., 2000; Bechara, Damasio, & Damasio, 2000) describe the body map in the brain, but include the physiological aspects of emotion demonstrating that the emotion is a physiological sequence of activities that we perceive as our feelings. Emotional actions consists of a physiological response to the world or internal states. One highlighted region of cortex which represents the body states is in the insula, the state of viscera, pulse and other internal factors are perceived through the posterior insular cortex while anterior regions interact with other neural systems to assist in the perception of feeling these emotions (Craig, 2002; Damasio et al., 2000;

MacDonald, Leary, 2005; Immordino-Yang, McColl, Damasio, & Damasio, 2009). Thus, the physical as well as the emotional body is represented in the brain. We perceive the world through our body. As the body moves through the environment it is changed usually in less drastic ways than losing a limb, but nonetheless, it is changed. These movements are represented in the brain mapping the environment through the body onto the brain. Thus from Merleau-Ponty to the Damasios, the embededdness of the mind to the embodied brain is accepted as a modern neuroscientific fact.

Existing without direct experience. Returning to our idea of persistence, this mapping does not cease to exist when the region is not in use, and importantly neither does the activity of the region. This mapping of the body is preserved across time. It is integrated into an image of self (Damasio, 2010); it allows for the recreation of experiences outside their original contexts. I can close my eyes and imagine, I can day dream, I can dream. These decontextualized experiences are only possible because our internal representations of sensation are constructed as part of memory and creativity (Farah, 1988). I can see and feel without my sensory apparatus because my mind persists beyond external experience it is in the biology. Qualia do not require external sensation; they require internal representation.

However, we need to account for the fact that the body is extended beyond flesh. The blind man's cane, the painter's brush, the mathematician's formulas, and the writer's text are all internalized and represented in the mind and the brain. We feel the edges our cars when we drive as the blind many feels the edges of the cane. Vygotsky may envision these as extensions of mind through external tool (Vygotsky, 1997), but implicit in this

approach is that the external tool needs to be internally mapped. The outside world is remapped on the cortex through the association of sensory maps. A number of linguistic theories indeed ground the symbolic aspects of language in the basic sensory experience which eventually becomes part of the perceptual apparatus itself (Lakoff, 2012). As a side note, we may even examine this literally as we literally integrate human and machine we take advantage of this plasticity and are able to implant controls for robotic arms in the brain, and the brain then automatically generates a map of the additional limb based on experience (Davis et al., 2016). These external devices and tools are not solely external. The ways we interact with them become part of our mapping system (Obayashi et al. 2001; Farnè, Serino, & Làdavas, 2007).

Thus the body and its extensions into the environment is "minded" through the senses, but once the body is minded in the brain, these representations become part of the individual's brain's functional anatomy. Returning to Merleau-Ponty, the existing biological representations are a primary tool for perception. The phenomenology of mind is recapitulated on the biology of brain which we use to perceive. Perception is clearly not a bottom up process and at the very least involves a two way interaction between environment and brain. However, the minimal adjustments to neurology from experience indicate the vast majority of representation is top-down, as we shall discuss below. Representations of the world and our interaction with it are persistently represented in the cortex.

Literally removing knowledge. It is also of no argument that when parts of the neural apparatus are lesioned, knowledge of the abstract skills is also lost. The literature

for this is rich and I will not address this ad nauseam here, except to mention the simple

ideas that lesions in lead to the loss of memories, skills and self. The most obvious of

which are loss of memories or abilities to generate new memories though neurological

damage to the hippocampus but also association cortex that plays a role in the memory

reconstruction (Scoville, & Milner, 1957). The classic cases of language skills after

lesions or strokes affecting language related areas of cortex resulting in a loss of reading,

speaking, understanding skills just to name a few (Caramazza, & Berndt, 1978). There

should be no doubt that the mind and skill persist in the anatomy of the brain. If

knowledge is destroyed in the brain, it is lost unless other regions or external resources

work together to reconstitute it; but, in this sense, the knowledge is new, not rebuilt from

some abstract separate mental phenomena.

These neurologically grounded phenomenologies give us a space for persistent

representations of knowledge. Thus, Merleau-Ponty gives us a more acceptable monism.

The mind is not separate from the brain but intrinsically connected and the nature of

minded knowledge necessarily involves neurological representation.
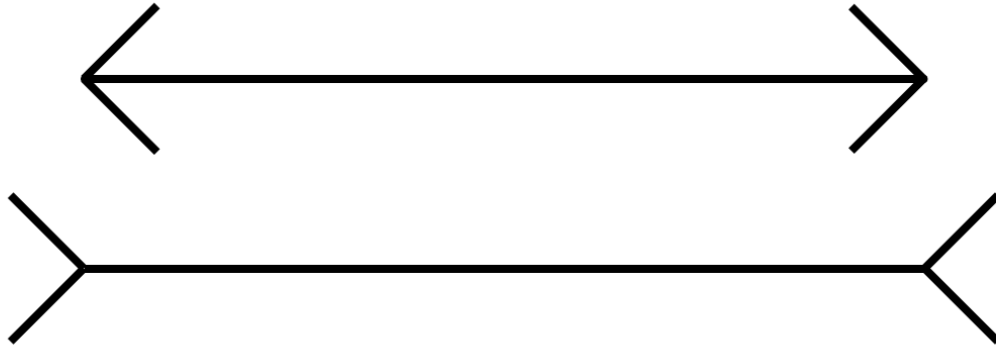
Figure 4. Müller-Lyer illusion. The top line is the same length as the bottom line but persistent representations in our mind do not allow us to perceive this even though we may measure the two lines and know the truth.

Not conscious knowledge is still knowledge. All of this discussion recognizes conscious perception as representing knowledge, but for these perceptions to be possible they must be accessible and available. But what of that knowledge which is not brought to conscious awareness. In the present exploration we are searching for latent persistent representations of knowledge. By their very nature these are assumed to be outside conscious awareness. Because I do not actively think of a paint brush does not mean I do not have knowledge of painting at that time. Knowledge does not arrive deus ex machina as needed. Unnoticed and unperceived storage of information is still knowledge. I am not always aware of my limbs nor is the amputee, but the persistent representations remain beyond my conscious awareness (Ramachandran, Stewart, & Rogers-Ramachandran, 1992). This is an essential question considering the current analysis searches for these persistent representations which cannot all be simultaneously perceived and in fact some are imperceptible.

Much of our bodily changes go unnoticed. This unnoticed change also becomes part of our knowledge what Michael Polanyi (2009) called tacit knowledge. In accordance with Merleau-Ponty's principles, Polanyi emphases the importance of tacit knowledge. Not only was the knowledge the we could grasp in our conscious awareness important for our engagement in the world, so was the knowledge gained beyond awareness. Examples were skills such as riding a bike or walking which do not require conscious awareness but are still essential in our engagement of the world. These are skills that can be engaged without conscious awareness. In fact, these unconscious or tacit representations are appropriately not minded, to mind them might distract from other

essential tasks, too much attention to the motor details of skiing reduce our performance and attention to other important environmental signals (Wulf, McNevin, & Shea, 2001). Too much attention to the tones of singing in trained singers reduces their ability to sing (Atkins, 2017). Our knowledge thus extends beyond the conscious to that which is enacted beyond awareness.

But, lets not stop there. What is not conscious does not need to be engaged in the moment. As mentioned above these representations of knowledge have persistent form. Knowledge is not something only engaged in the moment, but something that is ready to engage. We need to rapidly switch tasks when the opportunity presents itself and we can only do so if there is an existing representation to switch to. There is some previous experience which has been imprinted on the brain and is active that enables the specifics of our engagement.

At the moment you may be saying that this does not address the idea that knowledge is always dynamic and active. Knowledge could be stored in non-dynamic ways in the cortex such as in an inactive web of interactions that lay dormant until they are needed. It is however very clear that knowledge is not simply written and stored in the brain in files that can be accessed later. Even when knowledge is not engaged its nature and content change because systems of knowledge are always adjusting.

Instability of knowledge. Taking the example of memory, Elizabeth Loftus and colleagues (Loftus & Loftus, 1980; Loftus & Pickrell, 1995; Colins & Loftus, 1975) has convincingly shown how memories are not recalled but are reconstructed. If knowledge was stored and static then eyewitness testimony would accurately capture actual events,

however, eyewitness testimony is notoriously unreliable. This is not only due to differences in the encoding of the memory because given time the same memory will change. The flashbulb memory experience has similarly been shown to be unreliable and also alter over time although our confidence that it is unchanged appears high: memories of thousands of individuals who observed the terrorist attacks on 9/11 in New York reveled that changes continued to happen to stories for at least a year before the memory stabilized (Hirst et al., 2009). There are also no known cases of memetic memory (photographic memory) as all those who believe they have it are unable to reproduce the experience under experimental conditions (Gray & Gummerman, 1975; Patihis, 3013; LePort, 2012).

A second example is the activity of skill learning. It is well documented in learning theory that a practiced skill changes even when the learner engages in a different intervening task. Some simple skills such as finger tapping tend to improve after a break or sleep with no practice (Fischer, Hallschmid, Elsner, & Born, 2002) . All evidence points to the idea that outside the actual learning conditions the motor or cognitive sequences resonate in the mind outside active experience. Running a rat though a maze and recording the sequence of neuronal activity in the hippocampus (a region of the brain with spatial maps) results in patterned sequences which reflect the movements in the maze itself (Ji, & Wilson, 2007). We shall return to this idea later when we dive into the neurology, but it is clear that a model where skills or memories are discrete and experience dependent misses this temporal aspect of knowledge.

There is strong theoretical reasoning therefore to examine persistent representations of knowledge in the brain and to assume that this knowledge is an active representation even when it is not engaged. Knowledge is not a static representation it lives.

Transition to levels. To make statements about brain activity as representing mental activity we need to unify rather than just show a strong relationship between mind and brain. But, in doing so, as mentioned above it is not useful to simply state that mind is brain in the reductive materialism sense. The mind needs to somehow exist with the brain. We want to maintain that "every mental state (event or process) is a state (event or process) of the central nervous system or part of it" (Bunge, 1980, p. 6), but we also want to exert the idea that understanding the neural components is insufficient to understanding the brain. Something qualitatively different from brain emerges with the neural architecture. And thus, it is necessary to turn to a theory of emergence. But, to dismiss emergence as magic and mysticism (Gallistel, March 2017) depends on the grounding we use.

To elucidate the topic of emergence as a theory for mind brain relations, lets continue with Polanyi who pointed to the importance of "levels" of representation. While I shall not stay with his explanation because it remains a dualism of a new kind, however it is a convenient place to begin to make the relationship clear and set up the terms of engagement which we will resolve.

Mind from brain. As I mentioned above, without careful attention, dualism can reemerge in our understanding of the brain. But this new dualism seems to suggest a different relationship. The mind emerges as if secreted from neural interaction. It then is often acceptable dualism used by various approaches to discuss neuroscience.

Mentalism: Mind constrains brain. As we discussed above, the phenomenological view suggests that experience is tightly bound to brain but we have yet to describe this relationship, if neural events are not the same as experience, how do we define them? Polanyi began bringing into this discussion the idea of "levels" . This is not levels of complexity or scale but levels which each have their own laws or rules which them must follow; levels are qualitatively different. If we allow mind and body to exist in different qualitative levels this proposes a way to think about mind and brain as in some way separate influences on each other. It becomes important when discussing neurological representations of skill to examine what influences neurological representations. It is a possibility that mind "emerges" from the complex interactions of the brain. If we allow this supposition, it is possible to think about these different levels having influence on each other. Lets hold on to this idea of a moment as it is currently a very popular way of thinking about mind-brain interaction.

So, what is meant by different levels of organization? Polanyi and others have attempted to start this discussion for the physical world. At different levels of organization and complexity different qualitative properties appear to "emerge". In the simplest sense, water molecules have hydrogen bonding at room temperature that leads to the viscosity of liquid, but this bonding does not create the shape water takes when it fills

a flask in a bottom-up fashion (Polanyi, 2009). Rules at the microscopic level do not dictate the behavior of water at the macroscopic level. While hydrogen bonding explains the relationship between molecules, it does not dictate shape water takes as it entered a flask; the flask is what dictates the shape that the water takes. The flask acts as what Polanyi terms the boundary condition to the overall shape of the water.

In an attempt to be theoretically exact and perhaps to ground the social sciences in the philosophical foundations of the physical sciences, Polanyi explains the boundary condition as taken from mathematics and physics: it is the space in which a differential equation is applicable. This differential equation constrains the potentially limitless and infinite degrees of freedom available to some system. In other words, unbounded by other rules, water molecules could take any possible shape at the macro level. In a weightless environment they would float and only be constrained by their hydrogen bonds, in a vacuum, they are likely to spread out in a random way only following rules of diffusion. The flask, gravity and environment thus, act as a boundary condition for the shape of the fluid, it reduces the degrees of freedom in the shape that the liquid can take in a particular environment.

Polanyi extends this discussion to include the tool maker and inventor as the boundary condition for the material world. Physical properties of metal allow it to be molded by humans, humans act to constrain the behavior of the metal, limiting the degrees of freedom. No one would seriously question the qualitative assumption that the man and the metal or the flask and the water are in some sense separate. However, he

37

proposes that this same relationship exists between a machine and its parts; bringing us closer to a mind brain comparison.

Metal does not form gears, the boundary conditions set by the human allow for the formation of gears. Once molded into gears and the gears are arranged, another relationship emerges, that between the machine and its parts. Now, we move into the clearest connection Polanyi makes with mind brain relationship. The function of a clock constrains the possible arrangement of the parts which make it. The time keeping function is an emergent property not found in the gears and not found in the metal, and this time keeping property constrains the possible arrangement of gears. While the gears make the machine possible, the function of the machine "constrains" the possible functional relationship among the parts to perform a purpose. If the clock ceases to function, it ceases function as a clock. According the Polanyi, this is not dissimilar to the relationship between genetics and the organism (an analogy we will return to shortly); evolution constrains degrees of freedom in genetics. Without boundary conditions the possibilities are infinite; life is governed by boundary conditions. Each level alone has infinite possibility: the metal has infinite possibilities of form, the gears have infinite arrangement of possibilities, and genes have infinite ordering possibilities, but external forces at a different level of control can limit the boundary conditions for the level. Importantly, "No level can gain control over its [own] boundary conditions … a higher level can come into existence only through a process not manifest in the lower level, a process which thus qualifies as emergence" (Polanyi, 2009, p. 45) and this emergent level can then exert control through constraint over lower levels. It is in a similar fashion that

the mind is said to emerge from arrangements of neurons, and Polanyi and others have

suggested that this emergent level of representation constrains the possible organization

of the neural machinery and mind controls brain.

It would be radical material reductionism if we were to say that the simplest rules

govern the highest level, and as Polanyi noted the laws are different at different levels.

What happens at the chemical level does not govern all activity at higher levels. "A set of

conditions is left undetermined by the laws of nature" (Polanyi, 2009, p. 40) The basic

idea is that for one level to set the marginal conditions for the lower level it cannot be

predetermined by the rules governing that lower level. A new set of rules must exist at

this higher level. This new set of rules is said to emerge in the sense that they were not

there as predetermined in the lower level. "Within an organism, each higher principle

controls the boundary left indeterminate by the next lower principle it relies for its

operations on the lower principle without interfering with its laws and because the higher

principle is logically unaccountable in terms of the lower it is liable to failure by

operating through it" (Polanyi, 2009, p. 49) . So according to Polanyi, while the higher

levels are dependent upon the lower levels, they are not deterministically resultant from

them. This emergentist form of dualism helps alleviate us from the tension of some

magical thinking and removes tension from radical reductionism. And thus the pendulum

swings back in the dualistic direction.

However, it still does not deal with the theoretically hard problem. The governing

rules simply emerge at the boundary between levels; higher levels constrain lower levels,

but how did they emerge, in the first place? This question is not addressed by Polanyi, he

simply leaves it here. There is a type of dualism that results from his argument that is not resolved. Mario Bunge (1980) describes this as epiphenomenalism where the brain in a way secretes the mind that can then influence the brain. The lower levels somehow secrete a qualitatively different higher level phenomena that then govern lower level phenomena or as Polanyi puts it, set the boundary conditions. Each concentric level is treated as a closed system with a clear causal direction: higher levels control lower levels.

While it is clear that emergence, must play some role in moving from neural actions to qualia, this dualistic type of emergence gives us little theoretical traction. We know changes in brain states accompany changes in the emergence of mind, we also know changes in mind accompany changes in brain states. Causal direction is often unclear between these levels. It is to this causal question that we shall now turn. We shall also dive briefly into genetics as an example of problems with traditional ideas of causal direction in biology which directly relate to the examined relationship.

In the current paper, we are exploring ways to observe knowledge in brain. If we allow the mind to cause changes in brain or the brain to cause changes in mind then it is unclear what we are observing. This is of particular interest in the resting brain. One could make the argument that the resting brain dynamics are simply the result of the brain being manipulated by the mind when one allows their mind to wander; when the mind wanders it takes control. I will not be making this claim. Therefore, before moving further, causal direction must be addressed.

Eliminate causal direction. Alluded to by Polanyi is the idea of determinism from bottom up influences, but he never clearly explains a method of emergence that can result

in controlling levels. The current paper makes no causal claims of relationships (and in fact denies a causal relationship between them) but, to better understand mind-brain relationship we need to explore this concept in more detail.

Let's temporarily assume the theoretical distinction Polanyi sets up separating mind from body in levels of influence. If we accept this dichotomy, in the methods that follow, we need to ask, are we studying mind or brain. If observe neural dynamics at rest, are we simply observing the influence of the mind on the neural dynamics? What we have discussed so far is directional from neural complexity to the emergence of mind and then from mind to the neural components themselves. However, this issue of causal direction assumes a cause-effect relationship. This was once assumed to exist in genetics or environment which predetermined our development including but not limited to neurological development. While this nature vs nurture debate has long since been dismissed it is worth examining how it dealt with causality because this gives us some tools to interpret the mind-body causality relationship.

Simplistic understandings of genetics are that they are "blue prints" to development; this is the most basic causal argument in development and biology. The doctrine says genes are arranged in codons these codons encode amino acids that then build proteins that build the body. There is no stricter example of bottom up approach in biology. If we could only understand the genetic code, we could predict development. From the opposing perspective the behaviorists believed that an understanding of the environment led to a determined behavioral outcome. Watson famously said "Give me a dozen healthy infants, well-formed, and my own specified world to bring them up in and

I'll guarantee to take any one at random and train him to become any type of specialist I might select — doctor, lawyer, artist, merchant-chief and, yes, even beggar-man and thief, regardless of his talents, penchants, tendencies, abilities, vocations, and race of his ancestors" (Watson 1930, p. 104). Neither of these approaches answered questions of development. Instead it has become clear that a different form of causality and determinism was warranted.

In an attempt to deal both with the deterministic aspects of genetics and integrate the influence of the environment, Waddington (1942) attempted to deal with the trajectory of development by proposing the metaphor of the epigenetic landscape where genes interacted with the environment to carve out a figurative trough along the slope of life where one's development would continue down this trough and become entrenched unless some event shook up the landscape allowing development to take an alternative path (figure 5 a and b). The landscape itself it built through genes, but multiple paths are possible. Genes and experience helped us lay down a developmental path giving us choice points in development. While attempting to deal with the gene-environment interaction it was still far too deterministic to agree with emerging evidence. Thus there was not enough evidence to simply say that genetics led to possible futures. However, it does give us a way to think about neural systems for learning. As time progresses, those systems become canalized or entrenched. As we will discuss below, this approach also complements dynamic systems perspective where the system is sensitive to initial conditions and small differences early in development lead us down paths which are persistent with time.

Gilbert Gottlieb (1991) then proposed a new way of thinking about the interaction across levels in development. Essentially a description of causal influences as bidirectional and coactional. Genes did not only influence development but were influenced by experience. Across time, all levels of complexity from genes to environment influenced each other through adjacent levels of complexity. Notice this description of levels is not the same as that proposed by Polanyi. Within the individual another type of connection is hierarchically organized, but this hierarchy is still dynamic. Gotlib clearly illustrated that even from the genetic level development is not predetermined. From genetic to cellular to whole brain to environment there is bidirectional causality where all levels codetermine adjacent levels across time (see figure 5 c). This logic allows us to move to the mind-brain relationship. We cannot state that the brain changes behavior without simultaneously stating that the behavior changes the brain. This is true at the genetic level as well; we cannot develop proteins without changing the genetic material itself (Grigorenko, Kornilov, & Naumova, 2016). The expressions of proteins in the environment interact with genes to wrap them in different ways allowing for further gene expression.

To further illustrate this lack of genetic determinism, in recent years, extensive work on the human genome has demonstrated that the genome is changed through experience and in fact there may be epigenetic changes in the individual that are transgenerational (Ridley, Frith, Crow, & Conneally, 1988). Meaning that changes in the genome do not just go from mother to daughter based on amniotic experience, but also are carried to granddaughter in the genome . Additionally, current work in the area of the

Baldwin effect describes genetic-environmental interactions that are passed as memory engrams through the generations (Tonegawa, Pignatelli, Roy, & Ryan, 2015). These engrams are stored in cellular connections which are inherited and this inheritance can change in a transgenerational way. Thus, there is plenty of emerging evidence that knowledge structures in the form of engrams while inheritable are malleable and both genetics and environment play a role in emerging systems of knowledge storage.

This cocausal approach means that we need to think about any neuroscientific findings as part of a system. No single level causes something to happen at another level: "behavioral (or organic or neural) outcomes of development are a consequence of at least two specific components of coaction (e.g., person–person, organism–organism, organism–environment, cell–cell, gene–gene, nucleus–cytoplasm, sensory stimulation–sensory system, activity–motor behavior). The key concept to understand is that the cause of development (what makes development happen) is the relationship between the two components, not the components themselves. Genes in themselves cannot cause development any more than environmental stimulation in itself can cause development." (Gottlieb, 1991, p. 423).

Social cognitive theory directly borrowed these ideas from biology in the work of Albert Bandura (2001). In his approach internal factors, environmental and behavioral factors are acted cocausaly on development of self. However from this self, Bandura allowed hierarchical influence of the emerging self to direct the biological. "Cognitive processes are emergent brain activities that exert determinative influence" (Bandura 2001, p. 4). Bandura's "agentic" perspective of self allows for the emergence of mind

from biology through interaction with the environment which can then influence the biology. However, while Bandura clearly explicates the cocausal and bidirectional influence creating self, there is never any clear explanation for how self is represented in the brain or even how it is represented in the interactions. Instead, it appears to be magical and thus we have the reemergence of dualism.

So, from Polanyi we saw a causal direction which was resolved into a dynamic perspectives of development. But, we still have different levels of complexity and different rules governing these levels. Bandura separated the "levels" conceptually in a triadic model. However, this still remains problematic. This assumes that behavior and mind are separable; we shall now call into question this separability with a final approach for an acceptable form of emergentism that allows us to think about mind-brain in a scientifically useful way.

A.

B.

C.
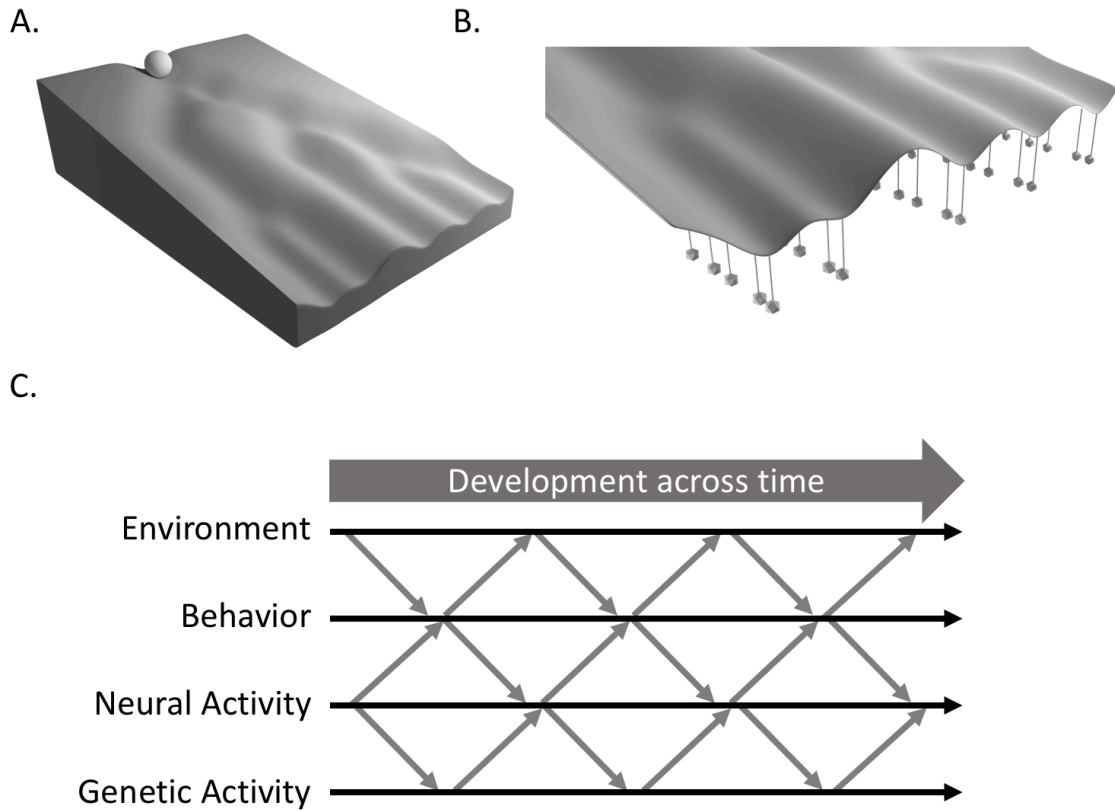
Figure 5. Development and cause. (A and B) The epigenetic landscape of Waddington. In A we see the entrenched valleys as possible directions for development and in B we see Waddington's theoretical foundation as genes and environment interactions pulling at that landscape and forming entrenchments for the marble of life to run down. (C) Bidirectional Influences. The influence is not unidirectional from genes to behavior nor from behavior to genes, but simultaneously in all directions. Levels influence each other bidirectionally and cocausaly.

Seperability dissolved. One may rightly ask at this point, is it not acceptable to

assume that mind brain relations are cocausal and bidirectional? Then we can understand

mind from changes in brain or understand brain from changes in knowledge and end this

metatheoretical discussion. But simply accepting this and moving on would drastically

limit the interpretability of the methods presented here. But, beyond that, they are

theoretically insufficient. If knowledge and brain are separate levels that leads to the

assumption that while they can influence each other, they can also change independently.

If we think about the flask containing water many aspects of the flask can change

independently of changes in the water. If we think of knowledge independently of brain,

then the knowledge should be able to change independently of the brain. Or the biology

of the brain could change independently of the knowledge. If this is the case, then our

behavioral or biological indicators of knowledge are not useful measures of knowledge. It

is of great theoretical importance therefore that we make some effort to dissolve the

separability.

Emergentist psychoneural monism. In our final exploration into the mind-body

problem we shall use the taxonomy of the mind-body problem proposed by Mario Bunge

(1977) which is useful in positioning ourselves within this subject matter. We have

dismissed the substance dualisms where the mind and the brain are separate substances

which are not grounded in empiricism, we have similarly dismissed monisms of idealism

and radical determinism. And finally, we have pointed to a more acceptable reemergence

of dualism which problematically still relies on a supervenience of the emergent mind

over the brain. We then addressed causal direction finding that perhaps mind and brain interactions are bidirectional. But still, this assumes some separability.

Here we shall use Bunge's postulates to take the ideas of emergence one step further than what we saw in Polanyi. These postulates are foundational to our argument and part of the separation of the two methods to be described later. The views here boil down to emergentist psychoneural monism. There are three postulates proposed by Bunge (1980) which will be ascribed to here:

(1) "All mental states, events, and processes are states of, or events and processes in, the central nervous system" (p. 506). The mind does not lie outside the brain, nor is it the result of the brain, it is equal to the processes and events of the embodied brain.

(2) "These states, events and processes are emergent relative to those of the cellular components of the CNS" (p. 506). The cellular components do not individually represent mind. They are emergent, but not emergent "from", they are emergent "with"; it is not that something new emerges from them it is more aptly put that something new is emergent from their organization into systems. But remember that emergent in this case is not separate or secreted.

(3) "The so-called psychophysical relations are interactions between different subsystems of the CNS or between them and other components of the organism" (p. 506) The mind is in the relations. It cannot be pointed to as any particular component but a system of components. This could also be seen as what Bandura was going for in Social Cognitive theory where the mind emerged as a level from the triadic relations, however he fell short of psychoneural monisms when he stated that this emergent property causes

48

changes. In other words his agentic theory is in opposition to these three postulates a whole. Importantly, this does not allow the "executive system" to act as a controller of the mind. The executive faculties of mind are a component not separate from it.

If we accept the above postulates then we can begin to think of neural events as psychological events and talk about "psychological events without leaving the biological" (Bunge, 1980, p. 506). Assuming these postulates we can now discuss psychological events as occurring on a neurological level without assuming a metaphor. We can say that cell assemblies, discussed below, do the thinking. It is important to note that minds are "not a supra organic level because they form no level at all" (p. 508).

Knowledge in active neural systems. I will be discussing neural events as psychological events, but importantly I am not saying that neurons or the material brain is equal to mind; a picture of the brain, no matter what its resolution, is not a picture of the mind. I am saying that the mind or knowledge is in the ongoing dynamic relations between elements in the system at all levels.

This is a repetition of similar observations made by Gottlieb above "the cause of development (what makes development happen) is the relationship between the two components, not the components themselves" (Gotlib, 1991, p. 423). But, to think of them as cocausal from this perspective is equally flawed. They are not separate levels that act on each other they are a system. Psychological events lie in the relations between components of the system of neurons not in the neurons themselves or in the mind as a separate level.

Along these same lines, understanding the physical aspects of the connections between neurons does not tell us about the behavior of the system. These types of reductionistic approaches have met with failure and demanded reinterpretation. In parallel to the human genome project where a complete map of the genome tells us little about development, we have found that a map of neurons and their connections does not explain behavior. The complete mapping of the 302 neurons and the 7,000 connections in c-Elegans worm has not explained its behavior not its learning (Bargmann, & Marder, 2013). As mentioned above, the genome changes with development and the genome and environment simultaneously influence and change each other. However we need to even make one more stipulation. The same neural networks with identical connections can have radically different behavioral results. Thus connections by themselves are not sufficient, we need to understand the flow of informations through these connections; small molecular changes even in social hierarchy of organisms can result in the same circuit resulting in radically different changes in behavior (Yeh, Musolf, & Edwards, 1997). The whole is not more than the sum of its parts it is the dynamic relations between its parts. The task then becomes one of understanding those relations. Approaches that examine these relations across time is one approach to get at this aspect.

What emerges is not something wholly new, but a level of organized complexity which has different properties from its component parts. However, it is essential to recognize that is still tethered to these component parts and thus changes in the component parts will exhibit different emergent properties for the system. In a sense, under an emergent materialism or psychoneural monism approach one can still "hope to

'reduce' the molar properties of the brain to the properties of its micro components and there links" (Bunge, 1980, p.205) and by doing so we are not dismissing or explaining away the mind.

Knowledge as an aspect of mind is also an aspect of neural systems. Knowledge is the temporal relation between components of the system but it is constrained by the components themselves. It is constrained by the brain and by the environment from cocausal influence. Now that I have laid down the metatheoretical approach necessary to understand this search for knowledge as it is seated in the brain, it is time to understand the neural system itself. As we shall see, this approach itself is still grounded in the anatomy of individual neuron, and synaptic structure. Bunge allows us to ground these ideas, but one more element is necessary.

Based on our arguments from phenomenology above, an additional postulate is added. All mental states (those of consciousness, tacit knowledge, and knowledge) are omnipresent. "Mental states are a subset … of brain states" (Bunge, 1980, p.22), but we add here based on the above analysis of the persistence of knowledge that knowledge, conscious, tacit, or outside current access is represented in these brain states; knowledge is beyond conscious mind or mental states. As an extreme example, an individual with locked-in syndrome where the individual is completely paralyzed but conscious still retain knowledge (Smith & Delargy, 2005). But how this is done will become clear in the upcoming discussion of biological foundations of knowledge. This paper assumes that all of these are represented by dynamic states of the central nervous system. The state of knowledge is represented in the ongoing dynamics of the central nervous system .

51

We shall now, in this spirit, examine what features of the physiological system allow for brain states and allow for knowledge to be stored. Neural components at the microscopic level constrain the observable dynamics at the macroscopic level. The microscopic will therefore also constrain the phenomenological.

Knowledge in Brain Dynamics

Appropriate level of analysis. The current approach will be to address the system at multiple levels simultaneously through interpretation of the indicator variables deduced from the fMRI signal.

The greatest question in cognitive neuroscience these days is what is the appropriate level of analysis? The international effort to map the human brain depicts this problem well. Some researchers are literally mapping every dendrite and glial cell connection preserved in individual brains (Helmstaedter, 2013), at the other end we are examining global interactions between regions that are similar across thousands of participants (Marcus et al., 2013).

While we must limit our analysis to the methodological limits of our chosen instruments and background. It is equally important to note what those instruments assume at a system wide level. As opposed to the approaches taken by behaviorists or idealists, this next section will attempt to do some evidence based reduction. Current science limits the representations of mind at the molecular level and takes it to the societal level. Brief mentions will be made to respect these extremes, but the core of our methodology lies somewhere between the structure of individual neurons and whole brain interactions.

What may initially appear reductive is multilevel and inclusive. It should be clear by the end of this discussion that knowledge is represented across levels from molecular to social and any artificial isolation for empirical reasons is a theoretical convenience and not reflective of reality.

Reactive or active? At this point, it is essential to describe what tools the brain has for these persistent neural representations. The point here is to see how neural representation enables persistence of representation to understand how we can probe this information using rs-fMRI. As mentioned above, it is unfortunately common to think of the brain as reactionary. As if it lays dormant until stimulated by the environment or as dualists would see it, stimulated by the spirit. This thinking has led to the unfortunate cultural belief that we only use a small percentage of our brain daily or that only specific neural regions are engaged during tasks. Nothing could be further from the truth. All regions of the brain are in constant activity and all regions of the brain are involved in all activity as they are parts of extended networks and establish a neural context.

One possibility for this misunderstanding may come from contrasts in fMRI studies. In a typical study the BOLD activation is represented in a subtractive method. The individual engages in two different tasks and the significant difference in BOLD activation between these tasks results in a map representing the differences between two states. However, the common misunderstanding is that this difference represents the activations necessary for task completion; if neural engagement was limited to only these regions many of the tasks would not be completed. While differential activations in these

regions appears necessary for task differentiation, it is clearly not sufficient for task engagement.

The entire network is necessary for each and every task, no regions are dormant in the brain until the right experience presents itself. Activity across the entire brain sets the context for every neural interaction. Furthermore, without activity connection between neurons disconnect and whither away, while new connections are always being made, their persistence is activity dependent (Hua, & Smith, 2004). Activity is intrinsic to the whole system and its elements. And, it is this constant activity that stores knowledge and which we shall probe. But, lets begin with a brief overview of how the brain is organized this will inform not only the theory but the methods to be applied. At the macroscopic level the brain has shown both remarkable preservation of functional specialization but also remarkable variability and plasticity.

Modularity. We shall begin with an illustrative look at locationism from the findings in the major language associated regions of the bran. The 1860s was a revolutionary time in neuroscience especially in the advancement of ideas concerning localization of function. Language difficulties resulting from brain damage known as aphasias lead to remarkable discoveries. Paul Broca discovered that a patient with localized damage to the ventroposterior region of the frontal lobe had lost his ability to speak (Lazar, & Mohr, 2011). He then evaluated the autopsies of 12 other patients who were known to have lost similar language function and as predicted they suffered damage to the same region which he confirmed. In the following decades, following Broca's work, Karl Wernickie appeared to have discovered a similar region responsible for speech

54

reception a well as semantic processing (Boller, 1978). While originally identified in the superior-posterior temporal lobe, the region historically moved from further superior regions all the way to the temporal pole; this reflected both the lack of clear definition, but also some methodological problems which were actually very informative (Mesulam, Thompson, Weintraub, & Rogalski, 2015; Mesulam, 2015, October). Shortly after Wernickie's discovery Lichtheim (1885) proposed one of the first extensive wiring diagrams of language regions of the brain using that wring diagram to predict that there would be similarly specialized areas as well as yet unidentified disorders of language. He proposed the idea that if connections between these regions in the white matter of the brain were broken specific types of aphasia could be accounted for because information could not move between these regions.

This type of thinking lead to dominant locationist paradigm and the field of phrenology (Anderson, 2014), this approach was quickly dismissed but we still work within its thinking. Locationism has some truth but is incomplete (Pessoa, 2012).

While the locationist perspective had been dominant it is not without problems. While Broca's area has been robust, the findings of this kind of research is often misinterpreted. We find, for example, that in a population Broca's area appears very localized, however when examining individuals, the distribution of function associated with Broca's area is more diffuse, involving both hemispheres and wider regions of the cortex (Lindenberg, Fangerau, & Seitz, 2007). However, the central hub for Broca's area remains consistent.

Wernickie's area has been another story altogether. Marsel Mesulam (2015) points out that damage to Wernickie's area proper results in a variety of inconsistent language deficits involving semantic and word comprehension. More consistently damage to the temporal pole and adjacent regions resulted in word loss. It was found that damage to Wernickie's area proper often involved damage of the underlying fiber tracts which connected regions of the temporal lobe with more anterior regions such as Broca's area. Sentence processing as a whole involves much more of the cortex and has not been sufficiently pinned down at this point; it likely involves the entire system as language is based on many levels of understanding (David, Lakoff, & Stickles, 2017; Lakoff, 2012).

In any case, the lesion studies have shown that some very specific skills such as phoneme recognition and production can be shown to have localization in specific regions, but most language disorders involve multiple regions and general large swaths of cortex. The general ideas behind Lichtheim's models are robust, there appears to be a sequence of processing units that when connections are disrupted result in predictable shortcomings in language function.

An interesting point to which we will return was Lichtheim's insight that perhaps the network had a hierarchical modular structure. At one level of analysis the nodes appear to work as coherent units, but if we zoom into the individual nodes in a network, they also have an internal modular structure where each module has a coherent function. This would not be confirmed for may decades.

This classic findings of localization have been repeated with other functions and as mentioned in the previous chapter, the sensory cortices are very reliably reproduced

across subjects. Interestingly, these sensory cortices appear to respect topological

boundaries consistent across individuals. The neocortical folding patterns in sensory areas

are more consistently found across individuals and the folding patterns of association

areas show greater variability (Van Essen, 2002; Van Essen, Drury, Joshi, & Miller,

1998), even between identical twins (Botteron et al., 2008). The further we move from

these primary sensory cortices, the more problems we have as association areas are more

variable and act as hubs integrating many sensory and other association areas (Van Essen,

Glasser, Dierker, Harwell, & Coalson, 2011).

Regardless of this known short coming, there is great consistency in functional

localization and folding patterns for some basic skills (Van Essen, Glasser, Dierker,

Harwell, & Coalson, 2011). Thus is would be best in our approaches to understand

function to attempt to align these folds regardless of brain size or other dimensions. The

locationist hypothesis has features which are fairly robust.

However, in Karl Lashley argued against the locationist perspective when he

suggested that the amount of damage was more important to memory and complex

cognitive skills than damage to a specific region (Lashley, 1929). He ablated regions of

rat cortex and put them in situations where they had to run through a maze to get to food.

He discovered that it was not the specific region which mattered but instead the extent of

the damage. This approach became what is known a equipotentiality and mass action.

Lashley proposed that with small localized damage, the brain was capable of

compensating by utilizing cortex elsewhere as a mediator. For this to happen, learning

must be distributed and it must also be degenerate, meaning there are multiple ways to

get at the same skill (Price, & Friston, 2002; Edelman, & Gally, 2001). This does not deny localization, but generalized learning requires an interaction of many network components. Cognition is a brain wide function not a regional function.

Currently we accept models which are somewhere in between. Specific skills appear to be highly localized but also recruit extensive regions of the cortex. From both a learning perspective and an evolutionary perspective this makes sense. Of central interest in learning theory is the ability to generalize beyond the context of learning (Edelman, & Gally, 2001). If a single path or pattern was responsible for storing knowledge, then the brain could not handle variation in context. Similarly, if there is damage due to stroke or traumatic brain injury skills would be lost and the ability to recreate or preserve the skill would be lost. And we know that even losing the majority of one hemisphere can result in neural reorganizations of necessary skills (Immordino-Yang, 2007). We cannot simply just connect distal regions of the network if no connection exists. [2]There must be some existing framework allowing for neural reuse and generalization.

Network configuration. There is no doubt that the brain works in a network type fashion: there are regions of highly localized specialization which are interconnected. Implicit in this type of organization is a specific type of network connectivity. While at one time it was thought that the brain was organized in random network configurations, it has become clear that this is not the way it is organized. A random or orderly network organization would result in much larger brains with wasted material and energy

---

[2] This degeneration hypothesis must necessarily include external connections. Tools out in the world can facilitate connections between brain regions.

resources (Raichle & Gusnard, 2002); the amount of energy required to run such a network would likely cook the brain (Tomás, March 2017).

Watts and Strogatz (1998) examined a promising network type that is found in many biological systems but also shows great benefit in many other network ranging from power-grid construction to disease proliferation models. Between completely random and completely organized is a system with very high levels of clustering. This type of network is known as a "small-world" network and it has the benefit of reducing material costs, increasing signal processing speed, synchronizability, and computational power. Small-world networks have the feature that they have a preference for a high number of short paths between near processing units and less paths between clusters. While early models were done with the connectome of the c-elegans, these patterns were also found in the mammalian brain (Bassett & Bullmore, 2006). It is easy to imagine how this might account for the modularity we see in the human brain.

What is more is that this small-world network configuration in the brain appears to be fractal in nature. Just as Wernickie and Lichtheim suggested, the brain can be said to consist of interconnected modules and within those modules are modules also preferring short path lengths and if we increase the resolution we see the same pattern preserved (Bassett, Meyer-Lindenberg, Achard, Duke, & Bullmore, 2006). This gives us some interesting features to work with when conducting analysis. While fMRI has relatively high spatial resolution compared to other methodologies, it has relatively low spatial resolution when compared with neurons. Understanding that the structure of the network is hierarchically modular, fractal and small-world we can make some judgments

at this level of analysis that are not invalidated by scale. However, these judgments may be unique to scale.

Thus, what we are left with is a neural structure with network organization in a small-world configuration. It has both local modularity and flexibility. Its fractal organization allows for analysis at multiple levels. Importantly, studies from aphasia have shown us that the networks have sequential features after processing is completed or partially completed in one module, connections long distance connections with other regions are essential for sequential, parallel and hierarchical processing of information.

Locations of modules. While it is clear that some modularity is driven by genetic and developmental factors, much of neural organization is left to experience. Much of the flexibility in neural architecture is in the association cortices and our abnormally large neocortex, but as we discussed above with amputees and individuals with missing cortical tissue, the brain is incredibly flexible and allows for reorganization after injury.

Why are some places localized? While we discussed above that the system itself favors small-world network organization and thus modularization, we need to ask why in general the system reliably organizes some modules into the same locations across subjects.

Why are more complicated skills localized? Language works as a great example for localization of function. It is no coincidence that Broca's area is directly adjacent to the region of the motor strip associated with the articulators of speech, however this may not be the driving force of localization. A hypothesis put forth o evolutionary grounds is the neural reuse hypothesis (Anderson, 2010). Which basically says that evolutionarily

some regions are hardwired and new skills use those regions because those regions specialize in the necessary basic skills. For example, Broca's area may have some basic use in hierarchical relationships such as the hierarchy of actions needed for grasping and action preparation and sequencing (Thoenissen, Ziles, & Toni 2002; Nishitani, Schurmann, Amunts, & Hari, 2005), action recognition (Decety et al. 1997). More evolutionarily recently the visual word form area reliably activated in reading letters and words utilized previous visual regions important for visualization of specific shape types and probabilistic learning now necessary for letter and character recognition (Dehaene, & Cohen, 2007).

Why do they tend to fall on the convolutions of the brain? An interesting mystery has been to understand why modularity tends to follow the convolutions of the cortex. While no conclusive answer is present at the moment, Van Essen (1997) has proposed that part of the factor leading to convolutions is axonal tension. The cortex folds as it grows within the skull but if modularity has already begun to develop there will be greater tension on the short connections within a module. Regions of low axonal tension may be more likely to fold inward allowing their axons to wrap across the internal surface of the fold, while regions of high tension will tend to fold outward maintaining the close intra modular connections.

Interestingly, the use of resting state data has further confirmed much of these findings. If we examine which regions are coactivated during resting state, we find that in fact modules themselves tend to activate was a whole we also find that these correlations also appear to respect the folding in the cortical surface which also respect white matter

tract anatomy following Van Essen's approach to cortical folding (Van Den Heuvel, Mandl, Kahn, Pol, & Hilleke, 2009).

Neural components. To understand these high level interconnectivities we need to dive into the cellular components that make up the system. As mentioned above, while the smallest components of the network show different qualitative properties than the emergent structure of the network, the features of these small components allow the particular emergent structure to exist.

In an independent but parallel line of work to the modularity debate discoveries were benign made at the level of the neuron. In the 1870s the neuron doctrine was developing from staining techniques which allowed the detailed observations of neural structure. The inventor of this staining technique enabling the visualization of neural fibers believing them to be not only interconnected but continuous. This theory known as the reticular formation theory posited that the brain was one continuous net of these fibers.

The work of Ramon y Cajal in his intricate drawing s of neural slices showed the web of connections seen in this network.[3] It became a contentious matter as to whether these connections between neurons were continuous. The infamous debate between Golgi who believed the networks continuous and Cajal who believed they were separated by a synapse was not resolved until the 1950s when electron microscopes gave us the first detailed images of the synapse (De Carlos & Borrell, 2007). We now accept the synapse

---

[3] His illustrations became some of the most important and prophetic documents in early neuroscience as he observed details only reveled much later. This is also an amazing example where science and art meet as his observational studies were also beautiful.

62

as a physical structure at the junction of two neurons which binds neuronal connections making connections between neurons contiguous, but not continuous; this is known as the neural doctrine.

In his study of neural morphology, Ramon y Cajal generated basic conservation laws which became the foundation of modern graph theory and neuroscience. He conjectured that the neuron wiring was based on the conservation of space, time and material. So, even at the level of the individual neuron it was theorized that networks were constrained into particular configurations preserved in small-world networks which had not yet been discovered. Both macro and microscopic analysis came to similar conclusions. The brain is a network of connections with preference for local modularity and few long distance interconnections, and processing is likely done locally and then spread to more extended parts of the network.

Neocortical structure. While cellular organization across the brain is an intense and interesting area of study, the current methodology is limited to only that thin layer of cortical tissue on the outside of the brain. As it turns out, the cellular organization allows us to make specific interpretations concerning the propagation of signals in rs-fMRI.

The cortex is broadly made up of seven layers of neurons (Shepherd, 2003). These neurons are organized perpendicular to the surface with their cell bodies in the cortex. The most common type of neuron here is the pyramidal neuron. It's typical shape involves a small number of long dendrites reaching toward the outer surface of the cortex were it is branched into thousands of smaller arborations making local connections other dendrites both of the same and different cells. Below the cell body is the axon which

stretches into and makes up the white matter of the brain creating the tracts that connect

modules and connect the cortex with the deep structures of the midbrain, not addressed in

this study. The more superficial layers tend to be excitatory and they tend to be the layers

that are represented in Ca+ imaging methods during rest. And these Ca+ images tend to

correlate with patters of activity in rs-fMRI (Mao, Hamzei-Sichani, Aronov, Froemke, &

Yuste, 2001). Thus while obviously not excluded, the inhibitory regions of the cortex are

under represented in the cortical surface imaging in rs-fMRI (Raichle, 2015).

Another interesting feature of these layers of neurons is that they tend to be

organized in columns. The organization of the columns is highly variable, but in general

they can show functional distinctiveness and may map directly onto the sensory apparatus

in a topologically consistent way. One of the clearest examples of this is in whisker

studies of mice on what is known as the barrel cortex (Lübke & Feldmeyer, 2007). Each

whisker appears to have a specific column of cells in the cortex that is relatively

independent and separated from its neighboring columns. A similar organization is seen

in humans and is reflected in maps described earlier (tonotopic, somatic and motor body

maps, visual maps to name a few) (Mountcastle, 1997). This columnar organization is

also essential for processing different types of visual information such as edges and

directional motion (Hubel & Wiesel, 1962). Again we notice the small world architecture

as these column show mush higher local connectivity and limited long distance

connectivity.

Because we are focusing on signal propagation through the network of the brain,

let's take a moment and discuss the various ways signals are propagated through neural

units. The most prominent method known is the action potential. A signal is received from incoming dendrites; if the sum of these incoming signals exceeds a specific threshold when they meet at the axon hillock, the cell depolarizes sending a signal down the length of its axon stimulating the release of neurotransmitters at the terminal buttons of the dendrites which trigger similar reactions in cells downstream (Shepherd, 2003).

As the signal travels down the axon it generates an electrical current on the external surface of the membrane (Taylor & Dudek, 1984). Excitatory synaptic input at the apical dendrites results in a negative polarity and the further down the axon a positive potential occurs. This creates an external DC current on the surface of the neuron. It is this current that EEG studies take advantage of. There are two important points to discuss here. First this electrical current allows for indirect ephaptic interactions and an action potential is not necessary for the current.

A ephaptic connection results when adjacent neurons change their own current not in response to the signal propagating from the input apical dendrites but when their own environmental conditions are changed as a result of neighboring currents. These neighboring currents allow for a lower threshold for stimulation in neighboring cells that may more easily result in action potentials in parallel fibers. Secondly, this current is present even when threshold is not reached and the neuron does not fire. Small electrical changes in the dendrites travel down the dendrite before exiting the axon hillock. These excitatory post synaptic potentials (EPSPs) are not sufficient on their own to generate an action potential but their shared input can be summed either across space or time and result in slow waves of excitation that are measurable at the scalp (Shephard, 2003).

Thus, signal propagate through the cortex through action potentials, haptic connections and EPSPs all of which affect the current in the surrounding tissue as well as the excitability of the neurons making it easier for a neuron to overcome threshold. When threshold is reached at the axon hillock, an action potential is sent down the axon through the white matter to other cortical or subcortical regions. All of these processes require the use of chemical resources and thus they all affect the BOLD response in fMRI. It is also becoming clear that BOLD response in resting state is the result of regional cortical excitability and not only action potentials, a point we will return to shortly.

There is some relevance of this in fMRI methodology to be discussed below. Adjacent cells tend to interact even when not connected, but the foundation of connections is from direct interaction. In general, activity tends to move through these elementary units in one direction.[4] The interpretation of the data entails that we understand the anatomical orientation of these units. But before this discussion, lets examine briefly the role that the neuron has played and continues to play in one of the most influential models of learning in neurons.

Hebb. Now that we have briefly introduced the neural structure of the brain, lets examine how this system can learn and store knowledge. The basic idea of learning is that there is a change in behavior or behavior potentiality as evidenced by a change in a stimulus-response relationship. As mentioned above, this must involve some persistent change in the knowledge structure and therefore the systems of neural tissues in the brain.

---

[4] This is not to say signals do not move in the opposite direction. Backpropagation of neural signals is common especially in the dendritic arborizations, as described above.

The neuron as a foundational element of learning was suggested even by those who first observed the cell structure. Ramon y Cajal pointed out that the structure of the neuron must be related to this capacity for the neuron to learn (Cajal, 1995). But the learning sciences in the Untied States took the path of behaviorism and the neurology of learning was seen as largely unimportant in the process. Both approaches were born from connectionist ideologies but each represents a different path from this perspective.

Early connectionism acknowledged but denied the importance of neuronal connections. At its core, any connectionism argument deals with changing in the strength of connections as a result of experience. Edward Thorndike pushed the focus in the direction of the behavior: stimulus and response. The focus on learning still retained its source in neuroscience with ideas of conduction unit, "the neuron, neurons, synapse, synapses, part of a neuron, part of a synapse, parts of neurons or parts of synapses— whatever makes up the path which is ready for conduction" (Thorndike, 1914, p. 54). But the specific mechanisms were unimportant. Instead general laws of behavior describing how repeated action, pleasurable action, and pleasurable results of action were likely to result in increased future potentialities for the behavior. The connection was between the "The connection of a certain act with a certain situation and resultant pleasure" became strengthened meaning the behavior was more likely to be repeated (Thorndike, 1914, p. 8).

This approach was then dissolved in the development of classic strict behaviorism of John Watson. The focus then squarely put the science of behaviorism in the elicitation and prediction of observable behaviors. Connection dealt with the stimulus and the

response to that stimulus. The connection was stronger when the behavior was more likely in the presence of the stimulus. B.F. Skinner continued this approach taking the connection now to the realm of the response and the reinforcer, but there was still an avoidance of the internal mechanisms of learning. Learning was a statistical process looking at the increased frequency of a behavior. In essence, behaviorist emphasized the strengthening of connections between some stimulus and some observable behavior response could over time to the strengthening of the connection between them; the intervening variable of the physiology was of little interest (Skinner, 1950). Donald Hebb, on the other hand brought that physiology central, specifically examining connectionism with the neurological intervening variable.

In the 1940s Donald Hebb reintroduced the role neuronal interaction played in learning. He attempted to make the theoretical jump from the cellular to the behavioral suggesting ways in which the neuronal structure and function supported learning and knowledge storage. Hebb's approach was still a form of connectionism, but instead of linking simple stimulus and response connection he described a connectionism between the smallest units: "The connections serve rather to establish autonomous central activities which then are the basis for further learning" (Hebb, 1949, p. XIX). It is this postulate of autonomous central activity which would stand as the basis for learning. Notice however that Hebb does not refer to static structure he refers to "activity."

Too often Hebb's approaches are reduced to theories of single neurons learning, however, Hebb's approaches were squarely at the level of the neuronal population. Some may consider his approaches reductionistic, but his argument, while based on the

microscopic level respects system dynamics while maintaining the centrality of the neuron in the behavior of the system. He is thus satisfying out approach established by Bunge in emergent psychoneural monism while rejecting ontological reduction, we are still embracing epistemological reductionism; here Hebb attempted to integrate the microscopic to explain learning, not explain it away (Bunge, 1980).

Neurophysiological postulate. At a very basic level Hebb's approach has been paraphrased as "neurons that fire together wire together." This basic postulate has, for their most part, withstood the test of time with only minor modifications (Sejnowski, 1999). In the "neurophysiological postulate" the persistent representation is in the strength of the connection between neurophysiological units. Strength being defined as a physical change in the units such that the firing of one unit would likely be coincident with the firing of another. In Hebb's words, "When an axon of cell A is near enough to excite cell B and repeatedly or persistently takes part in firing it, some growth process or metabolic change takes place in one or both cells such that A's efficiency, as one of the cells firing B, is increased." (Hebb, 1949, p.62) Note that Hebb does not limit nor suggest that this approach to learning occurs at the level of the single cell, instead in Hebb's words the process is assisting or "taking part in" the activation of another neuron. There was clear acknowledgement of the system wide interactions necessary for the formation of neural connections although the functions of the single cell were essential. Importantly, the post synaptic neuron was not simply caused to fire by a presynaptic neuron, but there was simultaneous and precisely timed activity in the post synaptic neuron that permitted this interaction.

This idea was based on the principle of coincident detention; two events which occurring at the same time would result in structural changes. But for this to happen, both the pre and post synaptic cell would need to be simultaneously depolarized. The signal did not move from cell A to B until repeated simultaneous stimulation of both A and B. This approach requires some mechanism whereby the post synaptic cell would be depolarized without a signal from cell A.

The basic idea is that the system will separately activate each cell. When the post synaptic cell is depolarized from an independent incoming signal, this will trigger an action potential or a EPSP which will make it easier for even weak inputs from the presynaptic cell to influence the post synaptic cell. If this happens repeatedly, molecular changes take place at the synapse which make it easier for the cells to fire together for time periods from hours to days even if no additional action is taken (Bliss and Collingridge, 1993). This is known as long term potentiation (LTP). With continual reinforcement the connection is maintained.

This process is made possible through back propagation, while the cell generally prefers to depolarize from dendrites to soma and the axons, there is no reason it cannot happen in the opposite direction and this appears to be a frequent process. Through this process, the depolarization (usually sub-threshold) moves toward the apical ends of the dendrites and in sense prepares them for incoming signal (Stuart, Spruston, & Hausser, 1999; Hausser, Spruston, & Stuart, 2000). In other words backpropagation prepares the connections for learning.

Because we are assuming we are examining indicators of pyramidal neuron activity in the cortex, this back propagation is core to our understanding the signal. They serve to integrate the arborations of the dendrites in the cortex and therefore serve the function of the Hebbian synapse connecting cortical cells. This back propagation serves many other functions but the combination of back propagation and Long Term Potentiation are just two of the neuronal tools that support the foundations of the hebbian synapse in learning.

Cell assembly. While the cell offers the necessary ingredients for learning, Hebb did not assume that complex learning was the result of individual cells, instead he focused his theory on populations of cells. The source of learning was more appropriately represented at the level of the neuronal assembly. These were tightly associated neurons "a diffuse structure comprising cells in the cortex and diencephalon ... capable of acting briefly as a closed system, delivering facilitation to other … systems" (Hebb, 1949, p. xviii). His suggestion was that over time the activity in a single assembly would build its excitation though recurrent connections which could then facilitate the connections between assemblies. Experience changed the connection weights between the elements of assemblies, but also changed the connection weights between assemblies. Similar to the other approaches we examined, these assemblies were fractal and small world in nature. Assemblies were highly interconnected regions with comparatively few connections between them. Many small assemblies connected to make larger assemblies. For Hebb, the assembly was the building block of knowledge structures and the basic perceptual element.

These neuronal assemblies acted as modules whereby recurrent activity would be propagated thorough tightly bound members continually strengthening their connections. An essential component of this idea was that these units became linked by their shared activity over time but were not activity dependent. Thus, at this point we are very clearly straying from S-R theories. Recurrent connections offer a type of connectionism which occurs in these temporary "closed systems" (Hebb, 1949). They are not dependent on external activity, but they represent the history of that portion of the network in a trace or memory. These assemblies are a type of persistent representation of knowledge.

Phase sequence. Finally, the coordination of these assemblies resulted in a phase sequence which unfolded across time far exceeding the activity of the single neuron components. Recurrent connections could now account for activities unfolding across hundreds of milliseconds and across many assemblies lasting multiple seconds. He went as far as to suggest in the vein of emergent psychoneural monism that "A series of such events constitutes a 'phase sequence' the thought process" (Hebb, 1949, p. xviii). Hebb suggests that "the train of thought is a phase sequence" (p.100). Each perceptual event is a sequence of unfolding neurological events in which successive recurrent activity grows to include additional cell assemblies. The phase sequence was important in skill and thought processes, but it was not triggered by the environment. Instead in Hebb's approach, the phase sequence was a slight restructuring of ongoing activity that would result in a temporary sequence allowing the organism's behavior to adapt. Repeated activity in an assembly and between them would lead to the fascination of future

activities. The organism would, through experience, develop a system which was readied for skilled engagement with the environment.

In other words, all knowledge and representation is dynamically unfolding over time, not a snapshot state of the network and not synchronized activity. Knowledge is a living and dynamically developing system. But the intermediate levels of the assembly alone did not contain thought in the larger conceptual sense; thought unfolds it does not exist as images. This approach recapitulated from the discussion above is often lost in explanations of the Hebbian synapse. Hebb did not assert that the association led to static representation and thus in this way he was not an associationist. The argument against associationist in memory formation has gained steam in recent years from the work of many including Charles Gallistel who asserted the now well documented approach that memory is not about associations but about conveying information forward into the indefinite future. This recurrent loop type of storage was further supported by the theories of Elman (1990) who furthered the argument that recurrent loops and activity can push information forward in time allowing the processing of sentences and narratives (J. Elman, classroom talk at UC Riverside, 2017).

One clear example of the neural activity unfolding over time is in the perception of single words. A remarkable study examining written word perception unveiled reliable patterns of neural activity for single word reading stretching more than half a second (Woodhead et al., 2012; Dhond, Witzel, Dale, & Halgren, 2007). Demonstrating the interaction of bottom up and top down mental processes as we see early activation of occipital lobe followed by frontal lobe activity and temporal lobe activity which returns

the volley to the occipital region completing one interaction of a perceptual loop. This would be a clear example of the phase sequence described by Hebb. And applying models based on Hebb's approach Elman suggests that with this recurrent activity pushing information forward through time we not have the ability to string words into sentences, to tell stores, and carry on conversations over our lifetimes.

Temporal. Time was a crucial aspect of Hebb's approach. While coincident detection was important for building connections, the reciprocal connections that resulted from coincident connections would lead to building of activity over time within and then between assemblies. This allowed for the temporal aspect of thought and action. The combination of the assembly and the phase sequence demonstrate the unfolding of activity over time. Remembering that even perception is a skill "perception of a simple pattern is not a single lasting state, terminated by an external event, but a sequence of states or processes" (Hebb, 1949, p. 99). These processes were ongoing and reverberation never ceased. The perceptual process "does not arouse inactive tissue but feeds into an activity that is already going on" (Hebb, 1949, p. 121). Perception in this sense utilizes existing neural activity and does not generate activity from some base inactive state. This ongoing neural activity now well documented was intrinsic to the brain. The term " intrinsic organization of cortical activity is so called because it is opposed to the organization imposed on the cortex by sensory events" (Hebb, 1949, p. 121). It is the systems activity when that system acts as in a more closed situation.

Anticipating the future methods to observe the actions of the resting brain as a relatively closed system, he suggested moments in sleep and infancy. We now know that

74

intrinsic activity is ongoing and highlighted in resting but wakeful state regardless of age. Intrinsic activity during sleep involves different processes because low threshold Ca+ bursting gives rise to synchronized activity during sleep (low threshold Ca+ bursting is a process that leads to rhythmic bursting of specific cells which are often ~100ms in length close to the time scale we see in resting state scans) (McCormick & Bal, 1997). It is perhaps more important to the current theory that this changes the system dynamics of the brain and when we sleep we are not in readied state for skilled engagement. While Hebb proposed ideas of observing the brain during a relatively closed experience, sleep or infancy were not appropriate places to explore this. It may be, that the resting state we observe during rs-fMRI is in fact this state Hebb described to understand ongoing neural dynamics emergent from intrinsic assembly and phase sequence activity.

Problems. Hebb's approach to learning has many problems but overall it has withstood the test of time (Sejnowski, 1999). An argument against thinking of system dynamics as the place for stored information is in recent studies of the memory engram and that it might actually be encoded at the level of the individual neuron (Johansson, Jirenhed, Rasmussen, Zucca, & Hesslow, 2014). One of the core processes to learning the learning of an expectation time between a stimulus and a reinforcer expectation. It appears that the neural system can train the spike timing of individual neurons and in this way the individual neural stores knowledge in the form of timing or even delayed response. By stimulating parallel fibers in the cerebellum at both the efferent and afferent ends, the timing of responses could change. The memory engram for spike timing was recorded in the molecular makeup of the synapse itself. Thus knowledge was represented

at not simply the neural level, but at the molecular level not only in the entire system but also isolated in the smallest molecular components of the system and directly dictate interspike interval a form of information storage. However, information about interspike interval stored at the synapse may lead to the timing of phase sequences making these approach not incompatible. It may lead to the extended temporal pattern of activity proposed above. At the time of writing this dissertation these questions are still very much alive and in their height of debate.

While this continues to be of import and may revolutionize the way we think about the stage of knowledge, the general heuristics established by Hebb remain strong and establishing these molecular memory engrams is still a representation of wider system dynamics (Tomás, March 2017).

Change is intrinsic and important for learning. The above approach also depends on not just a system with neurons interconnected, but neurons which are literally in constant motion permitting the possibility of connections. Neurons cannot just build connection when needed from nothing. The system must have a way to keep its hardware in flux allowing for learning to take advantage of new potential connections beyond just changes in synaptic strength.

The ongoing changes in neural populations are an intrinsic feature of the brain. Often, the public over simplifies neural plasticity suggesting that the developing brain is plastic only in early years and the anatomy increasingly fixed over time. While it is true that the gross anatomy becomes somewhat entrenched, at the micro level, this network remains active and continually populated by new neurons. Neurogenesis, the process of

76

growing new neurons, persists through the life span. The older ideas that we grow all the

neurons we will ever need was overturned in the 1960s by Altman (1962) who discovered

that the hippocampus, an important memory region of the brain, continues to grow new

neurons throughout the lifespan a feature previously thought to only exist in non-

mammalian species. Then axonal elongation throughout the life span (Lynch, Deadwyler,

Cotman, 1973) . Neurogenesis increases in old age and injury as the brain adapts to

changing conditions (Eriksson et al., 1996); we see regular neurogenesis in the

hippocampus, a crucial memory region in the brain and along the surface of the fluid

filled ventricles whereby the new neurons begin this migration to their cortical homes

(Parent, J. Vexler, Gong, Derugin, & Ferriero, 2002). Neurogenesis appears likely to also

increase in environments with increased complexity and enrichment such as those which

offer additional cardiovascular exercise (Clemenson, Deng, & Gage, 2015). Damage or

environmental conditions also appears to "awaken" neural progenitor cells allowing them

to migrate to needed regions throughout life (Alunni, & Bally-Cuif, 2016). The simple

fact that we can recover from stroke, that we can generate new connections to control

implants, and that we can reorganize our sensory motor strip after amputation shows how

flexible the system is, but these are longer term changes in the brain usually take hours,

days, or years. Can morphology of the brain change on a smaller time scale important for

learning?

Changes in the brains hardware continue at a far smaller scale than the neuron. An

important discovery while observed by Ramon y Cajal and painstakingly down into his

diagrams has not been revisited until current methodologies allowed increased

magnification, tiny appendages on the surface of apical dendrites in the cortex are an important source of variation permitting learning (Yuste, 2010). These spines develop at a stochastic rate across the dendrites, although the average rate of development varies based on brain region and they are highly motile. The number of spines at any particular time are dependent on a number of factors but a single neuron can have its dendrites covered with more than 200,000 spines at any moment. These spines are very dynamic structures. Through the molecular actions of actin engines, the surface of dendritic membranes is extruded into the extracellular space with finger-like filopodia which sway in the neural matrix as flexible and temporary extensions. Without the necessary reinforcement, these fingers retract back and are reabsorbed into the neuron. However, if repeatedly stimulated by neural impulse as a result of back propagation or developed connections, the appendages are loaded with the cellular soup of molecules necessary to engage connection and maintain stability with neighbors. Once established, they are resistant to elimination and have been directly observed to sustain their connections on the scale of months and years (Knott, & Svoboda, 2005; Segal, 2005; Yang, Pan, & Gan, 2009). The stability of these spines is either strengthened or weakened based on the cell's firing rate and electro chemical activity along that section of cell. If a cell fires and another cell with an adjacent filopodia or dendrite fires, this sets off a sequence of molecular transformations that affect the actin and myosin (skeletal elements of cells) in the spine stabilizing or destabilizing the structure. In the absence of a signal from cell activity the cytoskeletal elements breakdown and the spine is reabsorbed. Based on

activity in that network the newly born appendage is either reabsorbed or structurally reinforced.

It is interesting to note that behaviorism's emphasis on variability in behavior as a core principle for learning and development is recapitulated at this microscopic level. Random variation with selection seems to be a law of all biological systems and behavior is just one more extension of this system.

Because the growth of these spines is stochastic, the growth process is not driven by learning, only the maintenance is driven by learning. Thus this process of spine development helps to ensure variability allowing learning to take place along new routes. This natural selection of spines gives a persistent landscape of connections resulting from learned skill while maintaining ongoing variability necessary for further adaptation and engagement with the environment.

The time frame of spine development is crucial. The spines appear to come and go on a minute by minute basis. They are sensitive to molecular changes that happen in the time span of seconds and slow hormonal changes. Additionally, spine development is associated with events known to affect the rate of behavioral learning such as hormonal changes (Woolley, & McEwen, 1993), diet (McCutcheon, 1998), exercise (Pysh, & Weiss, 1979), time of day (Maret, Faraguna, Nelson, Cirelli, & Tononi, 2011), and exposure to stress (Radley, 2005). It has been suggested that the spines themselves may serve as the source of short term and working memory (Goldman-Rakic, 1995) and when preserved through repeated activation and necessary molecular changes transform into strong long term memory connections (Yang, Pan, & Gan, 2009).

Intrinsic activity. In addition to the ongoing structural activity, there is patterned neural activity that is endogenous to the neural units themselves. This is one source of ongoing rhythmic dynamics in brain activity. When separated from the network these neurons and interneurons continue to pass electrical signal down their axons and through dendritic arborizations at a rate intrinsic to the neuron and defined by their morphology and chemical composition. In this way, even individual neurons separated from a network contain information in the classical sense. What is important is not whether the neuron is active or not during a task, but the changes in rate of activation during a task. It is also of note that when connected to a network this activity pushes through the network in feedback cycles maintaining strength of holistic brain activity over time even during rest and sleep.

As mentioned above, Hebb proposed that endogenous activity is the default state of the brain. But where does this endogenous activity come from? How does the system maintain the dynamics of subsystems over time? How does it push forward stable representations of learned skills and existing knowledge? Structural connections must not only be made, but hey must be maintained. In addition to ongoing reciprocal activation reverberating through the neural system, the patterned activity at the level of the neuron may serve as just this tool necessary to give us ongoing stability in system dynamics.

Neural songs. It appears that neurons have a song to sing. Importantly, this song is not a consistent rhythm and maintain a specific repetitive timing, but does have patterned behavior in the form of small sequences (or motifs) which reoccur. There are moments when the same song is repeated by different groups of neurons but then these

same groups may drift to different neural songs (Ikegaya,Aaron, Cossart, Aronov, Lampl, Ferster, & Yuste, 2004). The songs appear to move between assemblies in the sense that one assembly correlates highly with one group and one point and then with another group at another point. These patterned activities give a foundation for activity covariation storing information.

One question would be whether these songs are the result of recurrent activity moving through the network or if they are intrinsic to some neurons. Using calcium imaging on slices of mouse neocortex Mao, Hamzei-Sichani, Aronov, Froemke, & Yuste (2001) noted that there was temporally precise spiking among neurons. After applying a glutamatergic blocker to the tissue, which disallowed excitatory signals to move between cells, a number of cells still continued to conduct action potentials. Interestingly they found that this "autonomous activity became more regular" in the absence of network connections. The authors also speculated that because the autonomous cells in the cortex had long distance connections directly to subcortical structures, they may play a role in synchronizing the system dynamics. In other words there are dynamics at the cell level that would never allow the system as a whole to reach equilibrium.

This activity spreads across the cortex in waves of activity. What is more is that this endogenous activity in sensory areas is only mildly modulated during sensation. One may think that the visual world drives neural representations, however Fiser, Chiu, & Weliky (2004) found that the ongoing dynamics of visual cortex are only weakly modified from visual information. This suggests that perception is largely driven by the state of the brain prior to visual stimulation, that our changes in perception reflect very

small modulations of ongoing activity. These ideas give even more weight to the ideas proposed by Merleau-Ponty (1996) in that perception is a skill based on previous experience and endogenous activity.

Further analysis of these spontaneous dynamics in isolated tissue samples has demonstrated there seem to be patterns of UP and DOWN states whereby the region of cortex tends to be more depolarized and more excitable during UP states. During these UP states the temporal dynamics appear to be predictable and depolarization spreads in a stereotyped pattern across the cortex (Harris, Csicsvari, Hirase, Dragoi, & Buzsaki, 2003; Luczak, Hackett, Kajikawa, & Laubach, 2004; Harris, 2005). These patterns in awake cortex greatly reflect similar patterns during sensory input, there is also pattern which is unrelated and yet recurrent and endemic (Luczak, Barthó,& Harris, 2009). And finally, these patterns appear to also be related to a gating of perceived sequences generating a prediction by putting some neural sequences into an UP state based on previous experience while simultaneously putting unrelated sequences into a DOWN state (Luczak, Barthó,& Harris, 2009; Buczak, Bartho, & Harris, 2013). In an analysis of visual cortex of cats Amos Arieli (1995; 1996) found that the spontaneous firing of cells in the visual cortex when there was no visual stimuli closely matched those when a visual stimuli was present (Kenet, Bibitchkov, Tsodyks, Grinvald, & Arieli, 2003). Together, these and a growing body of studies suggest that at the level of the individual neurons sequences of endogenous activity in the cortex reflect history of activations, make predictions, and have unique sequences all of which happen when no sensory input is present.

How do we explain this endogenous activity in the neurons? It appears that two main theories are likely to interact to give us a full explanation. The cells themselves are morphologically shaped in such a way that it affects this spike timing. Even the thickness of dendrites affects their physiological properties (Mason, & Larkman, 1990). Even if we just assume this activity is intrinsic to the neuron it is modified by changes in the system. Connections between it and other neurons result in structural changes which will affect the timing of the neuron, but also allow extended networks to take advantage of the timing of the neuron's spike timing.

Secondly, we can account for this endogenous activity as a trained set of previous experience at both the cell and the system level (although cell morphology is also a result of experience). As mentioned above the information stored at the level of the synapse as proposed by Gallistel (2017, March) allows for just such a situation. But, the recurrent activity model proposed by Hebb and Elman also give a place to store such information. In either method endogenous activity reflect persistent representations of knowledge in the brain reflecting the history of the organism.

Timing. Before diving into fMRI methodology, a brief mention of timing is necessary. While the action potential takes only fractions of a second, shared patterns of activity have been measured to lag across time from seconds to minutes and perhaps longer. This is partially accounted for in Hebb's theory through the idea of phase sequences and in Elman's approach to recurrent activity. Fast communication between neurons in local neuronal assemblies process information before an output pattern is carried via long distance connections to other regions.

Something as simple as reading a word unfolds over several hundred milliseconds. Activity that moves across the cortex in more complex tasks such as word or image recognition can take as long as 700 ms (Woodhead et al., 2012; Dhond, Witzel, Dale, & Halgren, 2007) . But even more basic skills such as perceiving an object has variation in the sequence of processing (Pessoa, & Adolphs, 2010). This scale is at such a large time window that it is easily experienced.

We can easily perceive the passage of time in neural processing when we might go for a jog or a walk and see what appears to be a snake out of the corner of our eyes only to notice a fraction of a second later that it was actually a twig. We notably take a second to react. These faster processing speeds allow for immediate reaction but slower processing speeds allow us to further process the information at a deeper semantic level. Perception appears to involve multiple waves of processing over a variety of time scales (Pessoa, & Adolphs, 2010).

For the most part, it is these higher cortical processes which unfold over a longer period of time that are of interest when we are thinking about learned skills in the classical sense. This is not to deny that faster timescales are equally important in skill representation but they will not be observable in the current methodology.

Slow cortical potential. But, what might we be observing rs-fMRI? There has also been a large history of evidence demonstrating that cycles of cortical excitability take place over long periods of time. The cellular dynamics described above enable the generation of what Birbaumer (1990) and Raichle (2009) call the slow cortical potential (SCP). As mentioned above, the activity of neurons results in a shift in electrical current

which can be recorded from the scalp using EEG. It has been known for some time that in the EEG wave there are slow negative fluctuations which exist on the time ranges greater than half a second and these appear to correlate with behaviors and cognitive skills.

Since the early days of research using electroencephalogram, researchers have observed spontaneous slow wave fluctuations in the EEG signal. The EEG signal is the result of Local Filed Potentials (LFP)(Shephard, 2003). The orientation of neurons in the cortex is perpendicular to the surface. This means that as an action potential moves down the neuron it creates a net positive electrical field at the surface of the cortex and a net negative in the deeper layers. As mentioned above these electrical currents also result in ephaptic responses in neighboring neurons making them more likely to fire from lower incoming signals. Now, an important feature of these slow cortical potentials is that they are the result of net negatives recorded at the scalp (known as sinks as opposed to sources of electro negativity). What could be the cause for these findings?

As mentioned above we also discussed that backpropagation along the apical dendrites along with LTP reduced the threshold for possible signal transmission; the apical dendrites are prepared for learning. Likely populations of neurons are involved in this process resulting from a summation of Excitatory Post Synaptic Potentials (EPSP) resulting in a net negativity in the dendritic arborizations (Raichle, 2010). It is also likely that when the EPSPs are not due to summation they may also be due to extremely slow EPSPs ranging from multiple seconds to minutes. Sustained input to the neurons with apical dendrites in the superficial layers lead to the summations and subsequent

depolarization of the apical dendrites and entrainment of local populations giving rather large electronegative responses recorded in the LFP.

A number of theories have examined the possible role of the SCP. Birbaumer et al. (1990) theorizes that these slow wave fluctuations may actually act as a filter to help deal with central problems in Hebb's model of neural assembly entrainment. The reciprocal excitation in neuronal assemblies described by Hebb, while amplifying the neural signal, if left unchecked would lead to uncontrolled excitability and seizures , but if these are associated with fluctuations in the excitability of other cell assemblies this would break the uncontrolled excitation by stochastically breaking up the signals from neuronal assemblies. This would allow for the repetition of motifs and not result in a constant increase in activity in recurrent networks.

But, more important to current theoretical question is an examination of the SCPs relationship to cognitive processes. In task paradigms, SCPs tend to be associated with the time period between a primary and secondary stimulus. In other words one stimulus acts to orient the organism to pay attention for a change in some other stimulus.

A real life example of this is offered by Raichle (2009): stopping your car at a red light results in motor preparation for the behaviors associated with a green light. However, these slow cortical potentials also have spontaneous activity.

Those spontaneous activity act to prepare the organism for environmental engagement. This has typically been shown in experiments where stimuli are occur on timing with the naturally emerging UP and DOWN states. The results are then compared. It has been found that when there is a significant negative related event in an UP state,

subjects complete the task significantly faster and with less errors. Additionally this is associated tightly with topographic locations on the cortex which have been previously associated with the task of interest. Thus, these spontaneous fluctuations may create preparatory states for engagement with different stimuli.

Further supporting this, Walter and colleagues (1964) associated the cortical negativity after a priming event with a second stimuli. He termed this the Contingent negative variation and this is a well-documented effect in priming. Later, this CNV as it is associated with motor activities was located BA 6, the premotor cortex, through an MEG study. These waves also appear to be modality specific and Gillard (1977) identified a wave associated with auditory stimulus while a separate wave was associated with an orienting wave otherwise known as an expectancy wave or readiness potential (Loveless Sanford, 1973).

Summary of anatomy section. We began our discussion with an approach to interpreting neural activity as representative of mind and stored knowledge. Once we accepted emergent psychoneural monism as a way to interpret the mind-brain interaction, we sought to examine the neural systems which enables the learning and storage of persistent representations of knowledge as activity.

We have seen that the brain has a modular structure that respects small-world architecture at the macro and microscopic scales. This small world architecture leads to the natural emergence of modules which allow for local computations and specialization. Evolutionarily older sensory regions of the brain show very little variation between individuals and this shared representation constrains the possibilities for organization of

learned skills and evolutionarily more recent modules. Modules are relatively fixed between individuals due to a combination of evolutionary processes such as neural reuse and physical axonal tensions in the brain. These locations are fixed through a bidirectional and cocausal interaction of genetics with environment.

We then examined how Donald Hebb laid a foundation for a neural model of learning where experience could change the organization of neurons in the cortex leading to cell assemblies and larger phase sequences which would correlate with skill sequences and knowledge.

Finally, we examined how the neural architecture itself not only stores information in physical connections, but that these physical connections allow patterned information transfer across the cortex in the form of action potentials, EPSPs and ephaptic connections. The electrical flow of information through the cortex is also not tied only to experience but has strong endogenous activity. This endogenous activity changes minimally with experience but it also persists outside the actual experience. The fMRI signal correlates well with LFP and therefore EPSP activity in dendritic arborizations. This activity may act to keep the organism prepared for environmental interaction. It appears likely that perception and therefore learning involves minute adjustments of this endogenous activity.

We have examined this activity at the level of the neuronal assembly but also as small as spines on dendritic arborizations in the cortex. If the system is so robust and resistant to change, how can it adjust to environmental conditions and is it possible for these microscopic changes to change the dynamics of the entire system to adapt to the

environment. To address this potential problem we will briefly turn to study of system dynamics.

System dynamics. While we shall not dive deep into system dynamics it offers a way to pull back and interpret large scale changes in complicated systems.

As we have mentioned throughout, the brain is in constant state of activity. It is made up of millions of small components which interact to generate system wide trends and eddies which may last second, minutes, or even days. There is no doubt that the brain is a complex system and it is therefore appropriate to think about it in terms of complex system dynamics.

The study of complex systems involves the study of open systems with many interacting parts resulting in nonlinear dynamics and emergent system wide properties (Strogatz, 2014). Complex systems although built from their parts are not reducible to them. The patterns of activity are not in any one element, but in the dynamic ongoing change generated by component interaction. These systems also show the ability to learn from experience. Finally, complex systems have a specific property of sensitivity to initial conditions observable in the brain in the context of learning and the primacy of early development. Overall there is no doubt that the brain is just such a system.

What is important to us is that complex systems have a feature known as attractors (Lorenz,1969). These are states which the system will return to after perturbations. The stochastic nature of some neural dynamics and bombardment from external inputs will likely perturb the system configuration however the system will return to its original more stable state after these perturbations. This changes our concepts

from the environment driving behavior to the environment "nudging" behavior (Thaler & Sustain, 2008). This feature also helps the system recover from injury as it exhibits degeneracy. Complex systems also have the feature that multiple attractors are likely throughout the system and the dynamics likely roll between a variety of stable states.

In the current model these stable states represent a neural readiness for engagement with the world in the form of patterned negative potential in dendritic arborizations on the neocortex. This neural readiness is in the form of persistent knowledge structures representing the history and development of the organism. Larger and more apparent patterns likely reflect less specific knowledge and as we zoom into the fractal structure of the brain higher resolution likely reflect more specific knowledge.

The current effort is to examine these attractor states as representative of persistent knowledge and readiness to engage with the world. It is in the dynamics of the complex system that I am assuming these persistent knowledge representations exist. And these dynamics exhibit multiple attractor states which are marginally stable but observable (Sporns, 2010, p. 1631).

To capture the features of this dynamic system we shall be using fMRI and a methodology which purports to capture the temporal and topographic dynamics of the brain when it is at rest, specifically by examining its lag structure.

We shall now turn to a detailed examination of fMRI, rs-fMRI and lag structure analysis which will prepare the methods which will be examined in detail during Part 2.

fMRI analysis

First let's examine why we are choosing to use fMRI to capture this persistent representation of knowledge in system dynamics. As described in detail above the cellular dynamics and learning mechanism present in the cortex lead to system behavior which is observable in SCPs. These slow cortical potentials are strongly associated with the fMRI signal but there are additional reasons for examining this data with fMRI.

Most obviously, fMRI is noninvasive and allows for comparatively high resolution data without the need to open the skull. As mentioned above, however, the typical resolution is still limited to thousands of neurons. The processing methods in Part 2 attempts to improve this resolution using surface based methods. Sadly, however, the temporal resolution is limited typical temporal resolution is every 1 - 3 seconds. While the current study uses images taken every two seconds due to the longitudinal nature of the larger study in which this is seated, most standard machines in research now allow .8 second images getting closer to the range we are interested in. Again, we attempt to overcome this method using interpolation techniques. Finally, resting state data has become a standard procedure in fMRI collection techniques and is fairly easily collected for a variety of developmental and clinical populations. The establishment of online data bases in recent years allow for the analysis of large data sets with minimal collection costs (Van Essen, 2013). In future work the procedures applied here with a small population of 51 participants will be extended to data bases holding scans for thousands of participants and the methods are easily scalable. Finally, the images collected from fMRI are fairly easy for the general population to interpret with minimal training. This

91

was of central concern to me as I work with educators who have a general interest in how the brain works and with minimal training they can begin to interpret findings.

To be clear, fMRI does NOT record neuronal activity. Functional Magnetic Resonance Imaging (fMRI) indirectly measures metabolic activity in brain regions to infer changes in neuronal activity in that region. This inference originates in the principle of functional hyperemia, in which increases in neural activity are accompanied by regional decreases in blood oxygenation and nutrients and a subsequent increase in blood flow (Roy & Sherrington, 1890). While the specific mechanisms of this process are still being debated (Drake & Iadecola, 2007; Raichle, 2015a; Raichle & Gusnard, 2002), there is no question that a strong coupling between these processes exist (P. T. Fox & Raichle, 1986). The fMRI scanner takes advantage of this knowledge by indirectly measuring the regional amount of deoxygenated hemoglobin in the blood. Basically, the fMRI scanner releases a magnetic gradient pulse that briefly aligns the spin of hydrogen atoms in the tissues. When the pulse releases, the atoms relax to their previous aligning with the scanner's static magnetic field and in the process affect radio waves that the scanner equipment converts into regional value changes (Lauterbur, 1973; Mansfield & Maudsley, 1976). While oxygenated hemoglobin does not disrupt this signal, deoxygenated hemoglobin becomes paramagnetic and each deoxygenated hemoglobin acts as a tiny magnet affecting the spin of hydrogen atoms in the surrounding tissue and disrupting the signal; this measurement is called the blood oxygen level dependence signal (BOLD signal) (Ogawa, Lee, Kay, & Tank, 1990). Thus, the differing amount of deoxygenated hemoglobin disrupt the signal to varying degrees and we can get a proxy of

changes in percentage of deoxygenated hemoglobin by measuring this signal disruption. As the amount of deoxygenated hemoglobin in a region increases, the BOLD signal decreases. As increased blood flow to a region displaces the deoxygenated hemoglobin with oxygenated hemoglobin, the deoxygenated hemoglobin in that region decreases and BOLD signal increases; more oxygen increases the signal and less oxygen decreases the signal.

This principle of hyperemia then states that regional differences in BOLD signal correlate with neural activity in those regions: relative increases in BOLD signal is indicative of relative increases in neural activity. What drives the use of this methodology in the current analysis of slow changes in cortical activity is not action potentials. It so happens that the BOLD signal correlates better with local field potentials than spiking output of a region and is therefore inclusive of sub-threshold input and other changes to local electrical potentials (Logothetis, Pauls, Augath, & Trinath, 2001). As mentioned above, these SCPs are likely the result of entrained learned sequences which represent the cortical dendritic organization and connectivity.

Standard functional contrasts are only part of the picture. In a traditional event-related fMRI study a simple task, such as moving the right index finger, is done by the participant and images of BOLD activity are taken every couple seconds. The three dimensional brain images completed during these tasks are then subtracted from images taken during some control condition such as rest or more appropriately a control task such as left finger tapping. In essence, the average value for each voxel (a 3 dimensional volume element usually around a cubic 2 mm) during one task is subtracted from the

average value of a corresponding voxel during another task. The difference between these images should reveal the functional localization of the neural activity associated with the task. As Raichle (2015) states, this leads to a view of the brain as "reflexive, primarily driven by the momentary demands of the environment" (p. 2). In other words, the brain is too often thought of as reacting to environmental stimuli as opposed to being nudged by the environment into different functional configurations. But, the regional increase in blood flow rarely exceed 5% of resting state blood flow (Raichle & Mintun, 2006). In fact, although the brain typically weighs 2% of our body weight but accounts for 20% of the energy our body consumes, cognitive effort does not increase heart rate, respiration rate, or blood pressure even when engaged for hours on end, unlike the effects of most physical activities (Sokoloff, Mangold, Wechsler, Kennedy, & Kety, 1955). This massive energy consumption by the brain that has not been attributed to tasks is referred to by Raichle and his team as the brain's "Dark Energy" (Raichle, 2010; 2015). This is a rather fitting allusion to the dark energy of the universe, which while accounting for most of the universe's mass and structure is unseen. Even though this insight is not new, the vast majority of studies have been event-based.

The brain's "dark energy" patterns. In a seminal study to understand if this "dark energy" has structure, Biswal (1995) asked his subjects to "refrain from any cognitive, language, or motor tasks as much as possible" while BOLD signal recordings were taken for 2-8 minutes (Biswal & Yetkin, 1995, p. 537). A subsequent second task was 20s bilateral finger tapping alternated with 20s rest. As expected, bilateral motor cortex was activated during the finger tapping. But, when no action was being performed,

94

these regions also showed a great degree of temporal correlation (>.35) at low frequency

oscillations (<.1 Hz) even after removing other physiological components. The identified

regions contrasted to other work on imagined movement and they were highly correlated

between individuals indicating it was not likely from imagining the finger tapping task.

This correlated resting state activity between regions was suggested to be reflective of

intrinsic connectivity between cortical regions (Biswal, Kylen, & Hyde, 1997). These

correlations are thought to result from functional connections between large scale

functional assemblies of neurons which may be dynamically reorganized while

performing a task (Bressler, 1995). Correlated signals between motor regions occurred

along with the task timing, but importantly, the signals in overlapping regions were also

correlated at low oscillatory frequency during rest.

A strong limitation of Biswal (1995), however, was that this particular study

examined only a narrow slice of motor cortex. Refining the methods Xiong, Parsons,

Gao, & Fox (1999) examined the entire brain for voxels which correlated with a region of

interest. This allowed them to determine not only connectivity between two regions but

also which areas coactivated with the region of interest (once again, a region of motor

cortex). They were able to identify a high degree of qualitative overlap between the

regions they identified and those identified by previous studies examining anatomical

analysis of connectivity. They also determined that whether or not the task-induced

activation occurred before the resting state activation, and despite between group

variations on expectancy for upcoming task, resting state networks were not significantly

different. They make the assumption that this connectivity is the result of "spontaneous

firing … followed by regional cerebral blood flow … [and] specific brain area affects remotely located neurons … through efferent output" (p. 151).

Defining connectivity. These seminal studies began an era of research on resting-state activation patterns which is characterized by assumptions about connectivity rejected in the coactivated cortical regions. Because the term "connectivity" can be and is frequently misunderstood, it must be explicitly addressed here.

Three types of connectivity measures are typically used in the literature: functional, structural, and effective connectivity. The first of these will be the basis of addressing the research questions of the current study but it is important to define this type of connectivity in relation to the other two types of connectivity restricting any interpretations of the findings. While the term "functional connectivity" is sometimes mercurial in the literature, the community has settled on a definition offered by Karl Friston in 1993. Functional connectivity is defined as "temporal correlations between spatially remote neurophysiological events" (Friston et al., 1994, p. 58). (Of course correlations are only standardized covariance and so this definition works equally well with covariance which will be relevant below). It does "not provide any direct insight into how these correlations are mediated" (Friston et al., 1994, p. 58). Functional connectivity can be described as covariance or correlation between voxels, averaged regions of interest, between regionally dispersed systems, and it may be a first order correlation within a subject over time or averaged across subjects. Functional connectivity is simply operationalization of correlations. However, functional connectivity is used to make inferences. The general inference is that regions which are

more correlated are more integrated. It is possible to think of correlated activation as brain states.

While functional connectivity has no assumption of causality, "effective connectivity" implies causation, it relies on "some model of influence one neuronal system exerts over another" (Friston et al., 1994, p. 68). It is important to note that the present exploration does not make such claims. As we will see below, the models suggested do examine a sequence of events, but this sequence of events is not considered causal in nature, we will only be exploring the degree of integration between spatially and temporally distinct regions of BOLD activation.

Secondly, functional connectivity does not imply anatomical connectivity. Anatomical connectivity often implies direct connection between regions. Two regions can be functionally connected which could mean that they have direct connections; conversely, this could also imply that these two regions are anatomically connected to a third region which synchronizes their activity, or yet another possibility is that each regional subsystem is time locked to external events which result in their coactivation. Of course it is likely that as we follow connections through neural networks ad infinitum we will most likely find disparate connections between regions, but these long distance connections are often too weak to consider connected in any practical sense, bit they are likely not meaningless (Sporns & Betzel, 2016).

I want to make clear that functional connectivity in the study in Part 2 addresses temporal ordering, but does not imply causality. We are only examining the neocortical surface but it is the subcortical structures along with the fiber tracts which act as

mediators and allow for casual interpretation. No causal activity is therefore applied in this study.

All this being said, functional connectivity has often coincided with both effective and anatomical connectivity. It is to these examples that I will now turn.

Resting state networks. As has been clearly established by now, when a subject is at rest (not engaging in any external tasks) the brain does not simply shut down, it is dynamic and active. Various regions show connectivity and if we use independent component analysis on activations across time for various regions, networks of functionally connected regions emerge. One particular network has stood out and been extensively researched. It was found that when a subject is at rest, a particular network of brain regions tends to be up-regulated while other networks show a decrease in activation. This network has been dubbed the default mode network (DMN). When describing network connectivity a number of measures can be used which essentially boil down to two basic measures: how interconnected elements internal to the network are, and how much the network activation is differentiated from the components of other networks (Bullmore & Sporns, 2009; Friston, Kahan, Razi, Stephan, & Sporns, 2014; Rubinov & Sporns, 2010; Sporns, 2011). Intrinsic network connectivity for the DMN has been related to mind-wandering (K. C. R. Fox, Spreng, Ellamil, Andrews-Hanna, & Christoff, 2015), meditation (Brewer, Worhunsky, & Gray, 2011; Tang, Hölzel, & Posner, 2015), creativity (Beaty, Benedek, Kaufman, & Silvia, 2015; Gotlieb, Jahner, Immordino-Yang, & Kaufman, 2016), autobiographical thinking (Spreng & Grady, 2010; Utevsky,

Smith, & Huettel, 2014), distractibility in ADHD (Fassbender, Zhang, Buzy, & Cortes, 2009), and working memory (Piccoli et al., 2015) among many others.

However, the DMN is not the only connectivity that is apparent during the resting state. One common approach to understanding this functional connectivity has been the use of Independent Component Analysis. This method is similar to principal component analysis, but because the distribution of signals in the brain is non Gaussian, ICA is the appropriate method (Beckmann & DeLuca, 2005). When conducting ICA the number of components extracted is determined by the researcher and some of these components appear to correlate with task based networks involving visual areas or sensorimotor networks (Beckmann & DeLuca, 2005). By increasing the number of components "sub network connectivity" can be differentiated. Extending the work of Biswal who showed correlations during active engagement in a task are maintained during resting state, Smith et al. (2009) conducted an image-based activation network analysis of thousands of activation maps from the BrainMap database. They then took these results and compared them to the ICA resting state results of 36 participants. By first partitioning the variance into 20 components they were able to show that the activation maps from functional studies grouped into the 20 components in a way that made theoretical sense. When diving further into the data with a 70 component model, they were able to show increasing parcellation of the functional data and this increased parcellation corresponded in an interpretable way to the functional data. However, those attributed to noise also were broken into the various components of noise such as movement direction, cardiovascular activity, and external noise form the machine. Task based activation

networks mirrored resting state networks and reflected a hierarchical arrangement of ICA analyses. They conclude that "the full repertoire of functional networks utilized by the brain in action is continuously and dynamically 'active' even when at 'rest'" (S. M. Smith et al., 2009, p. 13040). This resting activity has been termed "resting state networks" although it must be remembered that these are functional networks and not neural networks proper.

Functional networks are not neural assemblies. Even though it has been repeatedly discussed in the literature, too often functional connectivity is seen as actual neural connectivity in the physical sense. As mentioned above, functional connectivity does not imply this (Friston, 2011). However, the general idea is based n the idea of recurrent connections between neurons in the Hebbian sense (Park & Friston, 2013). It is interesting to note that even though these networks have been referred to as the "alphabet" or "repertoire" of brain states (Sporns, 2010), it is clear that they do not operate as assemblies in a phase sequence during functional interaction with the world (Park & Friston, 2013).

Furthermore, not all connections between brain regions are recurrent, so this classical measure using correlation will necessarily not capture strong connections that are not recurrent (Douglas, & Martin, 2007). But, even those recurrent connections are not time locked. The entire idea of recurrent networks is they can provide feedback to the system and adjust weights across time (Edelman, & Gally, 2001; Hebb, 1949). If all connections were recurrent and synchronous then there would be an unlimited increase in activity through feedforward and feedback excitability resulting in seizure (Traub, &

Wong, 1982). Clearly, synchronized activity cannot be only measure of connectivity. If fact, as we shall discuss below appearance of synchronized activity may result in both false positives and false negatives in regard to connectivity. As I have discussed above, neural activity, even during resting state is a sequence of activity across the cortex and patterns propagate across the cortex in a similar fashion to what Hebb described as a phase sequence, they do not shift on and off.

  Physiological noise in resting-state networks. One criticism of resting state networks that has been leveled is that these low frequency fluctuations actually reflect cardio vascular information and not neural dynamics. It is clear that some of the temporal dynamics of this signal are clearly a result of this (Beckmann & DeLuca, 2005; Di Martino et al., 2008). However, it has been clear this can only account for some of the correlated signal variance and physiological noise can be separated as an independent component. The concern is that respiratory and cardiovascular cycles are aliased on the fMRI signal when the TR is longer (i.e., 2-3 seconds) giving the illusion that neural activity in different regions is synchronized. Utilizing Independent Component Analysis Beckman (2005) conducted fMRI scans of the motor cortex at both a low of TR 120 ms and a TR of 3 seconds. Sampling at the higher rate allows for the decomposition of the signal into a larger range of frequencies and reduces aliasing. Being that resting state fluctuations are identified as lower than .1 Hz and cardiovascular fluctuations are usually around .3-1 Hz at larger TR aliasing is possible. Using the smaller TR, Beckman (2005) was able to show that low frequency fluctuations observed oil rs-fMRI are clearly distinct from respiration and cardiovascular activity.

In addition to this important finding, Beckman (2005) also was able to identify 8 prominent networks in the low frequency signal fluctuations which appeared to have interpretable functional significance. Importantly, this method was able to separate signals with spatial overlap.

Some studies have interpreted these networks to be the result of mind wandering (Mason et al., 2007), however the dynamics of resting state networks appears to endure during sleep and show increased fluctuations at these low frequencies of interest (<.05) (Fukunaga et al., 2006) and in monkeys when they are under anesthesia (Vincent, Patel, Fox, Snyder, & Baker, 2007b). This further highlights the idea that these resting state network dynamics endure and represent relatively stable neural configurations within and across individuals.

Does mind wandering drive resting state findings? Now we return to concepts mentioned in the first section of the text. Remember that at minimum neural activity is cocausal and bidirectional. The mind and biology are simultaneously creating each other and if this is the case, then the discussion of causal direction is mute because there is not one. However, we are taking a more extreme view in this paper, that of emergent psychoneural monism. In this case the actions of the mind represent the system configuration in the brain. In other words mind wandering is a part of the system of mind at that moment. Secondly, the mind wandering phenomena is but a small fraction of the neural activity at that time. It reflects where system dynamics are made conscious. While all neural events during the resting state reflect mind wandering, if we ask participants what they mind wander about after the resting state, it only reveals the fraction of

dynamic knowledge at that moment that reflects not only conscious but also remembered experiences. Mind wandering reflect only a set of the knowledge system unfolding during resting state.

As a final point, we may experience different degrees of control over mind wandering while in the scanner, but that does not tell us anything more than our mind wandering experience included feelings of perceived control.

Lag Structure

Standard resting-state network analysis examines the time locked correlations (zero-lagged) in activation between neural regions, however, one problem emerges from this research that is seldom addressed. Knowledge is not a brain state, but a process which spans time (Marinkovic, Dhond, Dale, Glessner, & Carr, 2003); thus, some of these resting-state studies may be missing measures of connectivity if they only look at coactivation patterns occurring at zero-lag. Let's return to figure 3: notice that in a standard zero-lagged analysis region C was not interpreted as functionally connected to either region A or B. However, if we allow for a time lagged analysis and shift the time series for region C back by 3 seconds, regions A, B, ad C are now perfectly correlated in activity. A zero-lagged analysis does not allow us to see this relationship. It should be noted that our toy-model is extremely oversimplified. In actual neural data the signals contain considerably more noise and will never reach this level of correlation. There are also additional restrictions on time shifts like that above.

While it may be that at one level of analysis zero-lagged networks represent a true emergent property representing one type on neural interaction, it may be more likely that

cognitive tasks which have a clear temporal sequence may be better illustrated if we could examine network connectivity that unfolds across time especially on larger timescales such as those found in reading. Emerging methodologies have begun to examine this issue by searching for maximal coactivations between brain regions across time (Chang & Glover, 2010; Mitra, Snyder, & Blazey, 2015a; Mitra, Snyder, & Hacker, 2014; Schneider, Havenith, & Nikolić, 2006a). These studies have found highly reliable patterns in these lagged analysis, but the zero-lagged networks appear to not be a component of the these lagged patterns. Zero-lagged networks seem to be a predictable emergent structure from lagged network interactions, but are not found to be a component of lagged network dynamics (Mitra, Snyder, & Blazey, 2015a). In other words, we cannot simply seek zero-lagged structures and look at their sequential interaction; zero-lagged networks emerge from the interaction of lagged structures.

These lag structures appear to correlate with differences in behavioral variables. In 2015 Mitra and colleagues used the lagged network analysis methodology to examine group differences between individuals with autism and those with typically development (Mitra, Snyder, & Constantino, 2015b). This study followed the procedures outlined in Mitra (2014), but used a significantly smaller sample size of including 2 groups of 23 individuals. Using this smaller groups size, group differences were still robust.

While Mitra et al's (2014; 2015a) analyses included whole brain coverage, these methods are not limited to whole brain analysis as they were originally developed for understanding the order of activation between neurons within incomplete networks (Nikolić & Nikolić, 2007; Schneider, Havenith, & Nikolić, 2006b). And in actuality

observation of any complex dynamic system will result in observing only a subset of the network. The brain itself is a subset of the body and the body a subset of the environmental interactions (Beer, 2000). Additionally, as mentioned above, the brain is fractal in its organization. Thus, these methods could theoretically be imposed on regions or selections of the brain.

Lag structure analysis. Recently Mitra, Snyder, Hacker, and Raichle (2014) addressed a major problem with resting state connectivity studies. An assumption behind resting state connectivity studies has been that neural region activity in resting state networks is exactly synchronous. A number of human and animal studies have demonstrated that this is not necessarily the case (Majeed & Magnuson, 2009). It is probable that activation in one region lags temporally behind but is synchronous to another region when we correct for the temporal lag. In other words, while a standard resting state analysis examines the correlation across all approximately 210 images during a 7-minute period, there may actually be a temporal shift between regions that this type of analysis would not capture.

Mitra et al. (2014) attempted to deal with this theoretical problem by obtaining resting state scans of 692 participants. The participants were then randomly divided to seven cohorts to test whether consistently lagged networks could be identified across groups. To summarize their analysis approach, the images were divided into 6 mm cubic regions of cortex. A time series of activation was extracted for each region. Using a cross covariance function, all possible time series were then compared and temporally shifted to maximize covariance. To obtain temporal accuracy better than the 2 second TR, the

covariance function was parabolically interpolated (see figure 4). The lags reveled by this method typically did not exceed .5 seconds, but are clearly slower than neural conduction. Covariance was used as opposed to correlation to retain information and resist the possibility of multiple extrema in cross covariance which is also rare given that neural data is aperiodic. Form this covariance analysis, an antisymmetric matrix is constructed representing the proposed delay between any two neural regions. This "Time Delay" matrix is then tested for significant transitivity. This matrix is then converted to a covariance matrix representing the standardized variance of lags within the time delay matrix. After this, PCA was applied to the matrix along with an amplitude weighted matrix to determine the percentage of bold signal accounted for by each principle component (this is completed on each subject). When projected onto the cortex, this then gives an image of regional covariance across time.

The zero-lag networks found in standard resting state analysis do not appear to exist as units at any points in the lag structure maps. However, lag structure maps can be used to predict standard resting state networks. This suggests that zero-lag resting-state networks are an emergent property of lagged networks and lagged networks are not emergent from zero-lagged resting-state networks. These resulting lagged structure were reliably reconstructed in all cohorts.

In a later paper, Mitra et al. (2015a) expanded upon this approach using PCA to extract a number of specially overlapping "lag threads". In this study 1,376 individuals were used and when randomly separated into cohorts, the results were reproducible indicating that lag networks are a fundamental property of neural organization. Overall a

number of lag threads were discovered which uniquely produced standard zero-lag resting state networks, but were not uniquely predictable from zero-lag resting state networks. They hypothesized that one of these lag structures may represent top down influences while another may represent bottom up processes in cognition. They suggest that with refined SNR techniques and/or a smaller number of ROIs, lag structure identification may be reproducible on smaller scales.

Finally, a smaller group of participants was used to examine lag thread differences in autistic vs typically developing individuals (Mitra, Snyder, & Constantino, 2015b). In this study, lag structure was used to examine between group differences as well as predict specific behavioral attributes. Each group consisted of 23 individuals. Significant differences were described in the lag structure between groups. For example, typically developing adults showed later placement of the frontal polar region in the lag structure than individuals with autism. Similarly the putamen was earlier in the lag structure for individuals with autism than it was for typically developing adults As far as behavioral differences, the relative lateness of the frontopolar region correlated (r=-0.82) with scores on an attention task; and the relative lateness of the putamen in individual's lag structures correlated (r=-0.65) with repetitive behavior. This demonstrates that the methods are applicable to smaller groups to determine group differences and correlate individual behavioral scores with individual lag structure elements.

Summary. In Part 1 we developed a theory of knowledge representation in dynamic system activity in the brain. We established the approach of psychoneural monism whereby the we can speak about neural event as psychological events without

relying in dualisms or ontologically reductive monisms. Knowledge was defined to include the inclusive category, of skills, memories, perceptions, conscious awareness, tacit knowledge, and knowledge not in action. While we recognized that knowledge involves a qualitative aspect we conceded that even the qualitative is grounded in the neurological and we can epistemologically reduce the knowledge to the neurological as long as we recognize this is only part of the knowledge experience; there must be a neurological foundation in the brain even if this foundation consists of partial networks to be completed by environment interactions.

Having established this metatheoretical approach we then examined how the brain is structured and how this structure supports knowledge retention. We examined a foundational theory of Donald Hebb in how the brain can learn and store representations. His theory was examined in a way to demonstrate that knowledge was not stored in connections but in the ongoing activity of populations of cells in a network. He proposed the idea of the cell assembly and the phase sequence which offered explanations to temporal dimension of knowledge storage in neural networks.

Having established this learning theory, we then examined the modular structure of the brain. The brain is organized in a system of hierarchically arranged fractal modules allowing for examination at a variety of levels. It tends to organize itself into small world networks which represent modules with a variety of functions that all depend on a similar analytic substrate. Because of environmental, physical, and genetic interactions, these modules tend to align on the cortical folding of the brain which is remarkably consistent between individuals, but also very diverse in the association areas.

This system of neurons and modules was shown to be very active throughout life. It was not only active electrochemically, but undergoes a continual process of neurogenesis, as well as axonal and dendritic formation. At an even more microscopic level we examined how thousands of spines are constantly emerging and either retaining their connections through activity or being reabsorbed. Spine production and retention is activity dependent. All of these changes can account for neural development throughout the lifespan allowing learning on scales from seconds to years.

These structural changes are important for the reverberating activity in the brain that is ongoing. We examined how some cells have a patterned song they sing through interspike interval timing variation in the form of motifs. These cells are active even when isolated from other neural tissue and may very well be a motor along with recurrent activity that maintain networks over time in stable active attractor states capable of learning and persisting.

This ongoing activity spreads across the cortex in the form of EPSPs which are sub-threshold back propagation along the dendritic arborization. This activity results in a negative potential recorded at the scalp with EEG which is well aligned with fMRI recordings offering us a noninvasive way to approximate these network dynamics. This activity appears to be preparatory for environmental engagement and when networks are in UP states response timings for those associated activities is reduced.

When an individual is at rest and relatively isolated from daily activities, these aperiodic oscillations can be recorded in the fMRI machine. These resting state fMRI recordings give us a window into observing the system dynamics that may store

knowledge and the ongoing dynamics is what stores knowledge in a persistent yet flexible form.

Two approaches to rs-fMRI were examined. Time locked correlations is the traditional measure of this activity, but it is problematic. It assumes that neural activity within a network is recurrent and this recurrent activity is synchronous. As was demonstrated throughout this text, networks are often strongly linked but show a propagation of activity across the cortex and recurrent activity itself also tends to be sequential not synchronous. It is for this reason that perhaps a lagged network analysis is a more accurate way of depicting knowledge storage in network dynamics. A series of studies conducted by Mitra, Raichle and colleagues revealed the reliability of this analysis technique and that it indeed can be used to analysis differences between populations.

In Part 2 we will attempt to examine this lagged network structure at the group level with a small group of adolescents. We will apply a novel analytical method to examine the structure respecting cortical folding and extract hidden signals in the lag representation. This approach is still exploratory and therefore we will use some reverse inference to determine what these high level structures might represent as far as knowledge in the brain.

PART 2: Group Level Representation of Lagged Activity

Part 2 addresses the application of the methodology and theory described and contextualized in Part 1. The overarching goal of this section is to describe the generation of the time delay (TD) matrix which represents lagged relationships between neocortical regions. Using this matrix, we will then order it along traditional 0-lag networks to see if specific traditional networks act as independent units in the lag structure; it may be the case that traditional 0-lagged networks show a lagged relationship to one another.

Subsequent to generation of this matrix, two procedures will be used to extract information from this matrix allowing us to visualize the lagged relationships between regions. These data decomposition techniques will include the use of matrix projection for high level average latency representations and independent component analysis (ICA) to explore the unique independent networks in the data. Along the way a number of decisions were made regarding the processing of the data and we shall explore the potential impacts of these decisions in turn.

In the process of constructing these group level representations, we will also generate the means to build regressors to use against behavioral variables which will be described in detail in Part 3. It is hoped that the methodologies presented here could be extended to any set of behavioral variables which represent broad knowledge structures or situated behaviors framed by them.

Novel Approaches to Lag Analysis

A number of approaches to lag network analysis are presented. The processes outlined in Mitra et al.(2014; 2015) was conducted on very large groups 692 and 1376

individuals respectively. Lag threads were identified using PCA in Mitra et al.(2015), however there was not a transparent way to use these lag threads as regressors with individual level variables. In an effort to develop a methodology which will allow the use of regression techniques, a significant amount of noise had to first be removed from the data. Our theory developed above also suggests a limiting of the analysis to the neocortex, thus allowing the use of surface analysis techniques that may correlate with preparatory activity in dendritic arborizations.

Cortical folding. Brain sizes and cortical fold locations vary significantly between subjects (Botteron et al., 2008) even though the functional alignment with folding patterns may remain relatively consistent. This is a significant source of noise which can theoretically be removed if we align subjects using cortical folding topography instead of relying primarily on affine transformations of voxel representations, thus analysis is limited to surface representations. Being that Part 1 indicated that rs-fMRI has shown strong correlations with slow cortical potentials, limiting analysis to neocortical tissue is theoretically grounded, although it differs markedly from the approach taken by Mitra et al.(2014, 2015a, 2015b); the reasoning will be explained below.

Limitation to neocortex. We have built a theory in Part 1 which focusses primarily on the neocortex and pyramidal cells as sources of learning and knowledge representation. While we know for a fact that learning and knowledge storage involves deeper cortical structures (Immordino-Yang, & Yang, 2017; Pessoa, 2009, 2013), this paper does not yet deal with how knowledge is represented in these structures and how this might reflect on changes in the fMRI signal. For example the subcortical nuclei are

not arranged in columns with dendritic arborizations across the surface, so it is unknown if signal would correlate similarly with the slow cortical potentials described above. Additionally, the procedures described below to remove additional noise and improve alignment are based on 2D vertices on surface meshes, and subcortical structures are represented as 3D voxels: comparisons of 2D vertex areas and 3D voxel volumes will require further modeling to determine the appropriate comparison ratio. Interpretation of fMRI findings in these structures would be important but difficult to interpret using the above approaches and analysis of these structures needs to be the result of future exploration.

Additionally, we have excluded analysis of the cerebellum. We could apply similar methodologies and the cortical folding of the cerebellum can now easily be modeled. However, the fact that the cerebellar cortex consists of a single layer instead of multiple layers of neurons at the surface as well as the fact that cerebellar neurons have been shown to have different rhythmic output than their input make this structure difficult to model using the lagged relation methods (Johansson, Jirenhed, Rasmussen, Zucca, & Hesslow, 2014). Furthermore, Mitra (2014, 2015) found that the cerebellar contribution to lag structure was minimal; however, this is likely a weakness of the methods and not a feature of the cerebellum. Here we shall unfortunately continue the trend of ignoring this important structure. Future studies will need to be conducted to integrate cerebellar lag structure with neocortical lags.

As such, the current analysis is limited to neocortex. However, examining part of a network does not invalidate the results. Understanding network dynamics here is

assumed to have contributions from both cerebellar and subcortical structures, thus the analysis is assumed to already have the extended network data represented in the neocortical lag structure. To analyze an open network such as the brain we are always assuming there are external features which influence the network even when we limit network analysis. We are examining a subset of the system which will reflect the open nature of the system from neural regions not included as well as body and environment (Sporns, 2010).

What follows is an attempt to discover and interpret group level lagged structure of the neocortical tissues from 51 self-identified bilingual adolescents. While the results may extend beyond this group, no assumptions of generalizability outside the specific identifying characteristics of this populations are made.

Methods

Participants. The data used in the present analysis were collected as part of a study led by Dr. Mary Helen Immordino-Yang and Dr. Xiao-Fei Yang at the University of Southern California's Brain and Creativity Institute. It is funded by a National Science Foundation CAREER Award (#11519520) to Mary Helen Immordino-Yang. The original study purpose was to examine social-emotional development in adolescents. A subset of individuals from this study were selected for the current study based on quality and completeness of data collected.

The group level analysis involved 51 participants who were self-reported healthy right-handed individuals with normal to corrected vision and normal hearing. All participants were self-identified fluent bilinguals of Chinese, Philippine or Latino decent.

All were born in the United States. Their ages ranged from 15 to 20 (m=17.31, SD 1.11) years. All participants were neurologically normal with no reported psychiatric or neurological disorders. None reported being under the influence of psychotropic drugs. Ethnic makeup consisted of (25) Latinos, (2) Filipino, (3) Korean, and (24) Chinese. There were (21) boys and (33) girls recruited from a series of schools in the Los Angeles area. These are represented in table 1.

Table 1

Descriptive Statistics Lag Structure Development Group

Measure	*n*	*Min*	*Max*	*M*	*SD*	*Skew*	*Kurtosis*
				Score			
Gender							
Male	21						
Female	33						
Ethnicity/Language							
Chinese Bilingual	24						
Latino Bilingual	25						
Filipino Bilingual	2						
Korean Bilingual	3						
Age	54	15.00	20.00	17.31	1.11	.19	-.66
Cognitive Measures							
WASI_Full	52	72.00	135.00	105.63	11.93	-0.21	0.75
WASI_Vocab	53	34.00	67.00	53.42	7.55	-0.59	0.44
WASI_Mat	52	10.00	76.00	51.88	9.89	-1.28	5.88

Bilingual status. All participants were self-reported bilinguals; however, the influence of bilingual or language status is not analyzed in the current study. Given the large literature on multilingual brain development, it is acknowledged that bilingual experiences and differing language experiences affect brain development as well as a number of cognitive factors this will undoubtedly have unknown impact on current results. General resting state data has found some differences in traditional resting state measures of bilinguals (Grady, Luk, Craik, & Bialystok, 2015; Berken, Chai, Chen, Gracco, & Klein, 2016); but, in these studies the overall representations of traditional resist state networks was still preserved with only minor variation. In reference to lagged analysis, no study to date has been conducted using this methodology which also accounted for bilingual status. With specific attention to mind wandering, however, there has been no difference based on bilingual status observed even when executive function improves (Shulley & Shake, 2016). In regards to traditional resting state measures related to reading and language status, Zhang et al. (2014) found no relation of rs-fMRI networks with the identity of first language spoken or with bilingual status. The self-reported bilingual status is listed here only for the sake of completeness, but there is no reason to assume that it affects or does not affect the outcome any more than we could equally control for socio-economic status, gender, or any other categorical variable known to correlate with neurological differences. This is a limitation of the current study in that it cannot be extended beyond this population except to other self-reported bilinguals. No tests of bilingual reading or spoken language skill was used to further determine bilingual fluency.

Procedure. As mentioned above, the tasks used for the present analysis were part of larger longitudinal study of adolescent emotional development; all participants underwent the same procedure for the first part of the day. A smaller group of 38 participants was given a series of reading tasks which will be described in Part 3; however, these tasks were all given after the fMRI session and so will not affect the group level analysis. The general schedule for each participant involved an at-home survey, before a full day of experimental participation. A maximum of two participants were run on the same day.

Early in the day measures not used in the current study were taken: 2 hours of emotional-induction interviews, 1 hour personal interviews, 1 hour of cognitive tasks (some of which were used in the behavioral study described in Part 3) and 1 hour of psychophysiological tasks. There is ample evidence that tasks preceding the acquisition of resting state affect resting state analysis (Stevens, Buckner, & Schacter, 2009; Tambini, Ketz, & Davachi, 2010; Gregory et al., 2014); however, sharing the same tasks throughout the day should remove, not add, noise to the current analysis as they shared very similar experiences and ate a similar diet the day of the testing. The order of the other tasks was not in a consistent sequence, but this was not addressed in the current study. It is acknowledged, however that systematic noise related to our behavioral variable measurements may be a result of the extensive morning interviews, but this was unavoidable in the current data collection.

The relevant reading task to be discussed in Part 3 was administered around 2 hours after the fMRI scanning which took place around mid-day. The day of the

procedure, each participant arrived at 9 am and the procedure ended around 6 pm. Participants were given lunch and paid for their participation.

Neuroimaging instructions. Neuroimaging was acquired around midday following the procedures discussed below. During the resting state scan, the participants were told to "feel free to let their mind wander" but to keep their eyes open. The resting state scan took 7 minutes. All participants use here reported remaining awake during the resting scan although no eye tracking or similar procedure was applied to verify their report. Being that open vs. closed eyes influences both 0-lag and lagged resting state fMRI results Mitra et al. (2014), this is a potential shortcoming of the current approach.

Neurological Measures

The acquisition and processing of the rs-fMRI involved a number of choice points described below. These processes were used to reduce the noise in the resulting group level time delay (TD) and 0-Lag matrices. As mentioned above all processes were limited to neocortical tissue.

Image acquisition. Brain imaging data were collected at the Dana and David Dornsife Neuroimaging Center at USC. Whole brain images were acquired using a Siemens 3 Tesla MAGNETON TIM Trio scanner with a 12-channel matrix head coil.

Functional resting state scans were acquired using a T2weighted Echo Planar (EPI) sequence (TR = 2 s, TE = 30 ms, flip angle = 90∘, acquisition matrix: 64 × 64, FOV = 192 mm) with a voxel resolution of 3 × 3 × 4.5 mm. Forty-one continuous slices were used to acquire data from the whole brain and brain stem per image. Two hundred ten images were acquired and the first four were discarded to allow for signal normalization.

Anatomical images used for alignment to cortical features were acquired using a magnetization prepared rapid acquisition gradient (MPRAGE) sequence (TI = 900 ms, TR = 1950 ms, TE = 2.26 ms, flip angle = 7◦) with an isotropic voxel resolution of 1 mm; 160 slices were acquired to cover the whole brain, dimensions: 256 × 256 × 160.

Preprocessing images for surface based analysis. Prior to transformation from 3D voxel based to 2D surface based, the functional images are preprocessed using standard preprocessing procedures.

Anatomical file preprocessing: MNI volume to surface. The structural and functional data were processed using the FreeSurfer (http:// surfer.nmr.mgh.harvard.edu) version 4.5.0 software package. Free-Surfer constitutes a suite of automated algorithms for reconstructing accurate surface mesh representations of the cortex from individual subjects' anatomical images and the overlay of fMRI on the surfaces for group analysis.

FreeSurfer identifies the edge of the white matter and the pial surface (or the boundary edge of the grey matter). Using the 3 dimensional image the pial surface is transformed into a series of vertices of roughly equal distance around the surface of the entire cortex. This surface map follows the sulci (valleys) and gyri (mountains) of the folded cortex. Connections between adjacent sets of vertexes map the curvatures across these gyri and sulci. This information is then used to inflate the brain so that all cortical features are visible on the surface. This appears as a topology map of the brain with different colors indicating the sulci and gyri. This inflated version is then further transformed into a sphere. The result is a topology map of the brain that can be compared to an average brain map. Each subject's spherical topology of the brain is then warped so

that the sulci and gyri are optimally mapped onto the average brain (supplied with the FreeSurfer software). The major topological landmarks are consistent between brains, but their exact location, thickness, and size vary between individuals. By aligning the brains of all participants to this average brain, comparisons in activation and anatomy are more likely to correlate with similar topological regions between individuals. The transformations from each participant's voxel based image to the surface based image are saved, allowing for comparison between participants.

For the current study, the average brain map is divided into 20,484 vertices of which only 18,715 are relevant because the remaining are excluded portions used only to close the gap in the mesh where non neocortical tissue is present. For each hemisphere the cortical mask is ~102,871 mm^2, this is approximately 10 mm^2 for each vertex, when the mesh is aligned half way though the grey matter perpendicular to the surface. Although this may seem large, it is comparable to the voxel size which was 3x3x4.5 which if perfectly aligned with cortical folding a single face would be between 9 and 13.5 mm^2. Thus, the current method retains approximately the same scale but likely has an increase in accuracy as it obtains averages across the remapped surface. While it would be preferable to increase the resolution, computational limitations restricted current analysis to 18,715 vertices.

Resting state functional file preprocessing: Volume MNI space. The functional files, in this case, 210 resting state images taken 2 seconds apart were also preprocessed to surface based representations to maximize registration between subjects of similar functional regions.

Template and skull stripping. The functional image taken at the middle time point is used as a template for registration to the anatomical image. The portion of the image representing the skull, sinuses and the non-brain tissue is stripped from the functional images resulting in an image consisting only of the contiguous spatial region containing the brain.

Intensity normalization. From this brain mask, 3 outer voxels are eroded and a mean activation level is calculated for all voxels inside this boundary at every time point then multiplied by 100. The intensity of each functional image across the time course is scaled to have the same mean activation level retrieved in the step above. This accounts for scanner drift (Smith et al., 1999). Subsequently the whole brain average activation level is stored as a waveform with 210 values each representing the average activation level at that time point. This will be used as a regressor during analysis.

Registration. The images are then registered to the anatomical image across six degrees of freedom. Basically, the middle time point three dimensional image volume is shifted along and rotated around the x, y and z axis to best align with the anatomical image (affine transformations). These changes are translated to the other functional images in the sequence. This allows for the transfer of intensity values directly to the vertices which were mapped in the processing of the anatomical image.

Motion correction. Each of the remaining functional images for the participant are then rotated and shifted to match the middle image. The changes made to the other time points are recorded as 6 waveforms which can be used as regressors to remove any intensity changes which correlate with head movement.

Slice timing correction. The scanner samples the 3D volume by taking 41 images of the head from crown to neck. This process takes 2 seconds during which the scanner takes images from crown to base of skull with a space between each slice, then immediately repeats the process interleaving scans between each of the previous measured layers. Values for adjacent voxels between slices are then interpolated. This process is standard and necessary, because of the time it takes to go through the entire brain twice during one interleaved scan. Each image collected thus represents an average across the two second time period during which the image is acquired.

Anatomical covariates. A mask is generated for the white matter and for the ventricles of the brain from the anatomical image (these are non-targeted tissues). The barriers of each of these is eroded by three voxels and then the average for each time point for the white matter and separately for the ventricles is recorded. This results in two waveforms. Activation in the white matter and cerebrospinal fluid (CSF) is assumed to not represent cortical activity and any patterns found in these regions is of non interest where they may influence the intensity of the cortical strip. Therefore these are later regressed from signal in cortical tissue. We do not average the voxels in this region, but use principle component analysis to generate 5 principle components of these regions of non interest to remove the maximum variance in these tissues from the cortical signal (Van Dijk et al., 2010). Breathing and heart rate variance can be approximated and removed utilizing the white matter mask as a covariate.

Whole-brain average as a regressor. While an average intensity is often taken for the entire brain as a regressor, this process is controversial and was not performed here.

Using the whole brain intensity as a regressor artificially inflated the correlations as well as often results in the creation of an artificial anticorrelation between identified networks that are a result of the preprocessing and not intrinsic to the data (Fox, Zhang, Snyder, & Raichle, 2009). Mitra et al. (2015) examined this process on lagged structure and found it did not influence the lagged structure significantly, however, our methods here vary and as such we will avoid the procedure due to potential problems. Breathing and heart rate influences are further assumed to be removed by the band pass filtering at .01 and the regression of the CSF and white matter masks.

Resampling onto surface map. All functional processes up to this point have been conducted with voxels in a volume, these were all standard practices. The analysis conducted here is completed on a 2D surface model of the cortex. Utilizing the pial and white matter boundaries identified above, the value of the BOLD signal at the perpendicular midpoint between these maps is recorded as the BOLD value for the associated vertex. The initial mesh is of higher resolution than the one used for data analysis allowing for more accurate alignment with cortical folds. The original mesh used for resampling is 132,246 vertices per cortical mask per hemisphere.

Smoothing. To increase the signal to noise ratio, the value of vertices are smoothed by a 5 mm diameter Gaussian kernel. What this means is that if we take a single vertex we replace the value of the vertex by averaging it with the surrounding vertex. As we move further from a vertex the surrounding vertices have less influence on this average. Notice that one problem we are avoiding by smoothing in 2D space is that with standard 3D smoothing the diameter of that sphere will cross into non-cortical tissue

(Glasser et al., 2013). Additionally, in areas where the cortex folds upon itself surface areas of two adjacent gyri may come very close. The smoothing sphere in 3D space may actually be averaging areas of cortex that are very far from each other along the cortical surface. The strength of free surfer is that it first computes the surface model of the brain and only then smooths across the surface, but the reader is reminded that a kernel of 5 mm is not equivalent in 2D and 3D tissue representations. Because we are using a high resolution surface map, we do not smooth any further as this would defeat the purpose. The main purpose of smoothing at this high resolution is to average out any noisy vertices which might not match the surrounding tissue.

Resulting regressors. At the end of the neurological preparation for functional files, we have the object of measurement which is the BOLD activation at the location of each vertex. Each vertex has a waveform showing activation fluctuations over time. Additionally, we have a number of additional regressors in the form of waveforms: 5 principle components of white matter activation, 5 principle components of cerebrospinal fluid activation, 6 degrees of freedom for motion correction, and 1 representing the intensity normalization.

Using a linear model to predict the recorded waveform for each vertex along these 17 regressors we retain the residual for each vertex as our signal of interest.

Bandpass filtering. As mentioned in Part 1, the signal of interest only occurs within a specific bandwidth. Therefore, band pass filtering is conducted on each vertex to remove all signals higher than 0.1 Hz. This increases the likelihood that breathing and

heart rate are excluded in the data as well as removing any fluctuations at the higher rate that are not associated with resting state scans.

The resulting mesh of left and right hemisphere cortical surface is 264,492 vertices with accompanying location matched across subjects. This mesh is then decimated to 18,715 waveforms which is the base data for the current analyses.

0-lag map generation. A zero lagged analysis is a simple correlation measure. Each vertex is compared to every other vertex in a correlation matrix using a two tailed Pearson's correlation due to the importance of both positive and negative correlations. While standard methods involve the masking out of some correlations if they are below a certain threshold (Rubinov, & Sporns, 2010), this was not done here because we are not making an assumption that they represent connectivity. The matrix is only being used as a comparison to the lagged structure. Indeed there are some arguments that masking should not be done because even very small correlations may represent true relationships and there is no clear reason to remove these relationships unless we are trying to use graph analytic methods (Rubinov, & Sporns, 2010).

After generation of a 0-lag correlation matrix for each individual, these matrices are stacked resulting in a 18,715x18715x51 matrix. The next step was to identify and remove 0-lag value outliers across subjects. A basic approach using Tukey fences was applied. For each cell in the 18,715x18715 matrix values greater than 1.5 times the inter quartile range across subjects for that cell were removed before averaging (Tukey, 1977, p. 43-44).

Averaging along the third dimension was then conducted such that each cell represented the average correlation value for that vertex comparison across all participants. This gives us the group level correlation map.

Lagged map generation. In general, lag map construction followed the process described by Mitra et al. (2014). This method is also diagramed in Appendix A. However, the process of outlier identification, setting limits for the cross covariance function, and problems with values landing on limits was not discussed in detail. Thus, some effort is made here to describe the process for dealing with these parameters.

Limits and missing values. Cross covariance is used as opposed to cross correlation because cross covariance allows for the later recovery of signal amplitudes, but it also is less likely to exhibit multiple equal peaks. When applying a cross covariance function to determine lag, two time series are essentially slid past one another until their covariance is maximized. This process was shown graphically in figure 3. This process results in a function similar to the one seen in figure 6. In the process of obtaining the lag value, the cross covariance function is applied, then the local maximum or minimum is identified. A parabolic interpolation curve is then applied to this point along with point immediately preceding and following this point. After interpolation a new maximum or minimum is then identified and recorded. The interpolated time point of this maximum or minimum is representative of the theoretical lag between the two time series.

When identifying limits for the cross covariance function and interpolating values two main problems presented themselves. While Raichael and Mitra discuss the limit of 5 seconds there is no clear theoretical reason for doing so. Setting this limit created two

127

problems. First was what to do with instances where the peak was determined to be at the boundary and second was how wide to make the boundary.

In the process of determining the lag relationship between 2 vertices the cross covariance would most often result in clear maximums or minimums. However, in a subset of cases the maximum or minimum covariance was at the edge of the lag window as shown in figure 7. In this case interpolation was not a reasonable procedure and dealing with limits had to be done in other ways. If we interpret the more extreme lags as noise then the choice was simply to remove the point.

However, it was also possible that values at these extremes were meaningful as they neared a true lag relationship. While it initially seems strange to think about measuring neural signals multiple seconds apart, there is no theoretical reason this could not be the case. As was made clear in the Part 1 a slow cortical potential may in fact occur even minutes before the signal continues, however, we limited our analysis to those occurring with lags on the order of a few seconds because this allows for the use of many more data points in the analysis. To explore this idea, the lag times were simply replaced with the maximum or minimum lag value (e.g. -5 or 5 seconds). This obviously led to a stacking of values at the extremes resulting in a histogram with three peaks: minimums, maximums, and at zero. This was a useful tool to examine the influence the lag window size played on the data structure. Through repeated modeling, it was found that expanding the window from 5 to 10 seconds had a greater effect on reducing the size of these peaked tails but minimal effect on the number of values at the center; this also rapidly increased processing time. This suggested that if limits were set to 5 seconds a

higher covariance could be calculated beyond the 5 second window, but the highest covariance was still near 0. When shortening the window to 2 seconds there was a large increase in both tails and the center.

Then an examination of the accompanying amplitude matrix which contained the covariance values associated with each lag metric was conducted. Computation of a TD matrix with a 10 second sliding window showed that the covariance amplitude trailed off dramatically the further from the center the metric was taken.

Neither of these approaches offered a definitive answer as to the best approach. Determinations of lag window were then based on theoretical and practical reasons. Computing the covariance at larger sliding windows was computationally more intensive and yielded little gains. A window of 2 seconds would have agreed with the finding that Mitra and Raichle have suggested that the majority of lags lie within this small window, however, it may also be removing important information. Being that this is exploratory it was desirable to err on the side of including too much rather than too little information. The smaller the window, the more information was removed. Therefore, the sliding window was limited to 5 seconds paralleling Mitra et al. (2014). Extreme values were replaced with the maximum or minimum lag assuming this may approximate a true lag.

Additional analysis needs to be conducted to determine what the appropriate window size would be but this is a question for further research. Upon reflection, it may be useful to determine the primary, secondary , and tertiary covariance peaks, and to map these for comparison. I will return to the question of what to do with the extremes when

we discuss independent component analysis (ICA) because the requirements of ICA

created additional problems that had to be resolved.
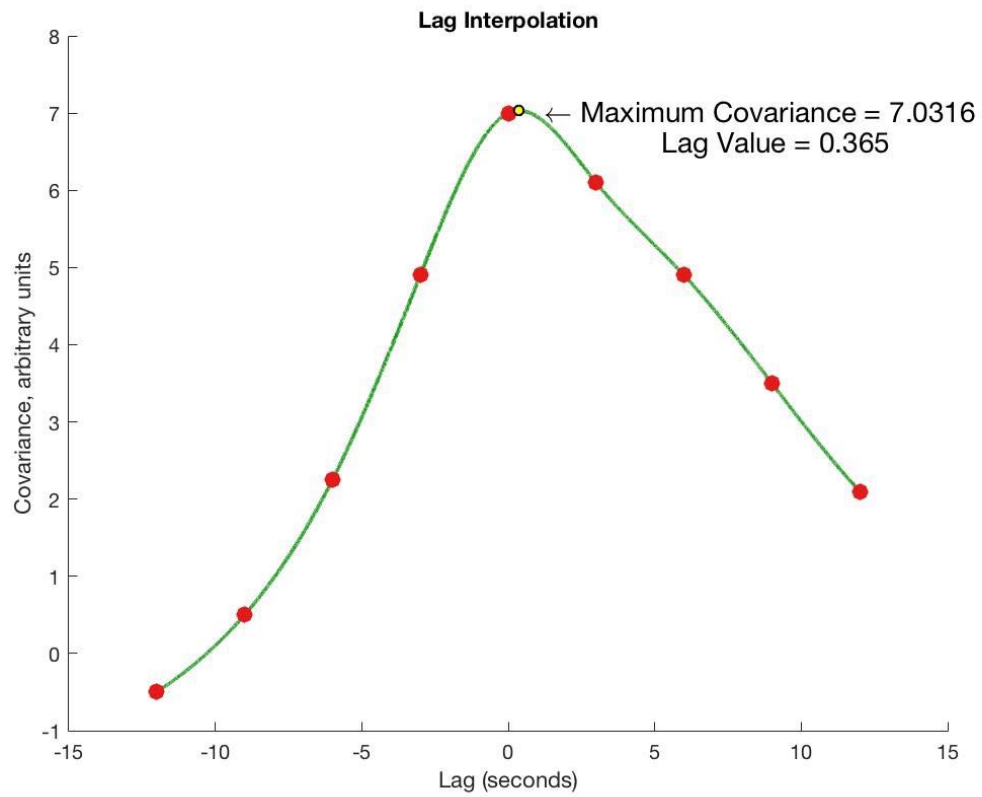
Figure 6. The covariance function generates a unique peak which can be interpolated using a parabolic function between measured time points for increased temporal resolution.
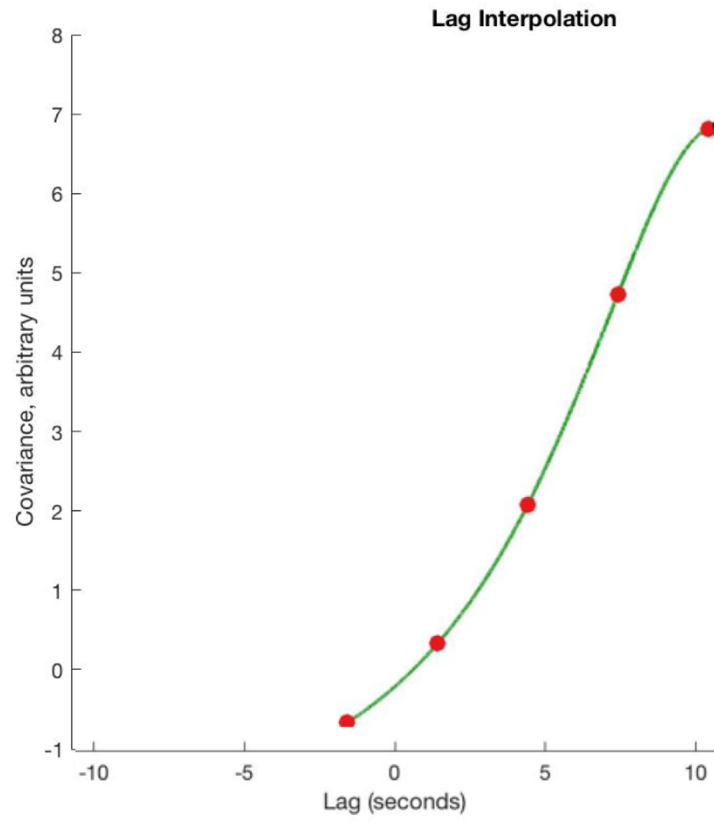
Figure 7. The covariance function may at times rise to the limit of the lagged window.

Group TD matrix. In the analysis which follows the construction of a group level TD matrix was required. In both the ICA and PCA methods, one possible approach was to stack the subjects' TD matrixes vertically along the second dimension and then run PCA or ICA on the resulting large matrix allowing for preservation of the subject level representations in the results (Beckmann, Mackay, Filippini, & Smith, 2009). However, this was not only computationally limiting, attempting to run ICA or PCA on a matrix which would be 954,465 rows 18,715 columns it may also identify differences between subjects and not assist in the construction of a shared group level representation. Therefore, stacking the TD matrices for each subject along the third dimension (resulting in a 18,715x18,715x51) and then averaging across this dimensions was the preferred methodology resulting in an abstract average subject. This approach was suggested by Svensén, Kruggel, and Benali (2002) but was warned against due to the need for temporal and spatial alignment. All participants were recorded using the same time period and the surface based methods lead to superior topological alignment and so this method was justified.

Stacking participants in this way also enabled additional methods for data clean-up. For each lag value comparing two vertices the SD was computed across all subjects. This resulted in a Standard Deviation Matrix representing the variation across TD matrices. The standard deviation was 1.30 seconds (SD=.76).

The next step was to identify and remove TD value outliers across subjects. A basic approach using Tukey fences was applied. For each cell, values greater than 1.5

times the inter quartile range for that cell were removed before averaging (Tukey, 1977, p 43-44).

This approach increased the likelihood that extreme values that were noise mentioned above were not being entered into the group level representation. If participant values were near 5 seconds and data replacement at limits replaced some values with a value of a 5 second lag these would still be counted. If however most participant values were near 0 for that participant then the 5 second replacement was removed.

The result of this process was a 18,715 x 18,715 matrix that represented the group average with no missing values.

0-Lag and TD comparison. To compare the 0-lag and lagged maps the resulting 18,715x18715 matrices were then sorted according to masks generated from Yeo et al.(2011) and then sorted based on the number of negative values in the map. This allowed for a visual comparison. The seven component resting state network map was used. Strong modularity would result in relatively similar colored blocks of cells along the diagonal representing the different networks.

As a reminder, in the computation of the TD matrix, we interpolated the time of maximum covariance using parabolic interpolation across three values. If the two times series are correlated, then they will show a maximum covariance at zero with both the first and last time points of roughly equal intensity. Highly correlated regions would show similar structure in both the 0-lag and the lagged representations.

Results and Discussion

Overall interpretation of the TD matrix. First we need to remind the reader what the TD matrix actually represents; an extracted region of the matrix is shown in figure 8. It is an antisymmetric matrix with zeros along the diagonal. Each row and column represent vertices on the cortex; there are 18,715 vertices in our analysis therefore the matrix is 18,715 x 18,715. Each cell in the matrix represents the temporal ordering of the two compared vertices where the covariance function is maximized. Along the diagonal are zeros, because each vertex is perfectly aligned with activity in that same vertex across time. The antisymmetry comes from the fact that if vertex A reaches maximum covariance with vertex B after a positive shift in time of .45 seconds, then it is necessarily true that from the other perspective vertex B is maximally aligned with A when we shift the time series of A back .45 seconds. It simply depends what our reference point is.

Now, let's reinterpret this matrix such that the columns represent regions and each row now represent a temporal relationship of these regions to the region represented by that row. We could reorder this row to help conceptually from lowest to highest, and now it would represent a timeline of activations relative to the vertex identified by the row. This is demonstrated graphically in figure 9. As mentioned above, the maximum value in the matrix is +5 and the minimum is -5.

A thread according to Mitra (2015) was a metaphor for the parallel running processes in a computer; in other words, the several programs which are running at the

same time. The concept of a Lag thread referred specifically to the principle component representation of variance in the TD matrix rows.

Sticking with this terminology, I will refer to the individual rows as micro-threads. It is worth reminding the reader that these are comparative terms not absolute terms. A micro-thread refers to an individual row in the TD matrix while a thread represents a deconstruction of the matrix into larger representative components. However, remember that a single row represents a vertex which is equal to thousands of neurons, so the scale is not absolute. Overall each thread or micro-thread represents separate parallel sequences of activity that spreads across the cortex. They are always unidirectional and cannot return to a single location more than once. Threads also do not represent the magnitude of activation, nor do they represent the magnitude of the covariance; these are further interesting areas of study not discussed here but clearly relevant and important work.

Because each thread represents a sequence of activity for each vertex on the cortex these can be mapped onto the brain in a way that allows us to visualize the topography of the activation. This could be done for each micro thread, but the use of 18,715 brain images is of questionable use. Secondly, each micro thread likely included noise and signal shared with other micro-threads; this will be dealt with below.

Anatomical Region

	V1	V2	V3	V4	V5
V1	0	-0.30	-4.20	0.21	-0.41
V2	0.30	0	0.71	0.18	-0.81
V3	4.20	-0.17	0	1.34	0.23
V4	-0.21	-0.18	-1.34	0	-0.05
V5	0.41	0.81	-0.23	0.05	0

Micro Thread

Figure 8. The TD matrix is antisemetrical and has zeroes along the diagonal.
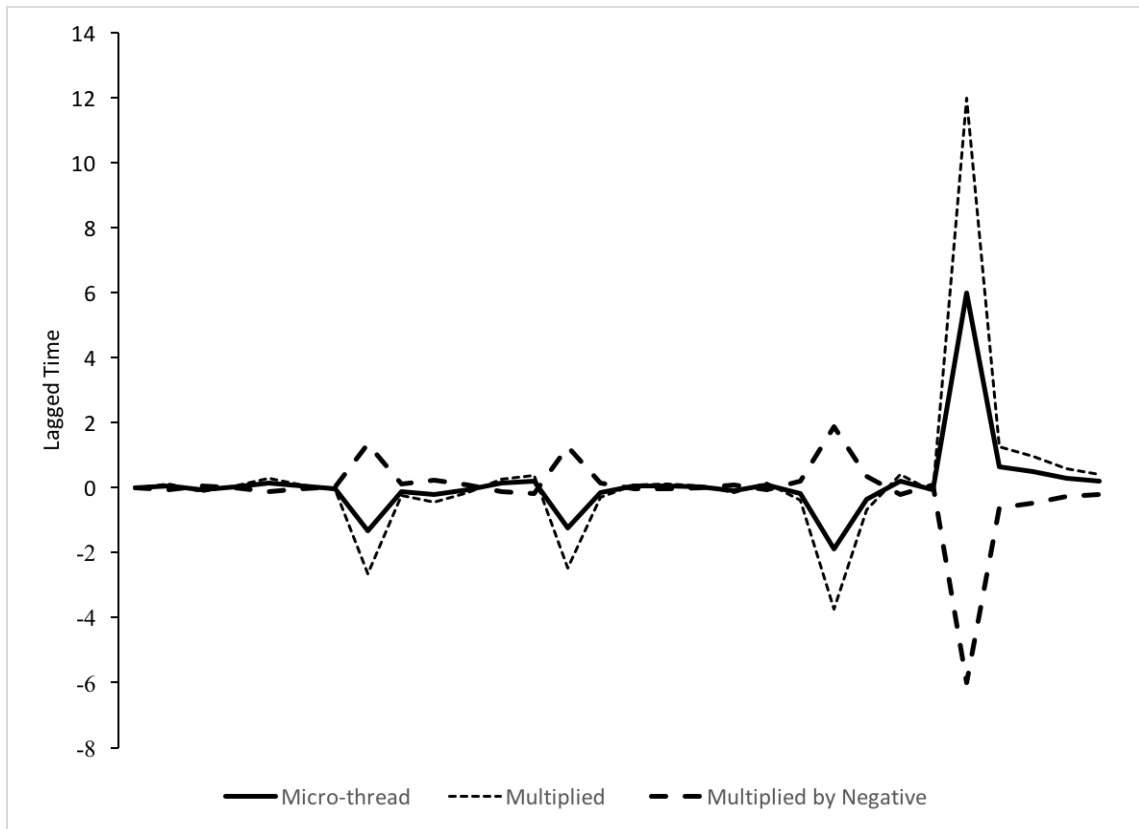
Figure 9. The amplitude of the signal for the solid line represents the first column of the previous TD matrix. If multiplied by a constant, as in done in ICA, the relative lag between the regions is the same, but the absolute lag changes as can be seen in the dotted line. The dashed line demonstrated that multiplying a micro-thread by a negative result in a reversal of the lagged sign. This is important because ICA does not respect the sign or amplitude of the source data. The points along the x-axis represent vertices on the brain; their order is irrelevant.

Relationship between lag structure and 0-lag structure. As mentioned above, resting state analysis has traditionally identified networks as spatially and temporally distinct. In other words, RSN were thought of as assemblies which work as a unit with extensive recurrent activity. If this was the case, then relationships between networks would be separated in time such that one network would reliably be earlier or later and all the units of that network would share a relatively short period of time.

If these networks acted as unified processing units, we would expect vertex relations to be isolatent or in a similar time range within the network. The values within blocks along the diagonal would include a restricted range in the lag representation and the range between lag structures would only minimally overlap, if they act as a unified network or use the coupling technique described in Part 1.

A second part of the RSN network theory is that the networks are not only internally isolatent but there is a difference in between network latency. Each network should be temporally isolated from the other networks. If this is the case then the off diagonal blocks of the matrix should systematically vary from zero.

Assuming these two ideas is central to some arguments relating behavioral variables to network structure. Anticorrelation between networks is often thought to reflect that they are not simultaneously active an important feature described above and further below in our discussion of mind wandering. It has also been theorized that the degree of correlation within a network shows how that network works as a unit similar to a neuronal assembly. Thus, in this approach, the internal integrity of the network is assumed to correlate with efficient network functioning.

Alternatively, if intra-network latencies are large and inter-network latencies are zero, then the above approach is an inappropriate interpretation of the data. This was the case in analysis done on Mitra et al. (2015) which was reliably reproduced by the authors. This same approach is tested here with our smaller group of 51 participants.

First establishing that traditional zero lag networks can be produced in the current population showed the correlation matrix representing the Pearson's correlation between each vertex. The table is first sorted by number of negative correlation values per row and then sorted by resting state networks following Xu (2107), as expected the network shows a high degree of modularity. At zero-lag the networks appear to be internally highly correlated.

However, in figure 10, we have reordered the TD matrix representing lagged relations in a similar way first by negative lags and the by traditional RSN.

As can be seen, the diagonal elements are not internally isolatent nor are the off diagonal blocks differing from zero. This supports the findings of Mitra et. al. (2015) finding that the traditional interpretation of resting state networks as assemblies or cohesive processing units is lacking.
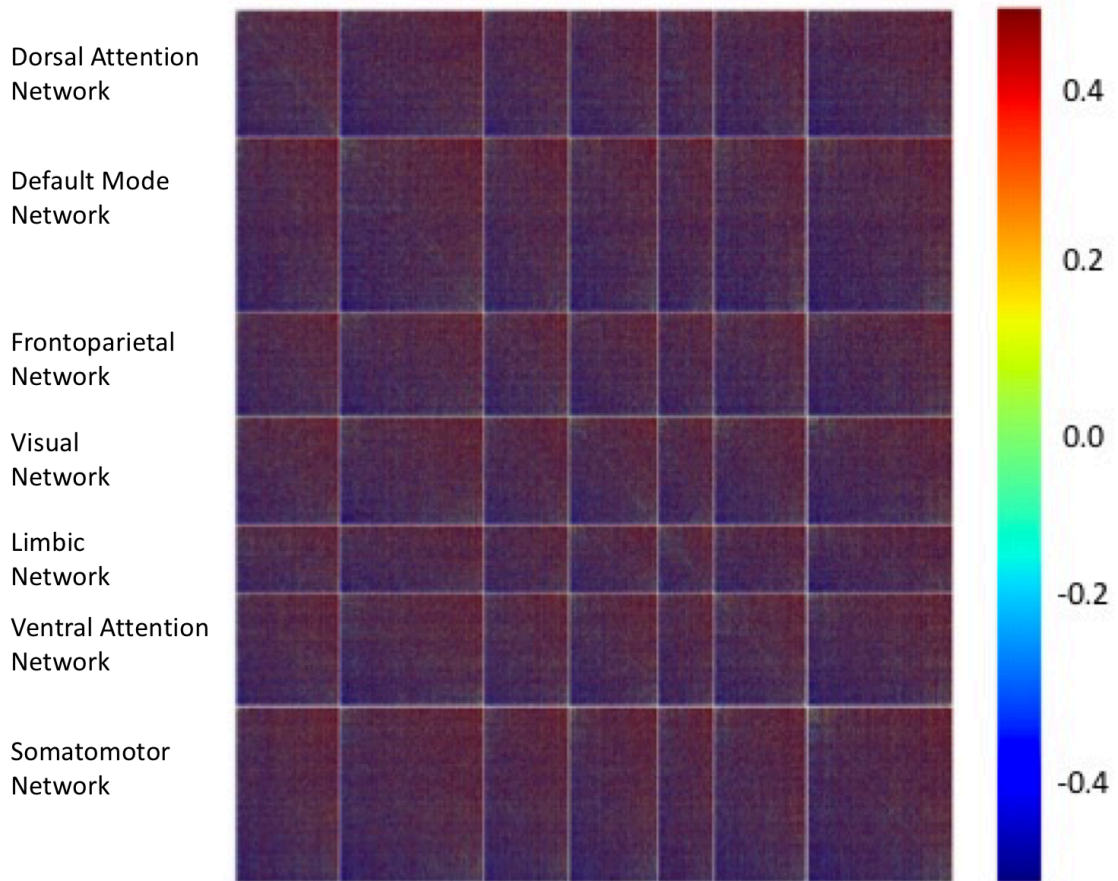
Figure 10. The blocks along the diagonal do not appear to be earlier or later on average than other blocks along the diagonal. If they were, they would exhibit different ranges of lag between them. Also, it appears that within the traditional 0-lagged networks there is the full range of lagged values that can be found in the entire TD matrix.

Discussion. How can this be explained? Remember that we obtained a cross covariance function for each time series. Let's say we shift two time series past each other and we get the covariance at a shift of -2, 0, and 2 seconds. If the two-time series are acting as a time-locked unit, then the cross covariance at -2 and 2 seconds should be equal; and if they are equal, the local minimum or maximum after interpolation should be at 0. If the maximum or minimum cross-covariance is anything other than zero, then they are either acting in sequence or they are unrelated. Figure 10 shows that within a network there are relatively few vertices with a temporal lag of zero. The distribution of the cells within traditional networks recapitulates the distribution of the cells in the entire TD matrix.

Although I will not go into testing these specific relations here, Mitra et al. (2015) point out some specific reasons this may be the case. First, and importantly, they demonstrated through that traditional networks can uniquely be reconstructed from lag networks, however the reverse is not true. This suggests that RSN are an emergent property from lag networks which are a more fundamental representation of neural activity. This does not invalidate RSN research, it only affects the interpretation.

Mitra suggests that the traditional resting state networks represent regions which represent "one way streets" or regions in which the dominant motif only goes in one direction. A motif is a sequence that has a stereotyped sequence that is found repeatedly; for example, if the sequence A-C-B is repeatedly found, this this is a motif. A one-way street means there are less reciprocal interactions within regions and the signal traverses the region mainly in one direction.

It appears that within traditional networks one-way streets predominate and between networks interactions are predominantly reciprocal. Mitra then ran simulations to test this finding that the apparent synchrony in RSNs can be uniquely predicted from lag network representations. However, lag network representations could not be uniquely generated based on the apparent synchrony found in 0-lag network representations. It is therefore their conclusion that lag structure is a more fundamental representation of neural relationships than the synchronous representations and resting state networks represent regions where one way streets are predominant.

Topographic representations. Having established that lagged network representations are a more fundamental representation of neural dynamics than 0-lag representations, we will now examine the group level data using three methodologies: projection, principle component analysis, and independent component analysis. Each of these methods represents a different aspect of the data and allows for limited interpretations. These will be discussed in turn.

Projection. The simplest high level representation of lag structure is the one-dimensional lag projection vector. Operationally, this involves the averaging of all lag values in a row giving us the average lag for each vertex. We could then arrange the vertices by their average lag values to determine which ones tend to be earlier and which tend to be later on average. This was shown in figure 10.

The projection method was developed for use with analysis of individual neurons examining peak off sets which were less than 2 milliseconds, but the authors suggest that this method is transferable to larger networks at various time scales. When examining a

population of neurons these offsets can be added to represent the relative firing time of the individual neuron to all other neurons in the data set. Some important caveats are listed for this method which was developed by Schneider, Havenith, and Nikolić (2006). The authors note that this is not a property of the neuron itself but is related to the functional stimulation, the behavior of the organism, and the environment which it is in. The projection vector is a property of the system we are examining, not the individual neurons or in this case the neuronal populations. This also has the same shortcoming of any averaging in that a value near zero could mean it tends to be sequentially active in the center of all sequences or it could be very early half of the time and very late the other half of the time.

This projection matrix is constructed using the group representation TD described above. The results of this vector are then topographically represented on the cortex in figure 11.
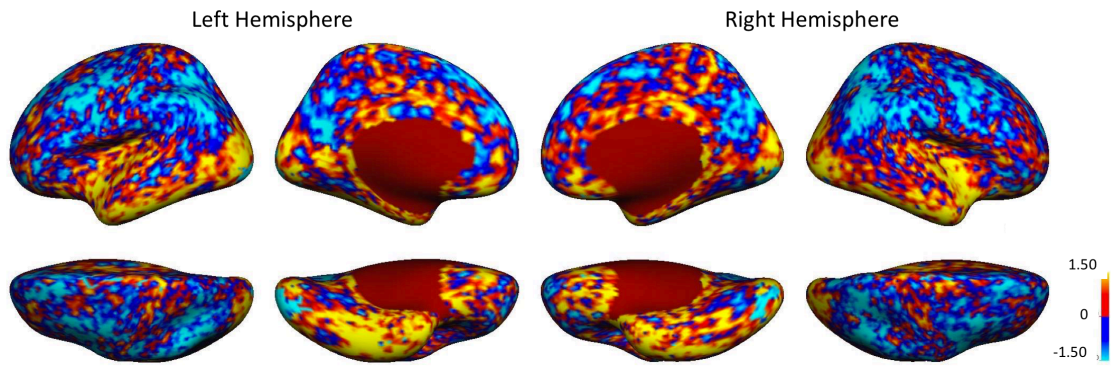
Figure 11. Projection matrix representing the lag of various regions on average.
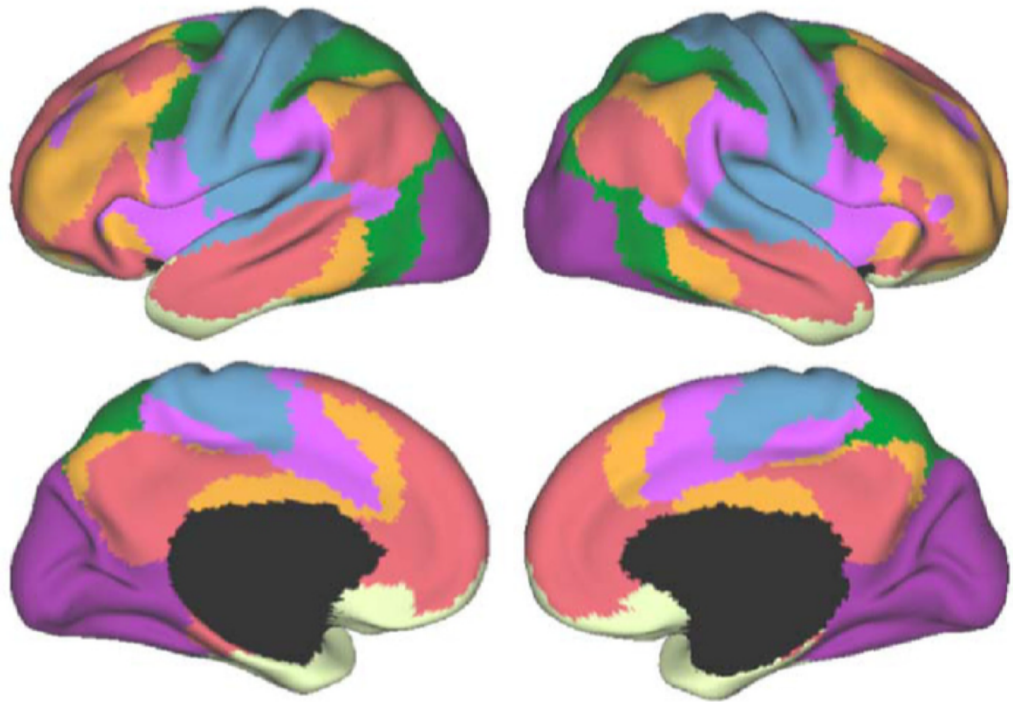
Figure 12. The various traditional resting state network boundaries. Note that they do not overlap with the regions in the projection map representing different lags.

Results. Overall, there are some immediately relevant findings from this procedure. At the group level, first, it is notable that there is great inter hemispheric symmetry at the gross level. The map also appears to respect some major landmarks.

Lateral maps. Along the borders of the Central Sulcus as vertices approach the pre and post central gyrus the regions tend to be activated earlier on average. This has functional significance considering these borders represent body maps of both movement and sensation respectively (Penfield, & Boldrey, 1937). Secondly we see early average activation of the insula which typically is associated with sensation from the viscera and internal body and the perception of emotional feelings (Immordino-Yang, McColl, Damasio, & Damasio, 2009). Interestingly the inferior and superior temporal regions are also early, these are typically associated with semantics and word meaning as well as auditory perception in the posterior regions (Mesulam, Thompson, Weintraub, & Rogalski, 2015). As would be expected the occipital cortex also shows early activation Mitra et al. (2015). These sensory regions are prominent in perception and imaginary visualization (Farah,1988; Kosslyn, Ganis, & Thompson, 2001). Interestingly a small region of the occipital pole is much later, if this is not noise, then one possible explanation is the recurrent activity in the occipital region where later visual regions continually feed back to the primary visual cortices might result in an on average later activation of this region. In any case these primarily sensory regions are clearly emphasized in the projection map as having early activation.

This indicates that perhaps these high level maps represent knowledge as described in Part 1 at the level of perception and general trend for the direction of information to move from perceptual regions toward higher abstract association cortices.

Medial maps. Switching to the medial surfaces, we can immediately notice that the cingulate gyrus tends to have earlier activation on average as well as the medial regions associated with body representations as was found on the lateral surface (McKay, Evans, Frackowiak, & Corfield, 2003). Also notice that the anterior regions of the middle frontal gyrus appear early as well as the orbital frontal cortex.

It is clear that while many of these regions are respecting the sulci and gyri of the brain there is still variation within these regions. Overall the topographic modularity is preserved in the lag structure. Also, the representation is similar across hemispheres and it respects the cortical folding.

Thus, there is plenty of evidence to suggest that we are not simply observing noise.

Resting state network comparison. Agreeing with the previous analysis, it is immediately obvious from an overlay of traditional resting state networks that the lag structure does not respect traditional resting state boundaries. In other words regions which are typically associated with the same network show the entire range of lag values. This is clear in the 7 component model as seen in the overlays in figure 12.

A benefit of using this projection technique is that it can easily be used to compare groups of subjects as Mitra et al. (2015) did in their evaluation of typical developing vs those diagnosed with autism spectrum disorder. Keeping in mind the

limitations above that this represent global system dynamics and ignores how some regions could be differentially early or late depending on the threads selected, this is easy to apply to any group of subjects across a behavioral variable as we will apply it in Part 3.

A clear limitation of this method is that it does not pull out the parallel processing of information which is of course essential to time series analysis. If we find differences at this level it will represent differences in regions that tend to be early or late but not regions that are both early and late equally across micro thread representations.

Singular value decomposition. While the projection map can be telling and has been used in Mitra (2015) to compare individuals with autism and typically developing individuals, it is very obvious that there is substantially more information in the group level TD matrix. For example, averaging across rows loses the information that a vertex may be early in some instances and later in others; information which is in the TD matrix. Therefore, the matrix must be decomposed into a set of "threads" which represent the data in the matrix at a higher level.

The first approach was to use singular value decomposition (SVD). This was attempted here to repeat the findings of Mitra where principle component analysis was used, however SVD was used which gives us the same mathematical results as a PCA but is more easily computed on larger data sets (Wall, Rechsteiner, & Rocha, 2003). The underlying assumption is that by using SVD each thread will represent the maximum shared variance in the TD matrix across micro-threads.

In Mitra's 2015 study threads were identified through the process of principle component analysis. The output of the PCA were thread representations. Each thread

represented the variance accounted for by rotating the matrix in hyperspace to obtain linear equations weighting each thread's representation across the cortex. While this approach has shown gross stable patterns maintained across many individuals, it represents a different level of complexity than what we will be examining here.

The PCA Mitra et al. (2015) conducted was performed on a TD matrix averaged across individuals, thus, removing individual variance. The goal was to determine global patterns shared across individuals and and representative of brain processes.

Another way of thinking about this is that the threads represent shared neural representations of persistent knowledge. Threads accounting for more variance represent the highest level representations of knowledge likely dealing with perception or gross level processes that are shared across many activities. The components accounting for less variance may represent more specific representations of knowledge or skills.

Analysis. Two problems emerged immediately. First, SVD is based on shared variance. Each component attempts to explain the maximum amount of variance with a set of linear equations. Each additional component adds another portion of shared variance until the number of components equals the number of predictors. Selection of important principle components is usually done using methodologies similar to scree plot which select only those components which explain the most variance.

When computed in the current data set no inflection point was clear in the results. The only component which existed before the inflection point explained only 0.004% of the variance. The method overall for this size of data set was therefore not useful. It may

be because the data itself is too noisy or it may be due to the number of regions being represented.

It is interesting to note that other simulations run on a further decomposed mesh of vertices only including 5,124 vertices did result in points of inflection, however this low resolution image was abandoned because each vertex represented a very large swath of cortex. This lower model is presented in figure 13, but as can be seen very low levels of variance are explained.

Additionally, in PCA or SVD, a problem emerges if we wanted to compare thread representations between individuals. The component representation would different for each individual. Thus PC 1 is not the same as PC1 in another subject. Similar networks across individuals may account for different amounts of variance between those individuals. Thus PC 1 accounting for the most variance in the first participant may actually be equivalent to PC 200 in another individual. One way to solve this would be to do a visual analysis of the components, but this proved to be impractical because there are no previous standards for lag structure and it was unclear which components were the same between individuals.

While a nested model may give us more information, this mode of exploration was abandoned. The relationship between PCs is also difficult to interpret. It was at this point that I turned to a different methodology to decompose the data.

Initial attempts to decompose such matrices into a minimal number of interpretable components were taken by Raichael and Mitra 2015. They applied principle component analysis to a voxel wide representation of the whole Brian including

cerebellum. Principle component analysis essentially rotates the matrix as to extract maximally orthogonal signal. There will always be as many resulting components as there are columns in the matrix. To reduce the dimensionality of the data Mitra and Raichle used the obtained Eigen values from each of the components ordered by their amount of variance explained. Using scree plot methodology 7 components were extracted and explained approximately 20% of the data. However, in the interest of maintaining special resolution the current methodology is working with a much larger matrix.

To reduce the dimensionality of the of the current data PCA was similarly applied. An average matrix was constructed by stacking 49 participants and averaging across the same cell. However, when PCA was applied to the resulting matrix, only one component could feasibly be retained before the inflection point. This single component accounted for .004% of the data. Successive components accounted for .001% additional variation in the data. It was unclear what this single component might represent. First of all, the obvious issue is that applying PCA to this data set and removing all components after the inflection point would simplify the data in a way that is not particularly useful. To use only one component is to remove most of the variation, not to better understand the structure of the data. It is also possible that the single extracted component is systematic noise. Furthermore, traditional singular value decomposition does not have a straightforward method to reconstruct the signal from each individual.
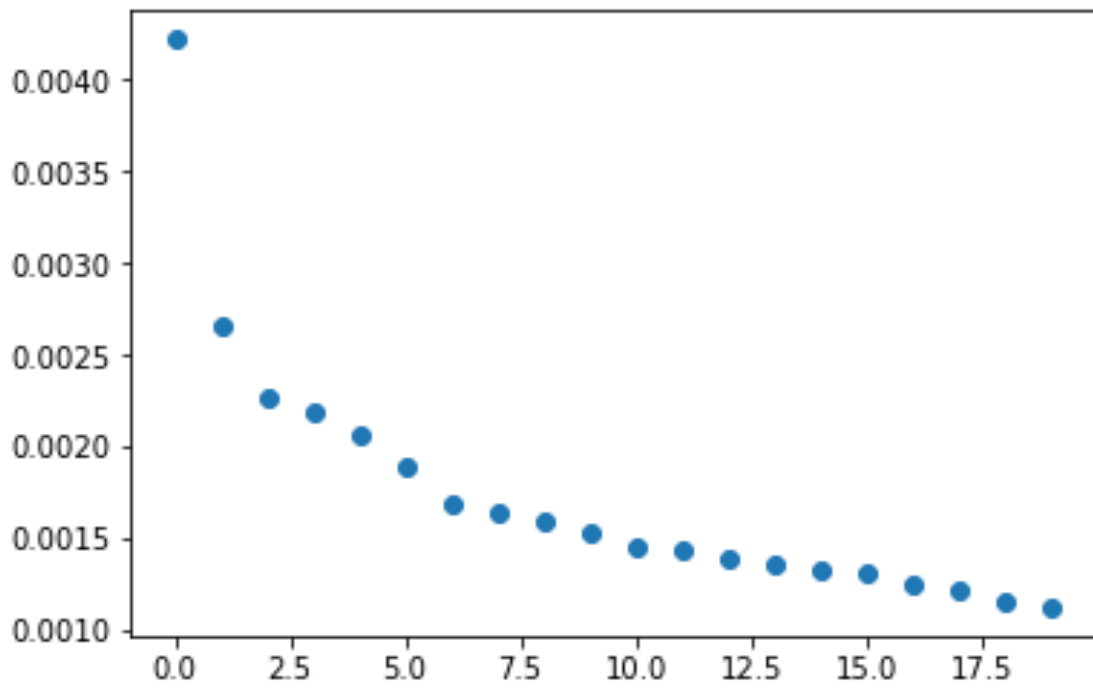
Figure 13. A scree plot of the PCA with the explained percent of variance on the y-axis. Notice the very small amount of variance explained. Because of this minimal variance and other factors described in the text, the PCA method was abandoned

Independent component analysis. The final approach used to reduce the data into interpretable threads was ICA. This is a novel application of ICA for a number of reasons and therefore some extensive explanation is needed to describe what motivated the analysis method as well as the interpretability of the results.

Goals of ICA. As a possible solution to extracting meaningful signal from the TD matrix a novel application of independent component analysis is proposed. ICA has a long history of extracting a small number of linearly mixed signals from mixed signal input. The classic example of ICA is the extraction of unknown independent audio signals from recordings which mix those signals in separate recording devices; this is known as the "blind source separation problem".

Independent component analysis is typically used for source signal separation. The observed values are assumed to not represent the "true'" values. Instead, the observed values are seen as a mixture of information from unobservable sources (Hyvärinen, Karhunen, & Oja, 2004). The goal is to find the mixing matrix that allows us to recover the unobservable sources. In other words, the observed variables are the product of the unobservable and the mixing matrix. We shall return to the details in a minute, but let's examine a classic example and then how it might apply to the TD matrix of current interest.

One of the key assumptions of ICA is that the source signals are independent. While neural events are never truly independent, we are making this assumption because we want to identify maximally differentiated patterns in the data set. These recovered systems are independent in the sense that they share more within than they do outside, but

they are still theoretically connected. Here we shall accept this assumption, although acknowledging that it is problematic. This assumption has also been violated when ICA has been applied to traditional 0-lag networks, but the assumption is not violated in the sense that we are searching for signal with maximum independence. Statistically, the sources are assumed to be relatively less Gaussian than the mixture of signals. This is in accord with the central limits theorem which says that signal mixtures are more Gaussian than the sources from which they are composed.

ICA background. The most common way of describing the ICA methodology is with signal recovery from a number of audio recordings (Hyvärinen, Karhunen, & Oja, 2004). Imagine 3 individuals in a room speaking: these are the sources which are independent. They are represented by independent sound waves which are not observed but assumed to exist. Recording devices or microphones are placed around the room, and critically, the number of them must match or exceed the number of source signals. So, let's assume that there are 4 microphones. Each microphone will record a mixture of the three voices if they are all speaking simultaneously. The recordings result in a sound wave that is a more complex mixture of some of the source sound waves. Individuals closer to one microphone will be represented differently in the recording. Each individual's voice is less Gaussian than the mixture of their voices. Independent component analysis takes advantage of this property of the mixture and recovers the three voices by seeking the mixing matrix though a learning algorithm which maximizes statistical independence.

Each of these audio signals could be represented as a vector of different frequencies in n discrete time bins. Arranging the four separate m vectors into a so called mixed matrix x of dimensions m x n. This mixed matrix is assumed contain information to extract a signal matrix s. The signal matrix must be no larger than m x n. More accurately the mixed matrix (x) is assumed to be the linear combination of the true signal matrix (s) and an unmixing matrix (A). This is represented in in the following equation: X=As

The goal of ICA is to find an unmixing matrix A which will satisfy the transformation between the mixed and signal matrices. A critical aspect of A is that the columns are linearly independent. This independence is stronger than simply not correlated. This matrix is also an invertible multiplier allowing this matrix to be independent of the particular mixture which constructed it. This allows us to use the matrix to reconstruct signals from similar mixtures. Importantly, while there is an upper limit to the number of signals which can be extracted from x (they may not exceed m), there is no lower bound. The various methodologies of ICA will allow for the amazingly accurate solutions to this equation allowing for the extraction of each speaker's voice if only three components are selected, but then if we add the allowable 4th component background noise can be extracted independently. If we add additional microphones additional sources of noise can be extracted, but through the addition of still more microphones different aspects of the separate speakers' voices can be extracted.

To solve this equation, we need a measure of independence. The typical measure of independence is entropy. A uniform distribution has maximum entropy. This process

156

involves the maximization of individual entropy while minimizing mutual information and thus maximizing the joint entropy (Bell & Sejnowski, 1995). Another way of framing this is to say that the goal is to minimize the information redundancy between the signals. The Gaussian distribution is by definition of maximum entropy.

Roughly speaking, entropy is a measure of disorganization or chaos in a system. The more organized the system the lower the entropy (higher negentropy). More organized systems show less normal distributions. Their outcomes are more predictable. The more random the system or the more normally distributed, the less predictable the outcome. As a note, this is also true of kurtosis. More peaky kurtosis is representative of higher predictability, values are more predictably in a smaller range. The goal of reducing entropy in each signal then is to search for increased predictability in that set.

Negentropy can mathematically represented as J(y)=H(ygaussian)-H(y) where ygaussian is a normal distribution sampled from the covariance of y. When comparing components, we want to minimize the redundancy between components making them each contain the maximal amount of information while minimizing the multiple information. To do this we want to generate an unmixing matrix where the sum of the negentropy of all the components is maximized and the components are also decorrelated. When negentropy is maximized the resulting component will represent signals embedded in the mixtures which are independent.

The contrast function chosen utilizes the log of the hyperbolic cosine to determine the contrast between components. This approach has been tested on a variety of real world and simulated data sets and appears robust (Hyvarinen, 1999).

There are various methods of ICA, Fast ICA methodology developed by Hyvarinen (1999, 2001) then uses a fixed point algorithm to iteratively find the best fit which maximizes the contrast function. Fast ICA method first estimates the unmixing matrix until a component of maximum entropy can be removed. Then the process is repeated on the remaining mixed signal until the requested number of components has been satisfied.

ICA varies from PCA because ICA attempt to make the resulting source signals independent and non Gaussian. It has been shown in comparisons of PCA and ICA for voices and image reconstruction that PCA does not in fact separate the signal into independent sources, instead it separates the signal into new mixtures which represent variance in the data (Hyvärinen, Karhunen, & Oja, 2004). In the voice example, PCA would extract new voices which represent the variance in the mixed signal. In an image example the so called Eigen faces are produced which represent mixtures of features an therefore each is a face unto itself. Conversely, in ICA the separate voices, noise in microphones, and background noise are each separated. In visual ICA facial features become independent components, and for neural studies signals originating from specific regions are extracted.

Application of ICA to TD Data. Some stretching of the mind is necessary to draw an analogy to the current data set. Each row in the TD matrix is not independent, it is assumed to be a mixture of signal from a particular neural region, as mentioned above, the data is assumed to have noise which is shared but also each micro-thread is assumed to reflect some influence from other micro threads. In our case, the original

"microphone" was the voxel. After removing potential noise sources and interpolating across the cortex we may now imagine that each vertex on the surface of the cortex is a recorder. But, the analogy is not this simple.

The data were then processed to discover the temporal relationships between vertices. We now have a different type of source. Each row represents a temporal sequence with respect to a vertex represented by that row. Each row now is a signal representing temporal and spatial aspects of the original signal. Mathematically, we still have the same situation, however. We are assuming based on the theory outlined earlier that there are temporal sequences shared between neural regions. To keep this parallel to the audio example given above, each row can still be visualized as a wave. However, the peaks and valleys of the wave now represent a temporally early or late dimension. Although not typically represented this way, a single row in the TD matrix can be represented as a wave as in figure 9. However, the values along the x-axis have no particular important order. They no longer represent time, but now represent spatial relationships.

This point may seem counter intuitive, but as long as we maintain the same x-axis order of neural regions ICA will still apply. This has been easily demonstrated in the spatial analysis of images where the 2D image can be broken into pixels and then unfolded into a single vector of pixels which can similarly be represented by a wave where peaks and valleys represent lightness and darkness of the image (Hyvärinen, 2013). The way we unfold the image is immaterial as long as we unfold all images the same way and then reconstruct the image respecting the original sequence. ICA will find

patterns in the data that respect paired relationships based on the intensity values but the order is immaterial. Remember the order along the x-axis in this neural analysis is not time. The x axis represents location in vertices and the intensity represents time. However, the equation does not know the location of the vertices; therefore, any spatial results will reflect shared sources of independent signal, not shared location. The equation does not know the location of vertices.

Application of ICA to current TD matrix. As the theory goes above, we are searching for relatively persistent patterns of neural activity which represent knowledge in the broad sense. An additional assumption is that brains developing in similar environments, with relatively similar genetic makeup (as compared to other species), and forming in relation to the needs of survival in a shared world and similar bodies will result in canonical organizations that maximize adaptability. In other words, there are lots of shared patterns in our brains in spite of our many differences. But, differences in the factors leading to brain development and learning will result in measurable differences in the expression of these canonical patterns.

By applying ICA to the TD we wish to uncover these sequences as relatively independent sources. Additionally, we want to be able to reconstruct the process for each individual so we can compare across individuals in Part 3.

Representing the current group, it would have been better not to average the participants to generate a group level TD matrix. It is preferable, instead, to concatenate the participant TD matrixes along the m dimension and then run ICA on the resulting rectangular matrix (Erhardt, Rachakonda, Bedrick, Allen, Adali, & Calhoun, 2011). In

this concatenation approach, each individual is represented and the unmixing matrix and signal matrix could have been deconstructed into portions representing each individual (Svensén, Kruggel, & Benali, 2002). However, because a decision was made to preserve the spatial resolution, the resulting mixed matrix representing the stacked TD matrices is 18,715 x 917,035. This proved to be computationally prohibitive during implementation; however, this should be considered in future modeling.

The first task is to recover these sources in a way that we can compare the components across individuals. Two main approaches have been used to deal with this both of which involve a dual regression methodology. The group's data are combined either through concatenation all subjects or stacking and averaging the subjects (Svensén, Kruggel, Benali, 2002). In the concatenation approach the TD are stacked as if they were all from one individual. Thus, our mixed signal matrix for the 51 subjects is 18,715 columns representing the neural regions, and 917,035 rows (18,715 rows x 51 individuals) representing the sequences. A second approach is to average all 51 TDs resulting in a matrix 18,715 x 18,715. There are costs and benefits associated with each.

As mentioned above, the construction of a group level through vertical stacking results in a matrix which requires more computational power than currently available. But, unlike PCA stacking the individuals in this way will not result in components being pulled out according to variance. Instead independent components would be removed and this would be a more powerful method if there were not current computational limits.

Therefore, the averaging method was used with Tukey fences as described above to start with a group level TD matrix with minimums and maximums of -5 and +5

seconds. Using ICA it is additionally not an option to remove values if we chose to do so. ICA requires a complete matrix. This process was still computationally intense therefore it was completed using external web servers available for research purses at Amazon Web Services.

One of the strengths of the ICA approach is that the resulting unmixing matrix can be used to separate components in appropriately matched systems. In other words, the resulting matrix can be used on a novel set of data with similar noise and signal properties. In the case of fMRI we are talking about similar machines, locations, and age group etc. Reconstructing the latent signal involves solving for s in the equation given above. Because we are using a reduced model of components where m<n A is not square, therefore the matrix has no true inverse. Therefore, an application of the methods described in Penrose (1955) were used to generate a pseudoinverse using least squares methodology. The Penrose pseudoinverse of A is utilized to be an appropriate solution to solving for s.

Our first step in ICA is therefore to compute A for our full data set. Once the group level unmixing matrix is constructed we can then use that matrix to reconstruct individual components and regress them across some behavioral variable. It is worth noting that these 'dual regression' models have been used for fMRI resting state traditional lag structure but not for the current TD matrix.

Decisions then needed to be made to decide how many components to extract. There is no accepted way to determine the number of components as this is not a similar

162

procedure to accounting for differing amounts of variance. We are looking for independent signals, not signals that maximize variance explained.

How many components? What is the correct number of components? Remembering that neural activity and structure follows a highly repetitive fractal nature while maintaining a small-world architecture, there is some degree of arbitrariness to the number of components to extract. We extract the number of components we would like based on the resolution we desire. An analogy can be made with human social networks. Is there a clear line between what is a community, group or culture? We could examine a school, a system of schools or students within a school, the boundaries are artificially constructed by the researcher using landmarks. Similarly, language studies pose a similar problem because the difference between languages, dialects, and idiolects is by no means clear cut and are clearly social constructs for the convenience of allowing us to examine language at a level we feel is appropriate to our study. The same applies here to neural activity. While standard resting state networks have been identified, nothing makes these networks ideal or isolated except that we deem them so for further analysis and have agreed upon appropriate levels of division. In actuality they have also been compared to other measures such as structural measures to determine their validity but early attempts had no priori assumptions.

Returning to the idea of how many components to extract, we could extract a number of components that are equal to the number of supplied mixtures. However, this is not particularly useful from a conceptual perspective. It is desirable to extract a number of components which can be represented in such a way as to organize them in a

hierarchical manner which we will attempt to do later. However, as mentioned above, using ICA on dense neuroimaging data (and this is clearly dense) Beckman et al. (2009) extracted between 45 and 125 components from traditional resting state data and them organizes them hierarchically. Either one of these extremes is far below the number of mixed signals, but there is a tension on both sides. Extracting too few components we may miss the necessary granularity to see within group differences. Extracting too many components will likely result in more noisy and uninterpretable components of which the validity will be highly questionable. Being that this procedure has not been attempted on this data set, we will make 4 different maps and then based on the interpretability of those maps compare components to our behavior variable. The numbers are somewhat random here but will double from 5 to 80 (5, 10, 20, 40, 80). However, in the reverse inference and the later regression of the results we will concentrate on the 5 component model because this is exploratory and because neural activity is fractal, this will still represent an interpretable level but better reveal hidden structure than the projection process used above.

Another alternative is to run ICA on each individual and then compare the components or use a clustering algorithm to find the most similar components between individuals (Esposito et al., 2005). The main problem is that this method results in different ordered components and because of variations in the mixing of the components between individuals the extracted components may not align because different algorithms may be optimal for extracting components among noise in each participant. Additionally, noise may be handled differently in different participants. Because of these

complications, this method was not attempted here. While this method may be ideal for understanding the individual, it lacks the generality required to compare between groups.

ICA interpretation. The results of the ICA cannot be interpreted the same as the projection vector nor the same as threads in a PCA or SVD analysis.

In ICA a multiplier is sought that would satisfy the equation such that statistical independence between the resulting components is maximized. This causes two problems with interpretation. The multiplier does not respect true amplitude of the signal nor does it respect the sign. This limits the information we can get from the ICA. Figure 9 offers some illustration of the concepts.

(1) First, the amplitude of the resulting source represents the relative timing of the units at different locations. We can multiply the signal by a positive constant and this will result is a spreading of the signal across time as in but will not change the relative timing of the regions. Any manipulation of the signal with a multiplier will result in some loss of information. We can still make comparisons but the actual timing is lost.

(2) Another problem with any multiplier is the sign of the multiplier. If the signal is multiplied by a negative number, it will essentially change the direction of the time series. However, the relative timing of regions will still be maintained in the absolute sense. The relative temporal distance between any regions will be maintained but the directionality will be unclear. Additional work will need to be conducted to interpret the correct direction. However, we will use the projection matrix to set a direction for easier reverse inference.

(3) Finally, the result will have a zero mean for every component. This will result in a shifting of the time series, but the relative position of the units in time will not be affected. This shifting does not affect the interpretation of the data in any way because each lag thread is essentially a time series of activation. As long as the association between a region and a value is maintained across instances, the columns may be put in any order and the information will be preserved. These points are important and I shall return to them later. They also illustrate some of the limitations of the current methodology.
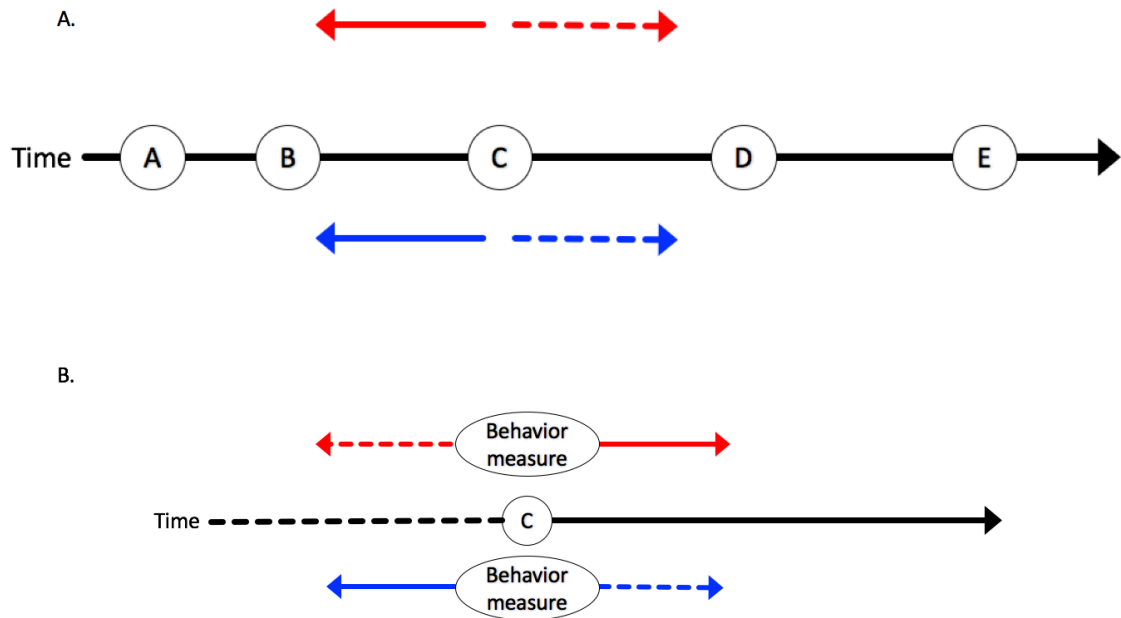
Figure 14. Demonstration of lag relationship between regions. A. Represents the situation in the projection vector. Regions have clear order. Positive correlations go in the direction of the time arrow. B. In the situation with ICA correlations represent the distance from some region, C.

Results. Once the method of data cleaning of the lagged representations was determined, ICA was completed on 5, 8, 10, 20, 40 and 80 components. Determining the number of meaningful components is a judgment call as described above. There is no theory driving these particular numbers. Increasing the number of components results in finding more source signals many of these may be the result of noise or portions of larger lag networks. Due to the interpretability the 5 component model was used in all further analysis although the output of the various number of components is included for the interested reader in Appendix E.

When reconstructing the signal, it is customary to add the mean for each signal back into the result, however the mean was left separate so that each component could be similarly visualized. Because we are looking at relative timing of regions visualization converted the resulting component signal into a z-score representation with the limits set to positive and negative 1.5 standard deviations from a mean of zero. Each of these components is also illustrated across time in a video located in the supplementary material.

Effects of Lag Limits. An initial simulation for 10 component models was used to evaluate the effect of lag limits on the resulting component structure. In this simulation all subjects were averaged across respective cells. The resulting components were then projected onto the cortex. A visual inspection of the resulting matrices shows both matrices have similar component structure. Choosing between a 8 and 10 second lag had minimal impact on the components. Keep in mind that in figure 16 the same components may be negative copies of each other, this is not a result of the lag limit difference, but a

168

feature of ICA which was described above. As can be seen the general shape and distribution of the components was minimally changed.

Results. Interpretation and reverse inference is limited to the 5 component model. The results of the ICA on a 5 component model can be viewed in figure 15. A possible approach to trying to classify these components is in their limits. Where does the thread begin and where does it terminate? What follows is a post hoc attempt to explain these threads. An individual with different training may see different patterns in the data that explain the observations; however, this is an attempt to begin classification. It is acknowledged that much more work is necessary to verify these additionally a larger data set is necessary to deduce the reliability of the component extraction.

Component 1. Component 1 appears to deal with body representations as initial activations and then at the other end is defined by the precuneus, and the inferior parietal gyrus, both association areas; but the precuneus is particularly important in complex social emotions and representations of self..

The motor strip (Penfield, & Boldrey, 1937), represented prominently here is early in the lagged sequence which may indicate the prominence of this in the later regions. This indicates that in this particular thread information in the sensorimotor regions may drive information processing in other abstract regions.

The inferior parietal gyrus and the inferior temporal regions come later and primarily concern semantic information and object recognition respectively. The inferior parietal gyrus also focusses on working memory and a variety of other association and abstract functions. Interestingly the superior parietal gyrus is also early. This region is

associated with mental manipulation of information (Koenigs, Barbey, Postle, & Grafman, 2009) including tasks such as mental rotation (Parsons, 2003). It does not appear to be associated with other types of working memory involving rehearsal or retrieval or long term memory. Additionally, this region is associated with body representations and maintaining memory of those representations (Wolpert, Goodbody, & Husain, 1998). In general, it also associates sight and action as in tasks like reaching and goal processing (Desmurget, Epstein, Turner, Prablanc, Alexander, & Grafton, 1999).

This component seems to represent the position and movement of one's body through space perhaps as a metaphor for more abstract processes. Motor tasks and peripheral attention regions of visual cortex are early whereas abstract regions such as reasoning in frontal cortex and representations of self in the precuneus and inferior parietal areas associated with working memory are later. This might help represent a source for embodied representations of knowledge grounding abstract thinking in physical interactions (Lakoff, 2012).

Component 2. The predominant feature of this component is the insula which appears as an entire unit to be activated early compared to other regions. The posterior central sulcus also appears to have early activation which is importantly associated with the abdominal region, but not the motor aspect of it. The cingulate appears activated early here as well. In this thread motor and memory regions are later.

The anterior superior region of the precuneus is activated early immediately following activation of the insular regions. The various regions of the insulation also deal with cognitive monitoring of emotions and the timing of the anterior insula in emotional

170

perception may vary based on culture as suggested in (Immordino-Yang, Yang, & Damasio, 2014).

The wave of activity in the precuneus is particularly interesting and is shown in detail in figure 17. This anterior superior region is earlier and is typically associated with more physical attributes such as admiration for a skill and compassion for physical pain. Later regions of this component involve the activation of the posterior inferior precuneus which deals with more abstract representations of self-including admiration and compassion for social pain (Immordino-Yang, McColl, Damasio, & Damasio, 2009). Immordino-Yang et al. (2009) also described the timing between these two regions as physical aspects of emotions may be processed faster than the social aspects of emotions.

Interestingly the inferior temporal shows significant early activation. This region is associated with rapid object identification and semantics (Grill-Spector, Knouf, & Kanwisher, 2004). Without subcortical region information it is difficult to tell, but this thread suggests that it may include rapid identification of objects and internal body states which would be relevant for perceiving feeling. The frontal regions and the sensory and motor cortices appear mottled at best and do not as a whole come early or late.

The insula and the fusiform face area have also been differentially associated with the subconscious processing of fearful faces (Pessoa, 2013; Pessoa & Adolphs, 2010). In any case, this component suggests that emotion and reaction to emotionally laden objects may be driving the start of this process. A more detailed examination including subcortical analysis might give additional insight.

One possibility is that this thread is associated with emotional processing. Early in the thread we see bilateral insular response at both the anterior and posterior ends, this coincides with activation in what may be the fusiform face area and anterior cingulate. This activation then spreads throughout these regions and throughout the process we see anterior superior precuneus activation spread toward the inferior posterior region. Just such a sequence may be associated with subconscious processing of visual stimuli for an emotional response ending in a feeling.

Component 3. The third component immediately appears to reflect visual processing demonstrating both a ventral and dorsal stream as suggested by (Goodale, & Milner, 1992). The ventral stream dealing with the "what" and the dorsal stream dealing with the "how". Of particular importance is the early occipital pole. Notice that for the other 4 components the occipital pole is late compared to the surrounding visual cortex. The occipital pole is often associated with visual processing at the fovea and deals with fine grained detail.

What is particularly interesting here is that the ventral pathway appears to have faster relative timing than the dorsal pathway, exactly what the theory would predict. Also, we note that the ventral pathway moves activity into the premotor regions predictably skipping the lateral parietal regions. This is suggesting of known anatomical connectivity between these regions (Goodale, & Milner, 1992; de Schotten, Urbanski, Valabregue, Bayle, & Volle, 2014). This dorsal pathway was suggested by the theory to involve the "how" of visual perception predicting the ways we may interact with the world. All other regions appear later and are not interpreted.

Component 4. This component is not quite as clear to interpret. The occipital region with the exception of the occipital pole appears early. In this sequence the temporal lobe is later as well as regions of the frontal lobe. Of particular interest is the predominance of the medial regions of the occipital lobe. There is also early activation in the posterior part of the insula and the inferior portion of the pre-central sulcus. This region is immediately between Broca's region and the sensory portion of the central gyrus associated with the mouth and larynx. These are necessary both in oral and silent reading as phonemes are represented as motor movements. Observing activation in the precuneus, we see simultaneously activation in the anterior and posterior regions which then moves more central to the structure. The meaning of this particular thread is elusive but it likely has something to do with secondary visual processing.

Component 5. This is the noisiest component and may therefore may be too noisy to interpret, however, overall there appears to be earlier frontal regions including anterior insula and earlier parietal regions including broad activation in the precuneus. A broad thought may be that these regions are associated with cognitive control and abstract thought. Early anterior cingulate also is associated with management of cognitive resources and conflict resolution (Koechlin, Basso, Pietrini, Panzer, & Grafman, 1999; Koechlin, Basso, Pietrini, Panzer, & Grafman, 1999). This representation may therefore vary most with abstract thinking such as math working memory and other abstract cognitive skills. The early frontal region activation may demonstrate a more top-down typically associated with frontal regions and executive control (Howerter, & Wager, 2000).

Overall. The overall finding here is that these components repeat the cortical folding patterns, but they are also very symmetrical between hemispheres. This indicates that what is being observed is likely not noise. The main findings here are not in any way conclusive but an approach to classification which may be useful in hypothesis testing when associated with particular components as we shall see below.
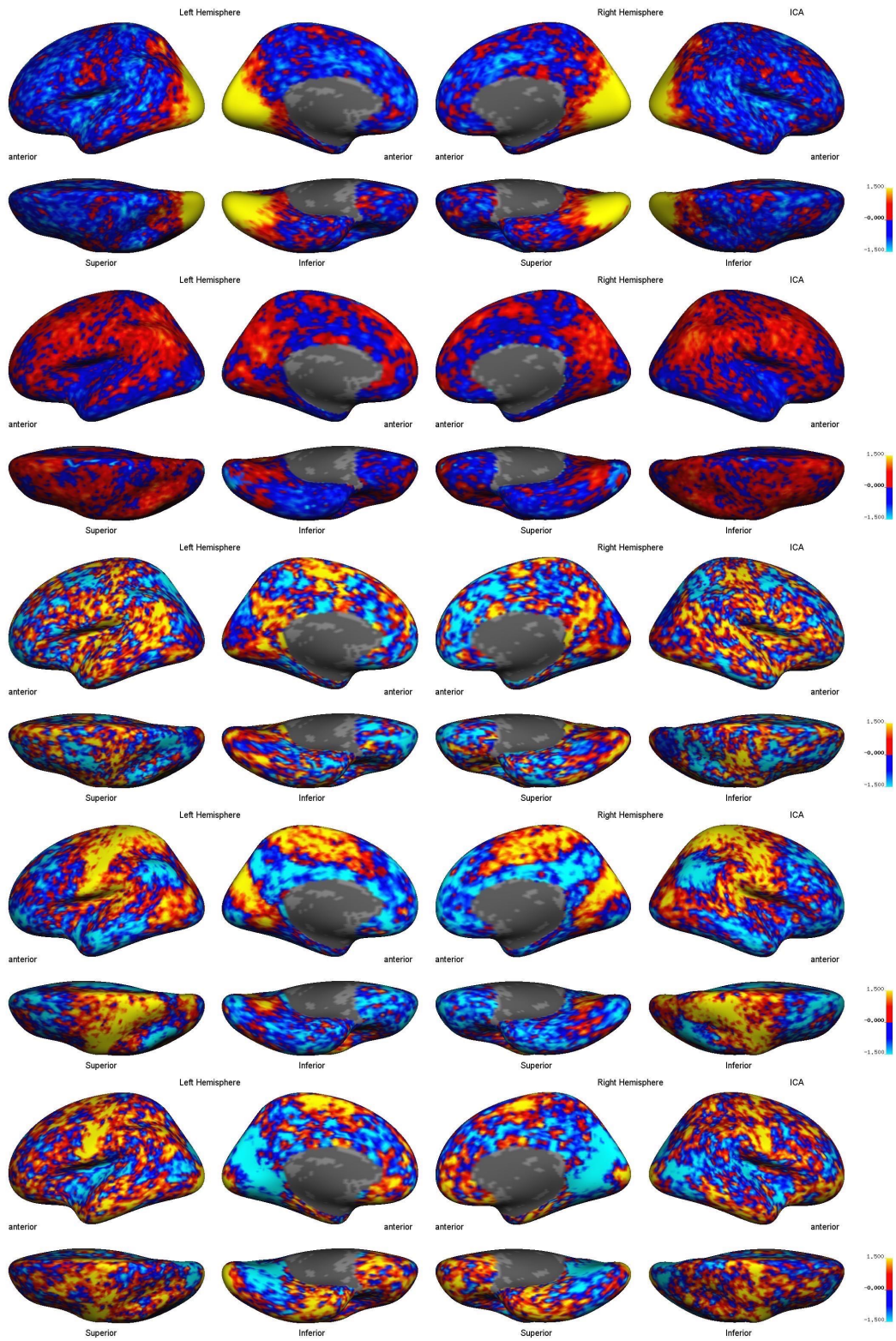
Figure 15. 5-component model of lagged structure
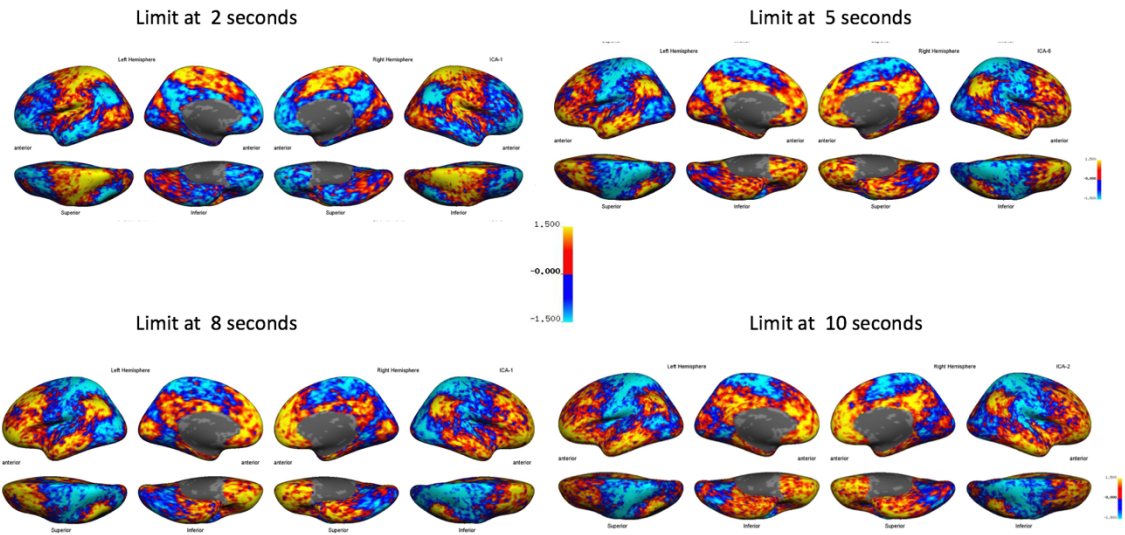
Figure 16. These are representations of the same component with four different lag limits set. As can be seen, the component structure remains robust although at 10 second it begins to get additional noise. Also, as explained above the flipping of some values is the result of ICA not the lag limit. The sign of the component is not interpretable.

0.002   0.004   0.02
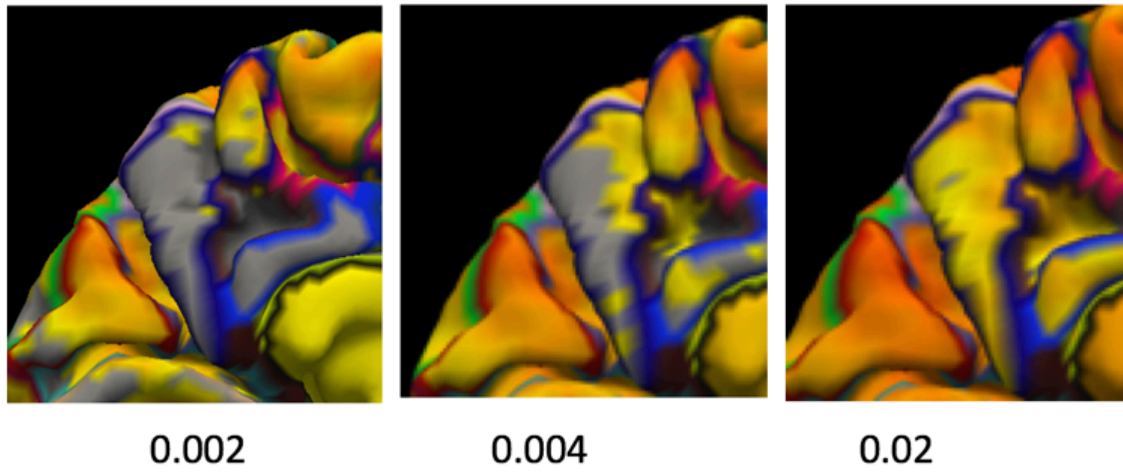
Figure 17. This is an example of a motif. The yellow is the leading edge of the time sequence. The Precuneus is outlines in dark blue. The time series appears to go across the precuneus in the same direction regardless of lag component identity. Note superior anterior precuneal activation at z=0.002 then the lag sequence continues into the posterior cuneus from 0.004 to 0.02.

PART 3: Mind Wandering in Behavior and Brain

This final section attempts to apply the methodology devised above to understand how the lag components from the projection and 5-component models, which are thought to represent high level persistent knowledge structures such as perceptual processes, might frame mind wandering while reading aloud. While a number of behavioral variables exist in the data set, mind wandering has been a task that has shown robust correlations with resting state. So it is here that we will attempt to apply the model. As we shall see our neurological findings do not correlate with any typically identified mind-wandering regions nor do they correlate with regions associated with reading. However, the literature summarizing reading and mind wandering in resting state networks will be presented below if for nothing more than to point out that lagged network analysis may unearth new relations. The methods here continue to be exploratory and the behavioral methods are also attempting to represent a specific phenomenon, mind-wandering while reading aloud. It is hoped that both behavioral and neural analysis will offer fuel for novel hypotheses using this method in conjunction with other more tested methodologies.

Mind Wandering

Our thoughts dynamically interact with both environment and internal states as we move between the continuum of shifting our attention by "looking in" or "looking out" (Immordino-Yang, Christodoulou, & Singh, 2012). While "looking in" can be a positive and useful skill as is found in constructive internal reflection (Immordino-Yang, Christodoulou, & Singh, 2012) or positive constructive daydreaming (McMillan, Kaufman, & Singer, 2013), sometimes those thoughts are decoupled from our external

experience in a detrimental way and pull us away from the focus of our current executive

goals reducing our performance toward the task to which we are supposed to attend

(McVay & Kane 2009, 2011; Mrazek et al. 2012; Unsworth & McMillan 2013). It is this

second aspect of mind wandering that will be the focus here. Specifically, we will be

examining this perceived intrusive form of mind wandering in the context of oral reading.

This seemingly trivial place to examine mind wandering has important

educational and practical considerations. It is not uncommon to experience a loss of

attention while reading silently to ourselves (Smallwood, 2011). Several pages into a

novel or expository text, we may suddenly become aware that our attention has drifted.

This can happen even more frequently when reading becomes automated because

automated tasks increase the frequency of off-task thoughts as do reductions in perceptual

load (Forster, & Lavie, 2009). Thus paradoxically, as fluency in skill increases

opportunities for decreased attention to the task are present. This is problematic because

while attending to simple tasks may require little attention, reading without attending to

content will not lead to comprehension. When we notice our attention drifting, reading

aloud is one popular way to reassert this attention. The assumption being that increased

attention is required for one to read aloud.

Specifically, one role of reading aloud has been used as a tactic to help students

maintain attention to text when they are struggling with mind wandering (Rasinski,

Padak, McKeon, Wilfong, Friedauer, & Heim, 2011); it is also assumed that prosody in

the oral reading patterns can be used to scaffold the reader helping to syntactically chunk

(Kuhn, & Schwanenflugel, 2010), interpret the emotional content (Binder, Tighe, Jiang,

Kaftanski, & Qi, 2013) and hierarchical arrangement (Van Dijk & Kintsch, 1983) of the text they are reading. However, recent research has suggested that reading aloud does not always decrease mind wandering and may in fact increase its frequency (Franklin, Mooneyham, & Baird, 2014). The current exploration may reveal some behavioral and neural differences between individuals that may account for the degree of mind wandering during oral reading.

There is a rich literature describing the construct of mind wandering including its behavioral and neurological foundations. First it is essential to point out that mind wandering is not equivalent to external distraction. When engaging in mind wandering there is often a decrease in the neural response to audio and visual distractors (Barron, Riby, Greer, & Smallwood, 2011; Smallwood, Beach, Schooler, & Handy, 2008), thus the phenomena is often termed self-generated thought because it appears to come from within the individual (Smallwood, & Schooler, 2015). However, framing mind wandering as self-generated also is a bit extreme. It appears more likely that mind wandering is the result of dynamic interaction between the environment and the brain. Specific contexts do lead to an increased probability of mind wandering.

Causes of mind wandering. The causes for mind wandering are unclear. It could involve a failure of executive control (Kane, et al., 2007, Kane, & McVay, 2012), differences in cost and values associated with a task (Klinger, 2013), or the ease at which we perform the task (Levinson, Smallwood, & Davidson, 2012), or even the extreme difficulty of the task (Feng, D'Mello, & Graesser, 2013). Alternatively, mind wandering

may emerge as a result of intrinsic brain states (Mason et al., 2007), which are likely

repertoire of tools available for skills engagement with the world (Sporns, 2013).

Executive control. Failure of executive control may be a significant source of

mind wandering when external tasks are cognitively demanding either because of

difficulty or sustained attentional demands. The general idea is that there is a limited

amount of executive resources, often associated with working memory, and as the skill

becomes more difficult or sustained, these resources are diminished and less resources are

available to keep the mind on task (Feng, et al., 2013). However, it must also be noted

that all working memory tasks are simultaneously tests of mind wandering. Mackay

found that individuals who mind wander more also score lower on working memory tasks

(McVay, & Kane, 2012). The causal direction is not clear. It may be that those who mind

wander more may do so during executive skills tasks and thus their scores are lower or

even a third mediating variable that affect both. Mind wandering may therefore be

independent of executive control, but we lack the current instruments to separate the two.

Low task demands. Conversely if the tasks demands are low, mind wandering

may also be more frequent (Feng, et al., 2013; Levinson, Smallwood, & Davidson, 2012)

. This is likely due to the automaticity of simpler tasks. Interestingly individuals with

higher executive control tend to mind wander more frequently in these conditions

suggesting there is some separability of the executive control and mind wandering

(Levinson, Smallwood, & Davidson, 2012). Enabling mind wandering during simple

tasks offers some clear advantages. For example, if we are driving we can then shift our

attention from the process of attending to shifting gears and the movement of our feet on

the pedals and instead engage in observation of the traffic and potential dangers.

However, the downside is that in the case of a car we can automate all aspects of driving

and then focus on phone calls, texting, or daydreaming without paying attention to life

threatening situations. Similarly, if a reading task is easy then we can free up out mind to

not focus on the decoding task itself but on the imagery the task evokes. In this way mind

wandering while reading can be useful for the individual as long as that process is

monitored.

Yet a third possibility is that more complex tasks of reading such as syntactically

parsing, hierarchically structuring the text, and even processing the text's emotionality

may become similarly automated allowing for a subconscious processing of the text

allowing the mind to wander, but leaving the reader thinking they have not been paying

attention. Overall, it is clear that in the process of reading, the skill level of the individual

interacts with text difficulty to produce mind wandering experiences related to difficulty

or ease.

Emotional states. Internal states of the individual may also result in increases in

mind wandering frequency. Clues to this come from the content of off task mind

wandering episodes. Most mind wandering appears to involve reflections about self and

these tend to have negative affect such as rethinking a mistake or evaluating previous

social engagements (Smallwood, Fitzgerald, Miles, & Phillips, 2009). This approach

suggests that it is not the features of task difficulty but that the emotional state the reader

brings to the task be intrusive (Smallwood, & O'Connor, 2011). Extreme cases of this are

in rumination found in individuals with dopaminergic disregulation disorders such as

anxiety, depression and schizophrenia (Curci, Lanciano, Soleti, & Rimé, 2013; Deng, Li, & Tang, 2014; McGhie, & Chapman, 1961; Ottaviani et al., 2015). It is unclear what causes these thoughts except that they seem to spontaneously emerge from the individual in inopportune times causing the mind to wander off task. It is also clear that this is an endemic feature of mind wandering and not just a clinical problem. These negative emotional states associated with mind wandering appear also more common in cases which highlight stereotype threat (Mrazek, et al., 2011). Putting someone in a state that makes them think about themselves in a disheartening way could move their mind into ruminative behaviors.

However, emotionality of the text may also be a feature of the mind wandering experience (Bal, & Veltkamp, 2013). When reading a text, the individual may become emotionally aroused by events in the text. The events in the text may also remind the reader of events in their lives which arouse emotions (Smallwood, & O'Connor, 2011). An interaction with the text results in an internally aroused state which could interfere with attentional processes. This is vaguely parallel to the well-known Yerkes-Dodson curve (Teigen,1994), which broadly suggested that arousal and performance followed an inverted-U curve where extreme high or low arousal would lead to poor performance. As one increases in energy there is a sweet spot of best cognitive performance. If the text is too emotive or the individual is too aroused, this may reduce the cognitive performance and lead to attentional lapses (Lenartowicz, Simpson, & Cohen, 2013). This includes the influence of arousing substances such as caffeine (Watters, Martin, & Schreter,1997). However, the reverse is also true where boredom appears associated with mind

wandering (Baird, Smallwood, Schooler, 2010). As the mood changes as a function of life or task context there is a change in the frequency of off task thoughts.

Temporal attention. The time traveling aspect of mind wandering also gives us some important clues to its causes. While individuals may be distracted by thoughts of the past as mentioned above, they may also be distracted by thoughts of the future (Klinger 1984, 2013). When cognitive tasks are low there is a prevalence of future related thought (Iijima, & Tanno, 2012). In either simple or complex tasks there is the idea of competing goals (Unsworth, & McMillan, 2013). The current task may not be important for accomplishing other goals such as a test later in the day, the need to use the restroom, or preparing for a date. These future goals unrelated to the task itself can be a clear distraction from maintaining attention. Additionally, the task itself may offer competing goals. The reward of task completion vs task performance is in the same vain as intrinsic vs extrinsic motivation (Unsworth & McMillan, 2013). In keeping with this approach, the oral reading may involve multiple goals: complete the task as quickly as possible, make sure the oral performance sounds good, or comprehend the text, just to name a few. It may even be that the way we teach reading where individuals can read aloud without comprehension check may encourage the separation of these goals. We have all had the experience of waiting for our turn to read aloud and the need to perform socially may exceed the need to understand.

Intrinsic neural states. While this external and internal state interaction may account for increased frequency of mind wandering, the persistent patterns of knowledge in the brain create conditions for any of the above approaches to mind wandering to

occur. This is not in conflict to what is mentioned above but changes the focus from a skill based approach which examines behavior performance to a neurological approach which examines neurological foundations for skilled interactions. In this approach there is a persistent neural pattern that is common among all those who mind wander more. The history of the individual may build neural systems that facilitate mind wandering during oral reading. If this is the case, then these systems should be observable in the resting brain.

Neural associations with mind wandering. As mentioned above the study of the default mode network has been core to examining this phenomenon. Typically, the focus has been on using 0-lag correlation studies to examine how well the components of the DMN correlate with each other and conversely how much they anticorrelate with other attention networks. In this framework the DMN is the network responsible for mind wandering and when it is internally cohesive and comparatively more active, then mind wandering is also present (Christoff, Gordon, Smallwood, Smith, & Schooler, 2009). Additionally, self-reported frequency of mind wandering correlates with connectivity within the DMN (Kucyi, & Davis, 2014), where the less distinct the attentional and DMN are from each other, the more likely the individual will mind wander. It is notable that within-network connectivity in resting state scans negatively correlates with greater visual imagery and internal language use. This is similar to the process of mind wandering (Doucet et al., 2012).

However, this type of research has unfortunately led to focusing on the DMN and neglecting other brain regions. Most studies appear to use regions in the DMN as regions

of interest, thus excluding other regions. A metastudy addressing this very issue examined other regions associated with mind wandering using task based paradigms. Differential neural recruitment during mind wandering extends beyond the DMN as it is classically defined. Fox, Spreng, Ellamil, Andrews-Hanna and Christoff (2015) examined other neural regions identified in mind wandering studies. Their study examined 24 studies which employed experience sampling, or retrospective analysis involving questionnaires which could be used to explore the previous mind wandering experience. To operationalize mind wandering, comparisons were made with high vs. low spontaneous thought frequency. They confirmed in their meta-analysis a bias toward only examining the DMN ROIs which often limited possible findings. The results indicated that 13 regions were reliably associated with the mind wandering experience. This included all classical DMN regions and additionally the dorsal anterior cingulate cortex, right dorsolateral/rostrolateral prefrontal cortex, left ventro lateral prefrontal cortex, secondary somatosensory cortex, left temporopolar cortex, left mid insula, and left lingual gyrus. It is unclear if lateralization is an important feature of these findings or simply the more statistically significant finding.

However, none of these studies examine the lagged structure of the brain that may correlate with mind wandering. In fact, some of these studies make the faulty assumption that the DMN acts as a unit and look at its connection with other networks over time when examining connections. The DMN and the Salience or Attentions network anticorrelation has been predictive of mind wandering while reading (Smallwood, 2013). Additionally, Beaty, Benedek, Kaufman, & Silvia (2015), suggesting that the DMN and

the Salience Network couple more efficiently in creative individuals. Research examining these networks in goal-directed cognition proposes similar coupling mechanisms (Spreng, Stevens, Chamberlain, Gilmore, & Schacter, 2010). This is based on the very precarious assumption described above in Part 1 that neural networks work together only in a time-locked manner as if they are neuronal assemblies in a task. However as described above, networks may also, and in fact are likely, to act in cascading or sequential manners with high correlations lagged across time that do not respect classical resting state connectivity boundaries. The present analysis seeks to examine just such a correlation based on the findings in the previous section.

   DMN components. Because consistent representation of the DMN was found to be implicated in mind wandering studies, it is worth breaking down the components as they are classically described (Greicius, Krasnow, Reiss, & Menon, 2003). The DMN consists of regions which tend to show strong within-network connections which tend to be non-reciprocal. To avoid confusion we will henceforth refer to the DMN as Default mode Regions. A medial temporal subset involves regions which are differentially recruited in other tasks requiring prospective and retrospective thinking about self, as well as constructions of mental scenes. A second subgroup, the dorsal regions have been associated with tasks requiring social judgements, social perspective, or social imagination (Immordino-Yang, McColl, Damasio, & Damasio, 2009; Yang, Bossmann, Schiffhauer, Jordan, & Immordino-Yang, 2012; Spreng, & Grady, 2010). A major hub linking these regions is the medial prefrontal cortex as well as the posterior cingulate cortex.

Other cortical regions. A number of regions outside the traditional Default Mode

Regions have also been identified and been thought to indicate network coupling (Uddin,

Clare Kelly, Biswal, Xavier Castellanos, & Milham, 2009). Primarily among these is

another set of regions that have been termed the Parietal Control Network. As the theory

goes this control network flexibly couples with the DMN to assist in the strategic

switching emphasis of internal vs external focus. However, if we recognize these

traditional resting state networks not as networks but regions with strong internal

connectivity which is non reciprocal then this interpretation falls apart.

Fox, Spreng, Ellamil, Andrews-Hanna and Christoff (2015) described some of the

possible reasons for other regions being implicated in mind wandering. The insula and

somatosensory areas reliably also appear in studies of mind wandering. It may be that

these regions often being associated with internal body states may account for the fact

that sometimes mind wandering can be stimulated by physical changes in the body like

those which are emotional. The inclusion of the insula in mind wandering is particularly

important when we examine the role the insula pays in perception of emotional and social

pain (Eisenberger, Lieberman, & Williams, 2003; Straube, & Miltner, 2011), features

associated with mind wandering contents. The lingual gyrus of the occipital lobe has also

been associated with mind wandering and has been attributed to visualizing (Ganis,

Thompson, & Kosslyn, 2004). The authors also point out that the temporal polar cortex is

also differentially engaged and while being associated with mentalizing, is also

associated with word retrieval (Mesulam et al.2013). Considering much of mind

wandering often involves internal voice this is not surprising. Overall, it is clear that mind

wandering, like all mental processes likely involves the recruitment of many neural regions, and due to the great variety in reasons and contexts for mind wandering, many more regions are likely to follow. No studies yet examine how mind wandering while reading aloud may be related to resting state scans at another time period.

Furthermore, to date, there are very few studies examining the temporal nature of mind wandering that do not rely on 0-lagged network analysis. The predominant method is to obtain resting state fMRI data and then use 0-lag methods to define networks or use a mask to define networks. These networks are then observed across time during resting state and their correlations across time are observed. This correlation is assumed to represent network coupling, how one network influences the other. However, there are problems with this approach as mentioned above.

Mind wandering and mind-brain relation. However, there is a conceptual hurdle to discuss when it comes to studying mind wandering during resting state. One could say that resting state is a mind wandering task. In this approach we are not observing a relatively closed system during resting state, but we are observing an active task driven by the individual. In other words, when we ask the individual to keep their eyes open but just let their mind wander, we are giving them a task to perform. We clearly make that statement when placing someone in the scanner for resting state scans. This idea comes from a dualist perspective of mind wandering. In other words, somehow the mind is separate from the brain, but perhaps emergent from it, drives the state of the brain into a mind wandering state. As we took some pains to explain in the first part of this document,

this dualist approach is rejected on philosophical grounds and is rejected by the current metatheoretical approach.

The approach taken here, is that when we isolate the neural system, ongoing dynamics will be the result of the organism's history, stabilizing within-network dynamics that are based mainly on internal attractor states. When the system settles into these attractor states mind wandering emerges as a behavioral and mental product. What is brought to conscious awareness and reported later is a small part of the process only reveling how the individual made sense of the experience and how well they can reconstruct memories of that experience. As a side note, after resting state it is common to probe individuals for what they were thinking about. Through working with the participants in this study and others, I have anecdotally noticed that they frequently do not know what they were thinking about and the probing may be forcing them to make sense of the experience or reveal a fraction of it. This might be because of intentional forgetting as they shift back to daily activities and social interaction as reported by Delaney, Sahakyan, Kelley, and Zimmerman, 2010), but whether this is intentional or incidental is also a question of dualisms. In daily life mind wandering is the result of an interaction of external and internal events which result in relative external perceptual isolation which may be accompanied by a sense of control or not. A mind wandering state is a resting state, but in the scanner there is less likelihood of external events leading to externally focused attention. Therefore, I am taking the approach that resting state is a relatively closed system that will allow for the emergence of intrinsic system dynamic attractor states which will be indirectly observable.

In what follows, I shall seek to examine what the characteristics of the population are and the task materials as they pertain to oral reading. As we can clearly see from above, a host of internal and contextual factors frame the mind wandering experience; it is therefore essential to characterize these factors in detail for interpretation of findings. I will then relate these behavioral measures to mind wandering. Having characterized this particular mind wandering experience as it pertains to oral reading in the current population, we will then seek to identify those differences in lagged network dynamics that correlate with mind wandering.

Oral reading and mind wandering. In this section, I shall examine the behavior of mind wandering as it correlates with comprehension, oral reading anxiety, and fluency; but, we also want to know the latent biological structure of knowledge which may correlate with these reading styles. Might an analysis of persistent representations of this skill in neural lag structures observed during rest reveal latent differences in the repertoire of stored knowledge worth exploring in readers whose minds wander more frequently while reading?

As I shall discuss, literacy itself restructures our brains and leaves a neurological representation of the gained skill (Dehaene, Cohen, & Morais, 2015). It is not a far leap to assume that variations in literacy practices would lead to similar persistent restructuring. The current study examines oral reading practices as an entrenched skill in individuals which may be evaluated through connectivity studies of approximated neural patterns when an individual is not engaged in an external task. This part of the exploratory study will examine resting state network activity over time as one indicator

of structural and dynamic differences and how it correlates with the frequency of mind wandering while reading aloud. We will explore how identified differences might contribute to the frequency of mind wandering while reading aloud.

Resting State and Reading. In an examination of mind wandering while reading aloud, it is also essential to review how resting sate correlates with reading in general. Mind wandering is potentially a difference in these network relations.

A number of studies have begun to examine inter-individual resting state network configurations and reading skills with mixed results. One of the first exploratory studies on this front involved resting state analysis of previously implicated neurological regions implicated in reading to better understand the relationship between regions and networks. Koyama and colleagues (2010) examined the resting state patterns of 25 adult English language readers. Six ROIs were selected based on a series of task based studies involved in word reading in a variety of alphabetic languages. These included the left FFG, left superior temporal gyrus, left temporoparietal junction, left pre central gyrus, left inferior occipital gyrus, and the left inferior frontal gyrus.

Particularly notable among these selections was the left FFG which has been identified as the "Visual Word Form Area" (Dehaene et al., 2010; 2015; Dehaene & Cohen, 2011; Dehaene, Le Clec'H, Poline, & Le Bihan, 2002). This region has been implicated as representing the orthography of a given language in a hierarchical fashion moving from single letter recognition to digraphs and whole words. Dehaene (2015) also suggested that the specialization of this area may be due to the adjacent fusiform face are and place areas allowing the reader to take advantage of evolutionarily established skills.

Other areas selected included traditional language areas of Wernicke's and Broca's areas implicated in speech perception and articulation respectively as described above. A region which was excluded from the data was the left angular gyrus which had been implicated in reading because of its hypoactive behavior in dyslexics; this region was excluded because it has not been implicated in fluent reading (Finn, Shen, Holahan, & Scheinost, 2014). In a connectivity analysis of these regions they were able to find strong connections between regions that were implicated in task based studies (Koyama et al., 2010). Also, they found that the increased network connectivity of these regions was inversely related to DMN activation. This would be expected as readers must focus externally to decode words. Regions of the frontal networks were inversely activated with reading networks, this suggested that word decoding skills are automated and require little guidance from frontal regions involved in problem solving. Unexpected was the finding that reading networks were not left lateralized with the exception of the FFG and IFG which were left lateralized but not limited to the left. There was strong bilateral activation for these resting state networks implicated in reading. A clear short coming of this study is that it did not take any behavioral measures.

In a later study, Koyama and colleagues (2011) examined differences across age groups. In this study 25 adults and 25 children were given subtests of the Wechler Abbreviated Scale of Intelligence (WASI) and the word reading section of the Wechler Individual Achievement Test (WIAT-II). Because general IQ and reading decoding skills highly correlate, general IQ scores were used as a between subject covariate to help identify difference sin resting state that were unique to word decoding skills. Correlation

matrices were constructed for each individual for all 11 ROIs giving 55 pairwise correlation coefficients each of which was then correlated with the reading scores from the WASI-II. Significant correlations were identified between reading competence and connectivity, the strongest of which was between the FFG and IFGop. This correlation was negative for children and positive for adults. This finding was interesting considering the FFG is important for visual word recognition. This suggests that the developed and integrated orthographic functions of the FFG become more important in reading for older adults who are better word decoders. For all groups stronger connections between motor regions and the classic language regions (Broca's area and other areas implicated in phonology) correlated with word decoding ability. This reading network connectivity was inversely related to DMN activation, supporting later findings that DMN activation may be down regulated when paying close attention to a reading task (Smallwood, 2013). This study examined only children 8-14 years and adults of 20-46 years. It excluded the current groups of adolescents that are under examination in this study from 17-19 years. In any case, this study strengthened the use of resting state connectivity measures as a way of examining network availability for reading tasks by including a reading task (albeit a very limited one) and revealing age related differences in reading network connectivity.

The current study examined network connectivity in bilingual individuals, therefore, it is essential to show that these results can be extended to bilinguals. Resting state functional connectivity analysis was carried out on 43 Chinese-English bilinguals aged 19-24 years (M. Zhang et al., 2014). They were able to show similar results with

this bilingual population even though one of the languages was not a traditional alphabetic language. (Although it has been reported elsewhere that both iconic and alphabetic languages rely on statistical mappings related to phonological representations and are not, therefore mutually exclusive systems (Dehaene et al., 2010). In this particular study an additional reading evaluation was used: the Test of Word Reading Efficiency (TOWE-SWE) and the Chinese Character Reading Efficiency (CCRE). Both tests were word recognition tests basically counting the number of words that could be read correctly in 45 seconds with test items arranged from easy to hard. Like Koyama (2011) a general intelligence measure was taken and used as a covariate. In this case Ravens Advanced Progressive Matrices (RAPM) was used. From the list of 11 ROIs in Koyama(2011), 8 ROIs were selected each with a 6 mm sphere. There was no significant relationship found between resting state connectivity measures and RAPM, but there were correlations found between reading scores and reading network connectivity. Of particular note, there was no significant difference between resting state connectivity maps associated with Chinese and those associated with English. These results bolster the validity of using resting state analysis to examine neurological foundations of reading ability. They are particularly important for the current study because they show that resting state connectivity results correlate with reading scores regardless of bilingual-monolingual status.

Important limitations of all these studies is that reading ability is simply defined as word recognition ability and decoding. However, as discussed above reading has many more skills involved than simple decoding.

It is hypothesized that some of these regions may be important in describing the resting state findings in lagged structure. Perhaps differences in the lag networks related to these other regions may be the foundations for mind wandering while reading aloud. However, I shall not be using general intelligence as a covariate as was done in the studies above. General intelligence is a combination of many skills and by regressing out this feature, it may actually remove regions of particular interest in this study. There is also no theoretical reason for doing so because we do not know how general intelligence correlates with lagged networks.

Aims. The basis for this particular study is based on the foundations built in Part 1 of this dissertation whereby sequential neural activity recorded in the brain at rest is a persistent representation of knowledge or a repertoire of available skills. In this vein, we shall attempt to use the regressors for the projection lag vector and the principle component model with 5 components. This assumes that these lagged networks are persistent representations of skilled engagement with the world. Although we are theorizing that the representation in Part 2 are perceptual in nature, perception is also a learned skill and part of the knowledge framework with which we engage the world. A more detailed analysis of higher component models should be the study of future investigations.

Methods

Participants. From the study used above to generate group level representations only a subset of 38 participants were used for this analysis. All participants were self-identified fluent bilinguals as described above. All were born in the United States. Their

ages ranged from 16 to 20 (m=17.65, SD 1.07) years. All participants were neurologically normal with no reported psychiatric or neurological disorders. All reported being able to read with minimal help from corrected lenses. None were under the influence of psychotropic drugs. Ethnic makeup consisted of (27) Latinos, (2) Filipino, and (9) Chinese. There were (18) boys and (12) girls from a series of high-schools in the Los Angeles area.

Procedure. The oral reading procedure took place in the afternoon approximately 2 hours after the fMRI scanning procedures. No assumption is made that the oral reading procedure affected the resting state scan, instead the assumption is that the scan captured persistent neural representations of knowledge during resting state that were available for the later reading task. The reading task uses non standard measures with an attempt to capture a specific type of behavior which was produced in Feng, D'Mello, Graesser (2013) and Franklin, Mooneyham, Baird, & Schooler (2014), both studies which examined mind wandering during reading. Therefore an extensive discussion will be included to describe the features of the reading material in the current study.

Preparation. The reading procedure took place in a small bare office with a small window at the participant's back. All instructions and debriefings were conducted by the same experimenter who sat next to the participant for the preparation and debriefing.

To introduce the participants to the task they were told the purpose of the task was to "assess reading patterns" and given a definition of mind wandering and a brief discussion verified their understanding of the concept. They were asked if they ever experienced the sensation of having read a passage but not paying any attention to the

text because they were either "zoning out, thinking of something related to the text, or thinking of something unrelated". They were then introduced to the scale of mind wandering and it was verified that they understood this scale before continuing. The participants were then given task instructions.

Participants were told that they were going to be presented with a story across a series of slides and were told that following this presentation, they would be asked what they remembered from the story. They were instructed to read the slides aloud; they were told that no silent reading was permitted, and they should refrain from reading sections multiple times to remember the content. Participants were asked to sit upright and tilt the laptop screen to a comfortable angle. Proper posture was ensured before participants began to limit any effects poor posture would have on oral reading practice; this was then verified in the video recording. They were asked to read in as natural a voice as possible and read the text as they felt "the author intended it to be read". They were told that after reading a slide they would press the spacebar to advance to the next slide where they would make a mind wandering rating and then continue to read the next section of text.

Oral Reading Task. The oral reading task took place only after the experimenter left the room; this was in effort to minimize oral reading anxiety and a sense of social awkwardness. The participants were instructed to press the space bar when they were ready to begin. The participant was then presented with the first screen of text from the story. When they pressed the spacebar to advance to the next slide, they would be presented with the mind wandering scale. Once participants made a rating, by depressing the corresponding number on the keyboard, the screen advanced to the next sections of

text. The final slide told the participant to leave the room and get the experimenter who was not observing but was in an adjacent room.

Debrief. After the experimenter returned, the participant was asked a series of questions. The first question asked the participant about the content of their mind wandering. They were then asked to make an aggregate rating of how much mind wandering they think they did and the final mind wandering question asked participants to reflect on their general frequency of mind wandering while reading for school or recreation.

Following this, the participants were probed for comprehension of the story. They were asked to retell the story in as much detail as possible, then probed once more for additional information. When no more information was given, participants were asked 18 open ended questions for an additional comprehension check.

Finally, participants were asked a series of likert style questions to explore how much anxiety they experience when being asked to read aloud. These questions were adapted from Saito (1999) and are available in Appendix D. Anxiety endemic to the task of oral reading may lead to differences in mind wandering.

After completing the reading tasks in a subsequent debrief, all participants informally reported feeling engaged by the reading task and not feeling exhausted from other tasks in the day. The entire time for the oral reading task and debrief lasted approximately 17 minutes.

Behavioral Measures

Mind Wandering Probes. In Franklin et al. (2014) mind wandering probes were presented to participants at predetermined points in the text. The current study differed from Franklin et al. (2014) in that it attempted to get at mind wandering as a continuous variable as opposed to a categorical. Mrazek, Smallwood, & Schooler (2012) similarly assessed mind wandering by using a 7-point scale ranging from one to seven ("completely off task" and "completely on task"). However, it was recognized during piloting that these ratings may be confusing to the rater as thoughts about the story may be interpreted as on-task although they may remove attention from the current practice of reading. Thus, the scale used here asked only for amount of general mind wandering which included both on- and off-task thoughts that interrupted the flow of reading. The rating scale was from 1-5 with one being no mind wandering and perfect attention to text, and 5 being so much mind wandering that they are not sure what they just read. This construct was general enough that participants could easily recognize whether it occurred. Participants in this study were presented with this mind wandering probe 17 times during the oral reading session at predetermined intervals avoiding breaking the story mid-sentence or paragraph. Intervals did not vary between participants. The time it took participants to make the rating was usually less than one half a second indicating that the process was a minimal interruption to the reading task.

The content of their mind wandering was probed immediately afterwards during the debriefing session by asking them the question "What did you mind wander about?" This allowed for validation of the type of the construct and later qualitative exploration.

To verify that they followed directions for the rating scale correctly, they were also asked how much mind wandering they thought they did during the task additionally this offered an aggregate metacognitive measure of mind wandering awareness.

A likert scale was used to assess how much the participants perceive that they mind wander on a daily basis while reading texts for school and for recreation. This 5-point scale ranged from "I never mind wander while reading" to "I struggle with mind wandering every time I read."

Comprehension measures. To check whether the participants attended to and understood the text, the reading task was followed by a free story retell. Participants were asked to "Retell this story to me in as much detail as you can." Students were then encouraged one after a brief pause by saying "what else can you remember?" Although no retell procedure as of yet has been determined to be optimal, these prompting procedures are consistent with a wide variety of retell approaches (Reed, 2011; Reed & Vaughn, 2012). Retells were recorded in audio format and transcribed. In a meta study, Reed and Vaughn (2012) found that 41 of their 54 studies evaluating retells used some quantitative measure based on number of words or propositions. All retells were therefore divided into propositions and propositions were coded as correct, correct inferences, or incorrect. A number of scoring methods have been developed for recall. Several of these were used here to validate each other. The first of these was simply the total number of words recalled which has been shown to correlate with both interest and retention and is a rough estimate of number of propositions (Naceur & Schiefele, 2005) A second approach taken in scoring involved counting the number of propositions. For this method,

procedures outlined in Gambrell, Koskinen, and Kapinus (1991) were followed: each correct proposition or inference was given 1 point, and incorrect propositions earned a negative points; points were then summed. Propositions were counted only once if they were repeated and while proper nouns were counted propositions, referents were not. Additionally, an overall rating of the completeness of the "main idea" was included. This was a summary statement ranging from 1-3 ("none," "some," "all"), indicating that the retell demonstrated understanding of the gist or overall main idea of the passage. This is similar to what is found in Woods and Moe (2009).

Finally, 18 open-ended questions were used to validate the retell measure. These questions addressed at least one proposition per slide. These answers were either marked as correct or incorrect. While retells indicate the number of propositions spontaneously recalled, questions about specific story elements may engage recognition of propositions understood, but not remembered. Thus, these additional questions further reveal the participant's comprehension of the text. Each slide was represented at least once in these questions.

Anxiety measure. Because anxiety may reduce the capacity of working memory (Darke, 1988) and therefore increase mind wandering (McVay & Kane, 2012), anxiety for oral reading was measured. There is no known measure for oral reading anxiety in first language, so one had to be adapted from previously used scales in foreign language reading performance. It is likely that there are some similar performance anxiety issues that the instrument would get at. Five likert style questions adapted for the oral reading performance anxiety were taken from the Foreign Language Reading Anxiety Scale

202

(FLRAS) (E. K. Horwitz, Horwitz, & Cope, 1986) and validated by Saito et al. (1999).

The questions were adapted from the FLRAS which was found to have strong concurrent

validity with the Foreign Language Reading Anxiety Scale (FLCAS) as shown in the

Pearson product-moment correlation coefficient (r =.64, n=383). The FLRAS showed

strong internal reliability of .86 (Chronbach's alpha, n=383). It has been tested on

Russian, Japanese, and French. However, we are using it with English which is the first

language for the participants. Additionally, changes were made to the questions so that

they related to oral reading in the first language and only a subset of questions were

appropriate. The participants were asked whether they "strongly agree" to "strongly

disagree" on a scale from 1 to 5 for the following four statements: "I start to panic when I

have to read aloud without preparation," "I can feel my heart pounding when I'm reading

aloud," "I feel very self- conscious about reading aloud," and "I get nervous and

confused when I am reading aloud." At the time of this procedure no known oral reading

instrument had been previously validated with the target population; while its validity in

the current study can be questioned it is nonetheless a proxy for oral reading anxiety.

   Other cognitive measures. Cognitive measures were taken for two reasons, first

they have historically been associated with neural connectivity in 0-lag studies, they

appear to correlate with mind wandering frequency, and they also correlate with other

reading measures. Two cognitive measures were taken. The Wechsler Adult Intelligence

Scale-Third Edition (WASI-3) was administered to get a proxy of intelligence (D.

WechslerPsychological Corporation, 1997). This has been used as a covariate in previous

studies examining neural connectivity and reading comprehension (Horowitz-Kraus,

DiFrancesco, Kay, Wang, & Holland, 2015; Horowitz-Kraus, Vannest, & Holland, 2013).

But, as mentioned above, these are not being used as covariates in the current study and

only included to see if they correlate with reading. There are notable issues with this

measure as it tends to only correlate weakly with other measures of working memory and

so lacks convergent construct validity (Kane, Conway, & Miura, 2007). Vocabulary, full,

and matrix results were taken.

As a proxy for working memory capacity the N-back measure was used. Variance

in N-back appears to vary independently from digit span measures, for example. But, it

still has some validity as a general measure of fluid intelligence and higher level

measures of intelligence particularly in terms of individual differences (Jaeggi,

Buschkuehl, Perrig, & Meier, 2010). The task was completed 4 times and results were

averaged. The basic procedure involves displaying a number of items on the screen

sequentially. As the items appear the participant is asked at random time points to identify

the item that was presented two items back. Participants respond to this task using a

keypress and then indicated their answer to the experimenter. To complete this task

successfully, they must maintain information in their short-term memory buffer and then

respond after a decision making process. It thus involves a variety of short term cognitive

skills. Due to the wide variety of ways that the task is implemented there is no reliable

psychometric data on the test. Because I am working with an existing data set, this

measure was the only one available as a proxy. As mentioned above, working memory

has been shown to correlate strongly with the amount of mind wandering (McVay &

Kane, 2012).

Reading material. The reading material was selected specifically for its emotional range. It was meant to be both engaging and stimulate a strong emotional reaction in the participants. This material was read aloud with intermittent mind wandering ratings as described above. The procedure was similar to the mind wandering study conducted by Franklin et al. (2014), in which participants read a detective story aloud; however, the story here was selected to have a wide range of emotionally charged content to elicit emotion. The material was selected after piloting a series of randomly selected excerpts from similar reading material with a small group of undergraduates. This material was reported as most engaging out of a random selection of 5 excerpts, but also very likely to induce mind wandering. Previously standardized fluency texts typically used in oral reading measures (Rasinski, 2004; Rasinski, & Hoffman, 2003) were not used because they lacked the emotional variation and were not sufficiently long to lead to multiple instances of mind wandering. Additionally, the detective story, nor the previously standardized fluency measures contain material which would be read in standard reading encounters where in the public newspapers.

As such, evaluating reading ability and mind wandering was done with an authentic and emotionally charged and ecologically valid reading sample, an excerpt of Ron Suskind's widely read New York Times article (2014) was extracted discussing his relationship with his autistic son and his son's developmental changes. The New York times was chosen due to its usual high level of readership and expected range in readability across the text. The New York Times tends to have articles ranging from 6th to 14th grade reading level. Because of this wide range, the readability will be analyzed in

detail below. The total excerpt was 1601 words. The excerpt presented participants with a clear exposition, climax and resolution narrative devices. The complete excerpt of this article is included in appendix D.

Presentation of text. The story was presented on a 12-inch laptop computer screen tilted so that it was a comfortable reading angle for the participants. Black text was presented on a white screen at a font size of 24 points, Ariel font, and no accompanying images. Slide presentation time was controlled by the participant who either pressed the spacebar or made a mind-wandering rating to advance to the next slide.

Although Franklin (2014) presented one sentence per slide, this was less desirable in the current study because of the loss of visual structuring of the text available to the reader which offers important cues. Because the Franklin(2014) study presented one sentence at a time, there was no need for the participants to "chunk" the information and was therefore less like authentic reading experiences. Slides in the current study varied in length due to efforts to keep from breaking paragraphs or meaningful segments of text across screens so some artificial breaks still occurred. The presentation consisted of 32 slides in alternating order beginning with story segment followed by a slide probing for mind wandering. The slides with story text displayed a mean of 104.56 (SD=33.32) words per slide.

The 16 mind-wandering probe slides displayed a likert scale of 1-5 centered on the screen at 28 point Ariel font. Above the scale were the words "no MW" and "Greater MW" above the numbers 1 and 5 respectively from left to right. Once the participant

made a rating, by using the keys at the top of the keyboard, the next section of the text was automatically presented.

MATLAB was used to present the stimuli and record keyboard responses and both audio and video format of the reader's face. Participants were video recorded from the camera embedded at the top of the laptop screen, and the microphone embedded in the surface of the laptop.

Story readability. This section will seek to answer two main questions about the selection of reading material: what is a holistic readability for the selected texts, and what is the ongoing dynamic readability measure to examine readability changes across the story. The first will address the appropriateness of the reading material and the second shall act as a dynamic variable compared to other ongoing measures.

Holistic readability measures. Measures of readability were applied to the text to determine an estimate of reading difficulty. In general readability metrics attempt to take into account both syntactic difficulty inferred through sentence length and semantic difficulty as inferred from the frequency word lists or the average number of syllables per word (Fry, 2002). Overall readability measures are preferred to leveling in the current study due to their reliable objectivity and application to older populations: grades 1-17 (Clay, 1991). Here, six measures were applied to the text to determine its general accessibility to the age group in this study addressing readability from word familiarity lists, syllable counts, and/or sentence length. Unless otherwise indicated the readability formula was applied to the first 600 words of the text, a standard practice for assessing readability (Clay, 1991). All participants in this study were either in the 11th grade or

207

higher. The goal of any readability measure is to indicate the projected years of formal education required to easily read the text therefore readability below 11th grade should be appropriate. This is a measure of the text; and not a measure of individual skill, to be described with other measures in the measures section below.

To obtain a reliable readability measure three approaches are used here to determine the appropriateness of the text for the participants under study: using previously established age level vocabulary lists, average word length, and a hybrid sentence length and number of syllables. Of the literally hundreds of readability measures the present measures are commonly used with the age group under current investigation, and are frequently used in the readability literature. Readability measures which are standardized only for younger age groups are not discussed.

Dale-Chall's index uses a list of "hard words" and sentence length to determine the difficulty of the text. This method was designed and tested on higher grade levels. A "hard word" is defined as any word not on a list of words easily readable to the average fourth grader. The number of words in the current material not found on the list was 88 (13%). This gave a level of 2.518 for the material and the adjusted score (+3.637) for grades higher than third bringing the final raw score to a grade level of 6.2. This scale increases the difficulty based on absence from the list of words and each time the same words appear they are counted in the final raw score. Utilizing word frequency measures, the current text is below the grade level of the students in this study.

Another approach is to evaluate the text based on the number of syllables in words as an indicator of word readability. These methods are applying Zipf's principle of

abbreviation which has repeatedly shown that more frequently used and therefore more familiar words tend to be shorter in length (George, 1935). Thus, fewer syllables is an approximation of semantic specialization and word frequency as well as ease of production. It is of course true that syllable length can often be misleading but it does tend to be a good statistical indicator. The FORCAST-Strict 73 readability formula was designed to evaluate training material for newly enlisted members of the US armed forces which tend to be around the age of 18, similar to our current sample. It tends to err on the side of assigning a higher grade level due to the average education level of the enlisted member for which this measure was designed (Caylor & Thomas 1973). This readability formula evaluates a text's readability by taking into account the number of 1 syllable words per 150. Averaging the 150 word segments from the 600-word selection resulted in 118 one syllable words per 150 words in the text giving a readability index of grade 8.2. The opposite approach is to look at the number of polysyllabic words in a text. The Simple Measure of Gobbledygook (SMOG) readability index utilizes this approach (Laughlin, 1969); in the selected text of 600 words there were 56 polysyllabic words; by entering this into the SMOG formula we get a SMOG index of 6.1. This measure was validated with standard comprehension measure of the time requiring 100% comprehension for individuals in the associated grade level. These measures of readability by number of syllables also suggests the text is within the readability range for this set of participants.

To attempt to account for syntactic complexity the length of sentences is also used. This relies on a supposition that longer sentences are more syntactically complex as

well as require maintaining more information in working memory while reading a sentence. This second point is supported by research demonstrating that "heavier" noun phrases require more working memory resources than light noun phrases (King, Just, 1991). Three indexes are in regular use that evaluate text through a combination of sentence length and syllables. The Flesch-Kincaid formula used in a variety of settings indicating the general readability of informational pamphlets, resulted in a score of 78.8 indicating a grade level of 5.5. This scoring method has been validated with older readers and has been adopted as a standard by the US army (Ley, & Florio, 1996). Fry's readability index is an approximation of readability taking into account both the average syntactic complexity indicated by the number of sentences per 100 words, and the average semantic complexity indicated by the number of syllables per 100 words. The first 600 words of this passage had 136 syllables per 100 words and 8.4 sentences per 100 words; when applied to Fry's readability graph this indicated that the text was at a sixth-grade reading level. Finally, the Gunning-fog formula which was originally designed to help evaluate the readability of newspaper writing also combines sentence length and syllable information. The Gunning-fog score includes the average number of words per sentence and the number of three or more syllable words out of the total number of words in a sample. The total number of words with 3 or more syllables was 46 and the average sentence length was 12; indicating a grade level of 7.6 again indicating that the reading level is below that predicted for this age group. (Note that in this index proper nouns, compound words and inflectional suffixes are not included in the syllable count).

Readability and comprehension scores. The Gunning-FOG formula, originally designed to help evaluate the readability of newspaper writing correlates high with comprehension (r=.91) This indictor takes into account both sentence length and percentage of "hard words" which are those with more than 2 syllables. The FORECAST readability index, has correlated poorly with comprehension, but was designed for young adult recruits in the US military. It correlates with comprehension at r=.66. However, the FORECAST formula correlated highly with the Felsch Reading Ease formula at r=.92. Another way to evaluate the two measures is through how much of the variance in text difficulty can be explained by the scores as measures with reading comprehension scores. The FOG index is determined by 90% comprehension. It has been cross validated with the Fry, Dale Chall and Flesch indices giving strong cross correlations of .95, .88, and .91 (Meade and Smith 1991). The Gunning-FOG formula also has the added benefit of taking into account average sentence size. Thus is includes a measure of complexity and word difficulty.

Holistic ratings of readability discussed above were between grade levels 5.5 and 8.2, all of which are below the target population. On average, the readability across all 6 measures is a grade level of 6.6. Table 2 summarizes the above information for the first 600 words of Suskind (2014). The current participant group ranges from eleventh to thirteenth grade. All measures indicate that the readability should be appropriate for this age group.

Fluency and readability. In addition to verifying the appropriateness of the level of the selected reading material, the current study does not only examine reading success

in terms of comprehension, but also fluency. While for the most part these scores are developed with comprehension in mind, limited work has been done to validate them with fluency scores. Because the current study also evaluates various indicators of fluency, a general caveat must be made regarding the use of readability indexes for difficulty of reading fluency.

Because fluency measures are of central concerning in the current study it was important to find measures that correlate well with fluency and comprehension to rate the text. Overall, reliability of readability measures for predicting fluency is mixed. Ardoin, Suldo, Witt, and Aldrich (2005) indicated that these widely used measures were also not equally valid. They tested the association of these scores with WCPM on 99 third-grade students of varying academic ability. FOG, SMOG and Forecast were modestly related to WCPM. Overall, these showed the expected inverse relationship between increased difficulty and WCPM scores. Importantly, their study also examined the validity of using windows of analysis for 40, 100, and 150 words to predict reading fluency. Two measures stood out and will be used to evaluate these moving averages: the FORCAST and the Gunning-FOG index. Each of these was originally designed to assess adult reading material adding to their ecological validity in the current study. I will briefly mention their correlations with comprehension and fluency measures.

Using a Kendall's tau value to represented the association between WCPM and readability estimates, both Forecast and Gunning-Fog showed a medium correlation with WCPM (.46 and .41 respectively) such that increases in the number of words per minute correlate with increased grade level in readability. Importantly, these measures did not

vary appreciably between measures containing 40 words or 150 words, changing to .48

and .34 respectively. Notably, this study also revealed that none of the measures of

syllables per word, length of sentence, or usage of word lists alone out performed either

Forecast or Gunning-Fog formulas.

Ongoing readability. While these measures are used to sample the text's

readability as a whole, the current study also seeks to understand readability as a moving

score across the text. Readability is thus seen as a dynamic measure changing over time.

The moving reading difficulty level across the story was measured in two ways. First

using a 100-150 word sliding window always rounding up to the nearest complete

sentence and secondly the readability was rated for each slide in the presentation. It was

important to get this moving average because each slide would have a measure of mind

wandering and its relationship to reading difficulty had to also be assessed. The

FORCAST index was designed for military recruits which are of young adult age. It was

designed because the existing measures for elementary age readers showed large margin

of error for older age groups. When cross validated against the Flesch and Dale-Chall

formats it was found to have high correlations in the .98 and .95 range respectively.

However for this older population it had a narrower standard deviation for grade level

being 2 SD instead of the 4 SD found in the Flesch and Dale-Chall for this age group

(Caylor and Sticht, 1973).

FORCAST was shown to have the highest reliability for readability within

subjects for a variety of reading materials (Ardoin, Suldo, Witt, and Aldrich, 2005).

However, due to its lower correlation with comprehension, the Gunning-FOG index was

also used which has a modest correlation with WCPM in the Ardoin et al. (2005) study. The Gunning-FOG formula additionally evaluates syntactic complexity by sentence length. The Gunning-FOG formula requires full sentence segments so the moving average will always be broken at sentence boundaries.

Settling on the Gunning-Fog and FORCAST formulas analysis will be completed by starting with the first 100 words rounding up to the next complete sentence. The FORECAST formula does not require complete sentences but I will use complete sentences to align it with the Gunning-fog index. A grade level is obtained for the first 100 words, then I will slide the window by one sentence and recalculate and so on until the entire text is completed. By sliding the window in this way the score will either rise or fall based on the most recent sentence. This dynamic representation can be observed in figure 18. Trends in mind wandering, and fluency will be compared to this moving average for each participant. The mean FORECAST index per slide was 9.105 (SD 0.654) and the mean Gunning-FOG index was 8.463 (SD 3.243). Wider SD is expected for this text in the Gunning-FOG formula due to the short length of sentences in some dialog.

Thus measuring the readability of the text gives us two very important points of information: the text is below the assumed reading level for all participants; the reading difficulty changes across the text giving us a useful dynamic measure.
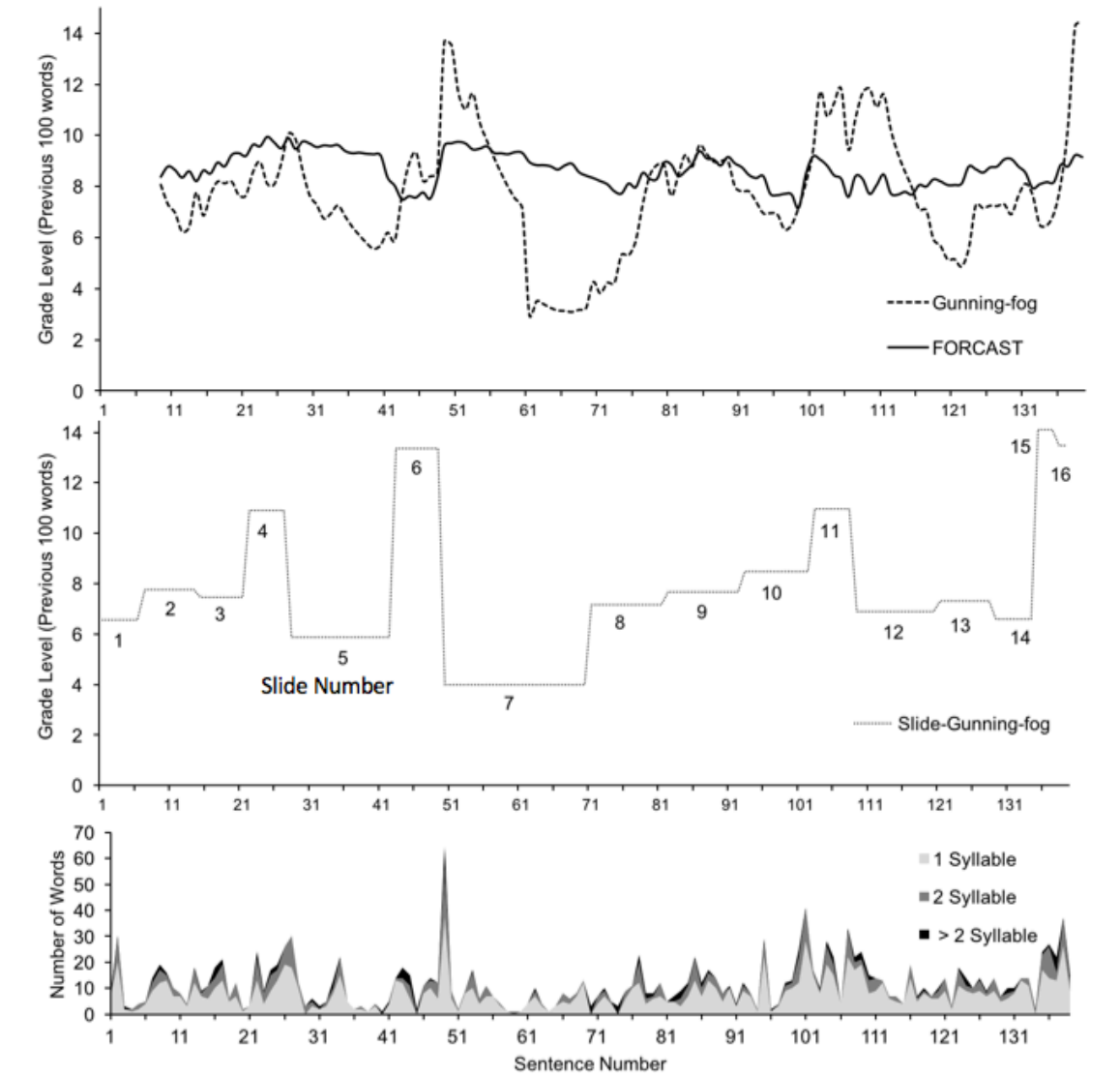
Figure 18. This was the graph which was used to examine ongoing readability. Mind wandering scores were overlaid for each participant, but no systematic relationship was discovered. This is only presented here as an illustration of the method.

Neural Analysis. All neural data for the current analysis was preprocessed using the methods described in Part 2. While the group analysis averaged and removed outliers as defined by the Tukey method, the individual maps were complete and unaltered. This was because it was not clear whether lag outliers may actually correlate with the behavioral variables of interest.

Projection maps. The projection maps for individuals were prepared the same way as the group representation above. Basically the 18,715x18,715 matrix was averaged across rows resulting in a 1 x 18,715 vector for each participant which represented the comparative lag time at each vertex.

The corresponding vertices were compared across participants using Pearson's correlation. This resulted in a vector of Pearson's correlation scores. However, because Pearson's correlations are not normally distributed a fisher-z transform was applied to the vector before significance testing.

Neural imaging involves many separate significance tests. Thus it is infeasible to conduct a Bonferroni on the 18,715 tests for each analysis not to mention the correction across analysis. While methods exist for controlling for multiple comparisons these were deemed inappropriate for the current data set due to the nature of the observed results.

While Mitra, Snyder, Constantino, & Raichle (2015) used a cluster based permutation method, defining cluster size in these detailed non smoothed data is not a useful procedure. Furthermore, because this is an exploratory study with a small sample the preference was to err on the side of making a type one error as opposed to a type two error. It would be better to identify possible results that could be eliminated later through

hypothesis testing than to eliminate results when the known distribution of these types of data sets is unknown. Furthermore, the cluster based methods were designed with a different data type in mind. The current analysis is not comparing signal strength but relative timing of regions and no known correction for multiple comparison in fMRI data has been validated on the type of data set to date. Therefore, all displayed significance tests were uncorrected.

There were individual vertices which while not connected, appeared to follow a pattern along well recognized anatomical and functional landmarks. This can be seen in figure 19. Along the inferior surface of the temporal gyrus a pattern of positive correlations can be seen for the fourth component and mind wandering. While the significance of this is unclear and possibly only the result of noticing patterns is noise, the data were not screened out. No conclusions are made about this patterning except to note its placement and trajectory.

The correlations and significance results of were mapped onto the cortical surface and are displayed in figure 19. The figure was thresholded to only display correlations which were above .40 and were statistically significant at a .05 p value. For display purposes all p values are in -log10 form.
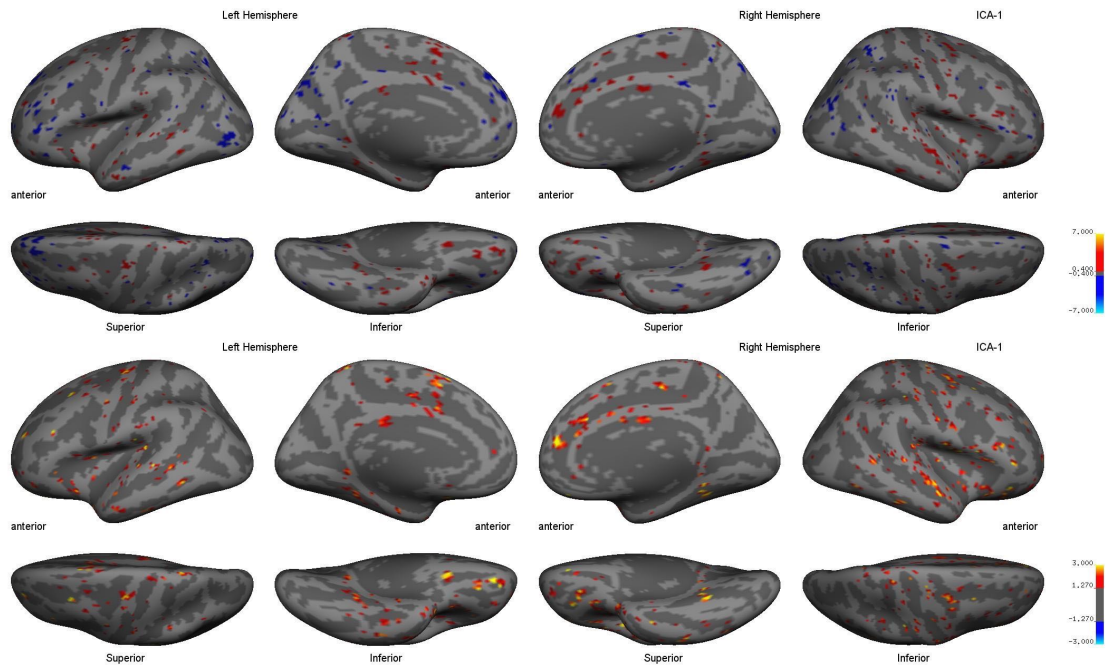
Figure 19. The top image represents the correlation map for the projection vector with mind wandering scores. The bottom is the associated significance map (uncorrected).

ICA maps. The results of the ICA in Part 2 gave a series of reconstructed

independent component signals. Through this process we were also able to obtain a

transformation matrix allowing us to convert the observed group representations into

these ICA components. Importantly, this transformation matrix can be applied to the TD

matrices associated with each individual to determine how the independent components

are represented in their lag structure. This methodology assumes that the anatomical

regions are well aligned, an assumption further supported by our use of the surface based

reconstruction method (Glasser et al., 2013; Beckmann, Mackay, Filippini, & Smith,

2009).

After reconstructing the component maps for each individual the vectors

representing each component were separated out and correlation maps and significance

maps were prepared using the method described in the previous section.

To reconstruct the components for each individual subject for which a behavioral

variable was obtained, the pseudo-inverse of the unmixing matrix (A) was computed. The

product of the A inverse for the 5 component model and the subjects' TD matrix resulted

in subject specific signals representative of each of the 5 components. Typically, the

resulting reconstructed signal has the mean signal added back into the signal to shift it to

the correct mean. This was deemed unnecessary for the subsequent regression as it added

little to the interpretability. For this step the TD matrix for each subject was unaltered.

The results of these comparisons are displayed in figure 20 and 21.

The resulting five component matrix was then regressed against the behavioral

variable using Pearson's correlation for each cell. This resulted in a separate correlation

map for each component. Before testing for significance a fisher z transform was completed on the resulting matrix. Pearson's correlations are not normally distributed and therefore this transformation is necessary to compare correlations across the surface. The resulting matrix was projected on the surface and thresholded at a value of .4 which is a moderate correlation giving a sparse result with minimal clusters to interpret. A difficulty in the interpretation is that the sign of the correlation needs to be interpreted with caution. Remember that the sign of the component maps was uninformative except as similar distance from the center value of that component.

The fisher z transformed matrix was then tested for significance. The resulting uncorrected significance values were converted to their -log 10 equivalents and thresholded at a p value of .01.

Larger clusters were examined with behavioral variables and are discussed below.
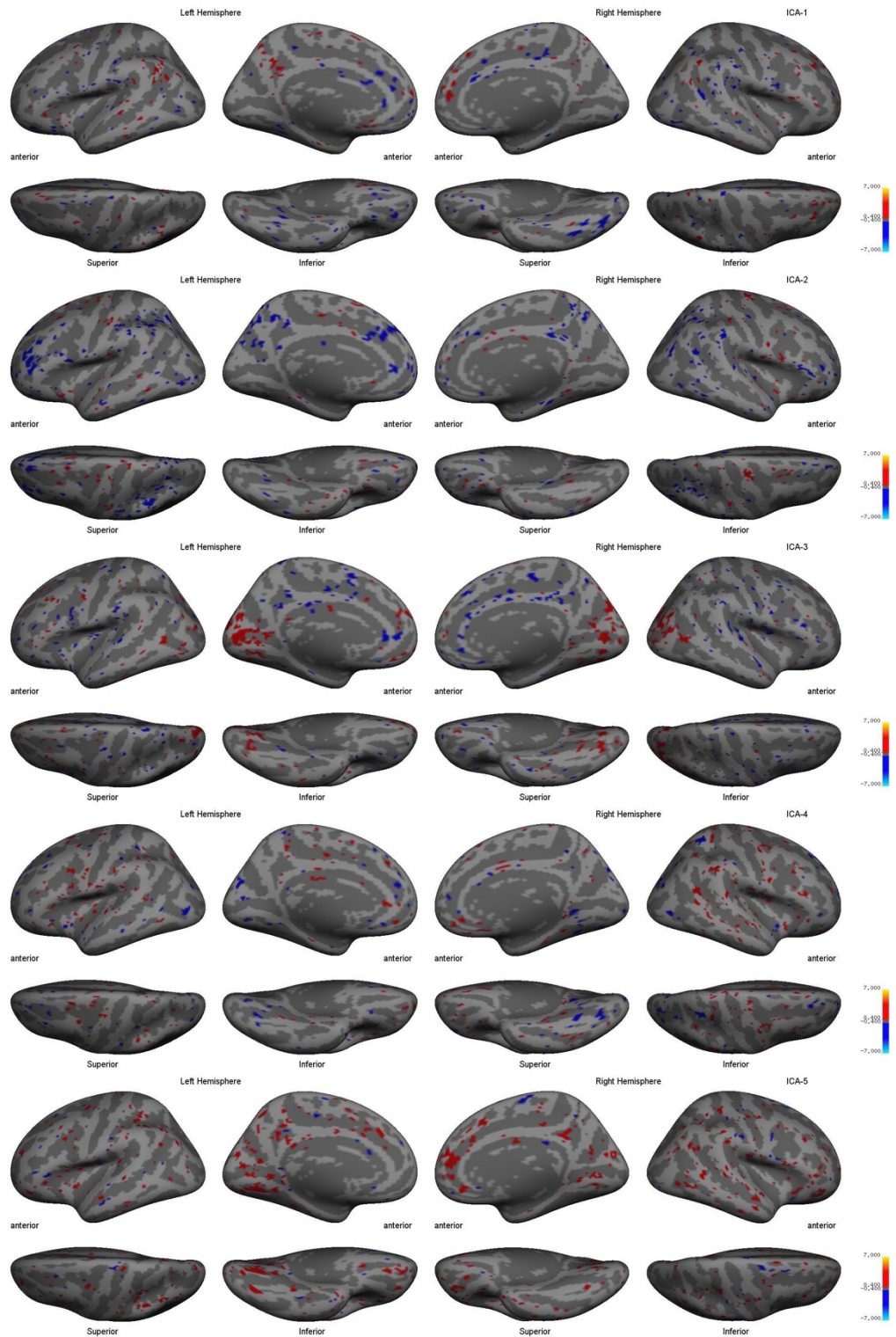
Figure 20. Pearson's Correlation with the 5-component model and mind wandering scores.
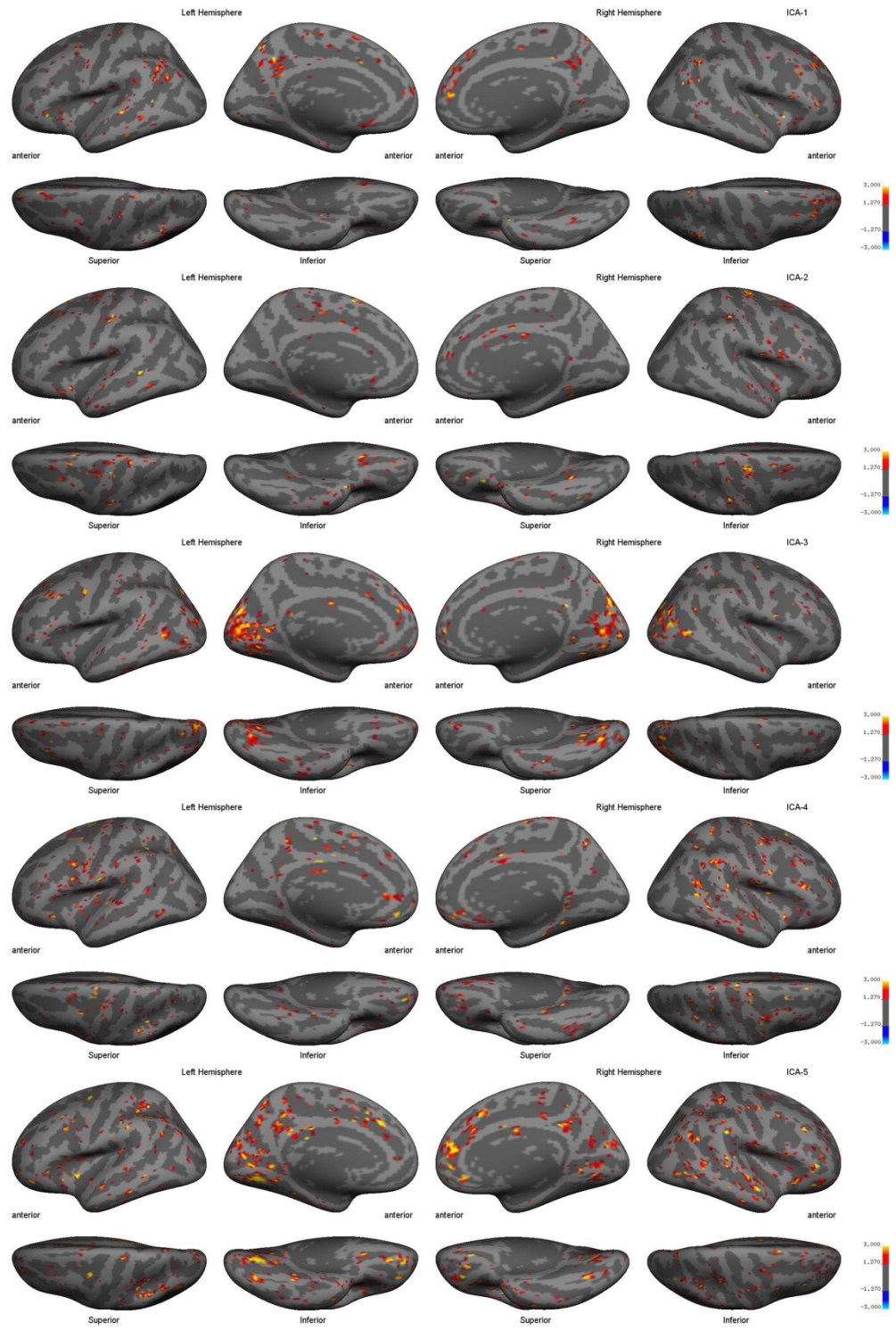
Figure 21. Significance Map for the previous Pearson's Correlation with the 5-component model and mind wandering scores.

Results and Discussion

      Behavioral results. Mind wandering was recorded on a 5 point likert scale. Each participant made 18 mind wandering ratings during the reading task. During debrief it was discovered that some participants interpreted the mind wandering scale differently. They assumed that they were always mind wandering a little because their attention was not perfect. Thus a number of them consistently gave ratings above baseline. Additionally, some individuals gave the highest rating each time they mind wandered even the smallest amount. Based on these findings the attempt to get at subtle differences between degrees of mind wandering was largely unsuccessful. However, it was clear that mind wandering was occurring. The meta-awareness of the degree of mind wandering was too difficult for some of the participants. The scale was therefore transformed to a traditional binary choice. Any rating greater than 1 was considered mind wandering, unless the individual gave rating of 2 as the lowest and no ratings of one. In these cases the participant was asked about the scale after the task and corrections were made, this occurred for 4 participants. An additional 3 participants reversed the scale so a similar transformation was made so it aligned with other participants. The score was calculated by then counting the total number of mind wandering incidents from the 18 slides. Out of a maximum of 18, the mean was approximately centered (M=7.84, SD=5.40). While the data were not significantly skewed at -0.12 (SE=0.38) it did display a kurtosis of -1.18 (SE=0.75). Overall, however the data showed acceptable distribution for within group comparisons. Thus mind wandering was successfully manipulated in terms of frequency but not degree.

General cognitive variables. Descriptive statistics are available in table 2 and the correlation between behavioral variables is available in table 3.

To evaluate intellectual ability the WASI-IV was administered to the participants. As a whole the participants scored within the average range for intelligence as measured with the WASI (M=103.97, SD=11.45). However, the results indicated a wide range of intellectual ability in the group ranging from 83 to 135. However, the distribution across participants was normally distributed with a skew of 0.48 (SE=0.38) and a kurtosis of 0.83 (SE=0.76). The vocabulary and matrix subtests positively correlated at a moderate level, Pearson's r(36)=.40, p<.05. The full score did not correlate with mind wandering scores, Pearson's r(36)=.10, p=.57. It similarly did not correlate with either the vocabulary subtest r(36)=.14, p=.39 or matrix subtest r(36)=.05, p=.78 indicating that mind wandering while reading aloud was not related to general intelligence measures.

However, as mentioned above, mind wandering has been found to correlate with working memory. Three scores were computed for each N-back session: the ratio of the times they correctly identified the target (hits), the ratio of times they incorrectly responded to the target (misses), and the response rate in seconds. The participants hit their targets more than half of the time (M=0.68, SD=0.20) but this was not significantly skewed at -0.76 (SE=0.39) with a moderate kurtosis of -0.56 (SE=0.76). The rate of false positives was also mediocre (M=0.15, SD=0.13). This also showed high but acceptable skew at 0.97 (SE=0.39) and a kurtosis of 0.17 (SE=0.76). The moderately high skew was likely due to floor effects. However, the measures of hits and misses showed enough distribution to warrant their comparison to the mind wandering scores.

Interestingly, there was also no relation between the frequency of mind wandering and the hits, r(36)=-.23, p=.18, or the misses, r(36)=-.07, p=.70, in the N-back task. There has been some research connecting n-back response time specifically to mind wandering (McVay & Kane, 2012). Here the response time was a mean of 0.87 seconds (SD=0.15) with relatively low skew of 0.27 (SE 0.15) and a moderate kurtosis of -0.84 (SE=0.21). There, however was similarly no relation between response rate and mind wandering frequency, r(36)=.18, p=.81. The N-back task is however testing a group of cognitive variables, so it is difficult to tell if it is accurately getting at the part of the working memory construct that tends to correlate with mind wandering. Overall, it is important to point out that the mind wandering scores reported here do not appear to be related to these general cognitive variables.

Table 2

Descriptive Statistics Mind Wandering Group

Measure	n	Min	Max	M	SD	Skew	Kurtosis
				Score			
Gender							
Male	18						
Female	20						
Ethnicity/Language							
Chinese Bilingual	9						
Latino Bilingual	27						
Filipino Bilingual	2						
Age	38	16.00	20.00	17.65	1.07	-0.88	-0.68
Cognitive Measures							
WASI_Full	38	83.00	135.00	103.97	11.45	0.48	0.83
WASI_Vocab	38	34.00	63.00	51.58	6.88	-0.68	0.32
WASI_Mat	38	30.00	76.00	51.97	8.19	0.19	1.80
NBack_Average Hit Rate	38	0.25	0.96	0.68	0.20	-0.76	-0.56
NBack_Average False Rate	38	.000	0.53	0.15	0.14	0.97	0.17
NBack_Reaction Time	38	0.623	1.19	0.87	0.15	0.27	-0.84
Text Comprehension							
Comprehension Questions [0-18]	38	8.00	16.00	11.86	2.27	-0.27	-0.92
Rating of Main Idea [1-3]	38	1.00	3.00	1.95	0.83	0.10	-1.52
Comprehension Total Retell Words	38	47.00	247.00	140.00	64.23	0.43	-1.14
Total Number of Correct Propositions	38	2.00	25.00	10.39	4.96	0.39	0.96
Total Number of Correctly Inferred Propositions	38	0.00	2.00	0.22	0.54	0.39	5.28
Total Number of Incorrect Propositions	38	0.00	5.00	1.50	1.36	0.39	-0.22
Comprehension Score	38	0.00	25.00	9.11	5.53	0.66	093
Percent Correct	38	0.50	1.00	0.84	0.16	-1.21	0.65
Other Measures							
Anxiety Rating [1-5]	38	0.00	5.00	2.86	1.18	-.42	0.25
Daily Reading MW Frequency	38	1.75	5.80	4.04	1.14	-0.43	-0.93
MW Ratings > 1 in task	38	0.00	17.00	7.84	5.40	-0.12	-1.18
CWPM_Total	38	99.09	271.83	155.53	29.37	1.46	5.63

Table 3
Correlation Table Representing Behavioral variables

Measure	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
(1) WASI_Full	1.00	0.76**	0.88**	0.52**	0.24	0.07	-0.03	-0.02	-0.01	0.28	0.56*	0.53*	0.41*	-0.41*	-0.10	0.35*	0.35	-0.130	-0.09	0.10	0.36*
(2) WASI_Vocab		1.00	0.40*	0.26	0.32	0.19	0.02	-0.43**	0.11	0.31	0.42	0.50*	0.59**	-0.57**	-0.11	0.50**	0.24	-0.242	-0.12	0.14	0.50**
(3) WASI_Mat			1.00	0.52**	0.23	0.10	-0.04	0.15	-0.10	0.19	0.43	0.38	0.17	-0.22	-0.06	0.15	0.25	0.085	-0.02	-0.05	0.19
(4) VF_animals				1.00	0.45*	0.20	-0.10	0.16	0.05	0.12	0.21	0.37	0.27	-0.25	-0.12	0.24	0.11	-0.070	-0.26	0.44*	-0.18
(5) VF_Prof					1.00	0.33	-0.16	-0.08	-0.03	0.18	0.33	0.44	0.27	-0.30	-0.17	0.25	-0.03	-0.093	-0.05	0.12	0.12
(6) NBack_aveHitRate						1.00	0.05	0.03	-0.08	0.19	0.20	0.02	0.18	-0.17	0.11	0.11	-0.25	0.025	-0.01	-0.23	0.21
(7) NBack_AverageFalseRate							1.00	0.28	0.05	0.11	-0.27	-0.02	0.05	-0.07	0.14	0.00	-0.03	-0.285	0.14	-0.07	0.05
(8) NBack_ReactionTime								1.00	-0.23	-0.09	0.04	-0.14	-0.14	0.23	-0.10	-0.08	0.27	0.169	0.03	0.18	-0.12
(9) Gender									1.00	0.36*	-0.06	0.16	0.35	0.08	-0.14	0.36**	0.07	-0.315	0.05	-0.29	-0.02
(10) ComprehensionQuestions [Scale 0-18]										1.00	0.67**	0.45*	0.44**	-0.02	0.43**	0.50**	0.47*	-0.055	0.34*	-0.32	0.48**
(11) RatingOfMainIdea [Scale 1-3]											1.00	0.64**	0.72**	0.04	-0.54*	0.79**	0.66**	0.109	0.50*	-0.14	0.61**
(12) ComprehensionTotalRetellWords												1.00	0.85**	-0.20	-0.14	0.75**	0.39	-0.160	0.53*	-0.03	0.22
(13) TotalCorrectPropositions													1.00	-0.31	-0.40*	0.96**	0.67**	-0.100	0.18	-0.06	0.47**
(14) TotalCorrectlyInferredPropositions														1.00	-0.08	-0.16	0.10	0.546**	0.28	-0.22	-0.24
(15) TotalIncorrectPropositions															1.00	-0.61**	-0.88**	-0.217	-0.08	0.12	-0.25
(16) ComprehensionScore [(13)+(14)-(15)]																1.00	0.84**	0.054	0.21	-0.10	0.46**
(17) PercentCorrect out of total propositions mentioned																	1.00	0.215	0.33	0.04	0.40
(18) MWFrequency day-to-day [1-5]																		1.00	0.050	-0.093	0.153
(19) AnxietyRating [1-5]																			1.00	0.36*	0.24
(20) MWratingsGreaterThan1 [0-17]																				1.00	-0.13
(21) CWPM_total																					1.00

**. Correlation is significant at the 0.01 level (2-tailed). *. Correlation is significant at the 0.05 level (2-tailed).

227

Comprehension and fluency. Reading comprehension of the specific test was conducted using a variety of methods described above. The utilization of comprehension questions, an overall rating of the main idea, the total number of word in the recall, and the total number of correct propositions showed strong convergent validity for reading. As can be seen in table 3, all the comprehension measures were at minimum moderately correlated at a $p<.01$ significance level. Many of these correlations were greater than .6 indicating strong convergent validity across measures. The one measure which was not useful was the number of inferred propositions which is only an additional measure in case actual events in the story were not recalled. Because of the high convergent validity discussion shall be limited to the answers to the 18 open ended questions.

Overall, the participants had a fairly good comprehension and memory for the story, with a mean of 11.86 (SD=2.27) out of a possible 18. This measure was not significantly skewed at -0.27 (SE=0.39) but had a moderate kurtosis of -0.92(SE=0.76). This shows that there were not ceiling or floor effects in this measure. We would expect based on previous research that mind wandering was going to be related to this comprehension measure, however this was not the case, $r(36)=-.32$, $p=.06$. This was the largest relationship between mind wandering and comprehension in the data. Why might this be the case? It is possible that while individuals may have a wandering mind, they are able to reconstruct the story from the bits that they are able to get. Another possibility is that the individuals perceived their mind wandering off task when they were simply imagining the story.

A second measure of reading skill was fluency. Only a single measure of fluency was used here and that was the total number of correct words per minute. In standard measures the participant reads for one minute then the number of correct words is counted. The correct words per minute was calculated here by taking the total number of words read correctly and dividing it by the number of minutes it took to read the passage. Reading rate was overall fairly fluid, with a mean of 115 words read correctly per minute (SD=29.37). However, the CWPM measure was not normally distributed with a positive skew of 1.46 (SE=0.38) and a similarly very high kurtosis of 5.63 (SE=0.75) indicating that most individuals were below that mean in a leptokurtic distribution. Comparisons are therefore questionable, but there was similarly no relation between mind wandering and this variable, $r(36)=-.09$, $p=.75$.

Overall the reading rate and the fluency were not related to mind wandering.

Dynamic and qualitative explorations. As described above a readability score was made for each slide. First, remember that readability formulas generally use sentence length and word length as indicators of grade level for the reading material. As can be seen in figure 18, syllable length and sentence length varied considerably throughout the story. Using the gunning fog and FORECAST method a sliding window was applied to the story of 100 words. In an exploration trying to discover what story feature may lead to mind wandering each participant rating were overlaid onto this graph. However, no systematic relation was discovered. Not a single participant's mind wandering scores correlated significantly with any of the measures of readability. This indicates that the difficulty of the reading material may not account for the likelihood to mind wander

while reading aloud. It was additionally observed that mind wandering was not more frequent in any particular place.

In an interest to better understand what textual factor may lead to mind wandering the debriefs were examined. There were rarely mentions of the story content or emotionality in the mind wandering explanations. 19% of the participants stated that they knew they mind wandered; they were not sure what they mind wandered about. This is interesting taking into account the theory presented by Delaney, Sahakyan, Kelley, and Zimmerman (2010) because if forgetting was part of the process of shifting back to task, we would expect these individuals to have low comprehension scores however this was not the case, although the group was so small statistical significance would have been difficult to reach.

An additional feature of the debrief in regard to story content was that the story appeared to have differential relevance to different individuals. Two felt like they mind wandered more during moments where Disneyland was discussed and three felt like they mind wandered more where a Disney song was being discussed. A single participant mind wandered about a friend with autism and how their life might be similar. Interestingly during the debrief we checked whether they rated that they mind wandered there, and none of them actually did. They also got all the important points on the particular slide. This is interesting because it says multiple things about the meta-awareness of mind wandering. Individuals may not know when they are not paying attention, they might confuse personal reflection with the story for not paying attention, and they did not even realize when they mind wandered. This is actually what may be

230

predicted by Kane and McVay (2012). Individuals with higher executive function may have mind wandered more because resources were available. This did not appear at the group level but there were likely a number of issues manipulating mind wandering frequency in the group. It would be interesting to see if mindfulness training, which is often associated with improvements in mind wandering, affects these meta-awareness abilities (Mrazek, Franklin, Phillips, Baird, & Schooler, 2013; Mrazek, Smallwood, & Schooler, 2012).

Oral reading anxiety scale. As mentioned above this scale was adapted from other sources. The adapted scale for oral reading anxiety included 4 items which were rated on a 5-point likert scale ranging from "strongly agree" to "strongly disagree". The items showed strong internal reliability .89 (Chronbach's alpha, n=38). Table 4 shows the correlations between these items.

In this measure, the higher the value, the more anxiety the individual reports experiencing while reading aloud. The mean score was 2.86 (SD=1.18). The results were normally distributed with a skew of -0.42 (SE=0.38) and with a kurtosis of 0.25 (SE=0.75). This measure correlated with mind wandering moderately, $r(36)=.36$, $p<.05$. Additionally, debriefs indicated that these individuals who reported the highest anxiety reported mind wandering about that anxiety or events in the past where they experienced oral reading anxiety.

Table 4

Correlation Table of Anxiety Questionnaire

Measure	1	2	3	4
(1) I start to panic when I have to read out loud without preparation	1.00	0.72**	0.61**	0.76**
(2) I can feel my heart pounding when I'm reading aloud		1.00	0.60**	0.62**
(3) I feel very self-conscious about reading aloud			1.00	0.67**
(4) I get nervous and confused when reading aloud				1.00

**. Correlation is significant at the 0.01 level (2-tailed).

Summary of behavioral results. Overall, it was found that mind wandering during oral reading could not be explained by cognitive factors although executive function and working memory have been associated with mind wandering in previous studies (Levinson, Smallwood, & Davidson, 2012; McVay, & Kane, 2012; Feng, D'Mello, & Graesser, 2013). Similarly, extensive exploration was conducted examining the difficulty of the text and there was no relationship between moments when text difficulty increased and mind wandering that could be determined even though this was found in previous studies (Feng, D'Mello, & Graesser, 2013; Levinson, Smallwood, & Davidson, 2012).

Reflecting on debriefs and the interaction between the emotional content of text there was also no systematic relationship. The participants were not particularly good at remembering where they mind wandered, but they tended to assign reasons for their mind wandering in a post hoc fashion which did not agree with their online ratings. It is possible that the text brings up emotional and personal content unique to each individual and when their mind drifts they tend to think this is the reason for their mind wandering experience. This actually agrees somewhat with what we know about the way memory works. Emotions have a way of drawing our memory in unknown directions similar to what happens in eyewitness and flashbulb memory studies (Loftus, & Palmer, 1996; Migueles, & Garcia-Bajos, 1999). Christianson (1992) suggests that emotional moments lead to preferential processing of specific details and these details may assist in the reconstruction of the text not attended to while mind wandering. This could potentially be a very interesting area of study to explore through the use of emotionally charged texts.

There may even be an interaction with meta-awareness which would be a promising avenue.

The only correlation with mind wandering during oral reading which reached significance was anxiety. There is a rich literature on the contents of mind wandering and negative self-thought (Smallwood, & Schooler, 2015). However, I do not want to put too much weight into this finding. It may be possible to think about oral reading anxiety not as something which causes or correlates with oral reading, but in fact is part of an identical construct (Poerio, Totterdell, & Miles, 2013). Using a slightly different neural methodology than the one below, which took into account the subcortical structures and had much lower spatial resolution, I did find an earlier activation of the insula in individuals who reported oral reading anxiety, however, as we shall see below, this did not appear in the current findings.

It was clear that there were different aspects of task, memory, emotion, or skill that led different individuals to mind wander. A much more extensive dynamic systems analysis of mind wandering in emotionally charged texts is clearly needed to better characterize how mind wandering changes as a function of all of these factors interacting.

Having attempted to characterize the current mind wandering phenomena in this group of adolescents we shall now turn to the neural data. First it is examined how the projection vector of lag structure correlates with mind wandering behaviors. Then we shall use the 5-component model representing underlying neurological processes that are ongoing at rest but readied for skilled engagements and how mind wandering while reading aloud might correlate.

Projection Maps. The projection map method described above was applied to each of the behavioral variables. In terms of mind wandering, the data is difficult to interpret. Some regions may have important findings and are mentioned here.

To evaluate the effects of any behavioral variables, the original TD maps for each individual was entered into the regression. No data points were removed from this data set and extreme values of +/- 5 seconds were allowed to remain as they may have been important for variation across the behavioral variables.

A Pearson's correlation was calculated for each vertex independently to the behavioral variable. Because Pearson's correlations are not normally distributed they were transformed using fisher z transformation before significance testing. The correlations were projected onto the cortex and then thresholded so that only those values above .4 were displayed. As one can see, the results are noisy. However, a qualitative examination of the map shows regions which may be of import. First, it is worth noting that there is not symmetry between the hemispheres. Secondly, there are two visually interesting features. First there is some clustering, and second there appears to be some scattered but patterned differences.

Note that in the posterior superior precuneus there is a cluster of negative correlation. This region is associated with autobiographical information, representations of self, social imagination and compassion (Immordino-Yang, McColl, Damasio, & Damasio, 2009; Yang, Bossmann, Schiffhauer, Jordan, & Immordino-Yang, 2012; Spreng, & Grady, 2010). There is also a region of positive correlation between the anterior and superior cingulate bisecting the frontal superior gyrus.

In the right hemisphere we see some patterning in two regions which stand out. There is a collection of positive correlation regions along the inferior surface of the superior temporal gyrus and some regions of negative correlation which appear to follow the middle occipital gyrus. Similar regions in the superior temporal gyrus have been associated with thought disorders and auditory hallucination implicating them in semantic and mental image formations (Takahashi et al., 2006; Takahashi et al. 2009). The relevance here is unclear but may have something to do with internal voice. The results however are so small that this is a large leap.

A positive correlation means that as the mind wandering score increases, so too does the lateness of that region relative to other regions. A negative correlation would mean as the mind wandering score increases the region is active relatively earlier in the sequence. It does not mean that a region is late or early overall.

These regions do not systematically fall within the DMN traditionally associated with mind wandering, nor are they associated with other resting measures which usually are associated with reading listed above.

It is worth noting that if we relax the constraints to notice the spread of the correlations in general the right frontal region shows a negative correlation and the superior temporal gyrus shows a positive correlation. The occipital cortex shows a negative correlation.

ICA. The analysis comparing the 5-component model to mind wandering was more promising, but still had no correlations which were in regions typically associated with either mind wandering or reading skill. The most obvious correlations are with the third and second component assumed above to deal with streams in visual processing and emotional processing respectively.

It is of interest that the third component shows some very clearly significant differences with bilateral symmetry. As we mentioned above, this component may reflect the two routes of early visual processing. The most prominent difference is the occipital cortex particularly the medial regions. These regions tend to be earlier in individuals with more mind wandering. Or put another way, the occipital regions typically associated with early visual processing are more temporally separated from the rest of the component. This result could actually account for findings that perception of external events decreases during mind wandering.

This has not been a region of study in reference to mind wandering, however, it appears that evaluating the timing of this region in relation to other regions may be warranted. Remember that we are ordering the components here for convenience only and aligning them with the projection. An alternative analysis of the data may suggest that the order is in the opposite direction. It appears that the indicated regions of the occipital lobe are further from the center of the component. If as suggested this component comes first, then a late engagement of other neural regions may allow a window for other internal or external processes to capture attention. If, however, the occipital region is later than other regions this would suggest a top down approach to this

particular component whereby the preparedness of the region is too late in mind wandering.

Another important feature is that this corroborates evidence given by temporal studies of attention. It was found that attention to a specific region of the visual field results in a heightened activation in peripheral visuals field 120-240 ms after. This timing difference could be part of the reason mind wandering individuals lose attention to task. Perhaps higher order cognition does not intervene early enough between foveal and peripheral processing enhancement (Woldorff, Liotti, Seabolt, Busse, Lancaster, & Fox, 2002).

Additionally, in experiments using-eye tracking with mindless reading, mindless reading is associated with longer fixations, increased blinking rates, and reduced sensitivity to lexical features (Reichle, Reineberg, & Schooler, 2010; Smilek, Carriere, & Cheyne, 2010). Other mindless reading tasks such as reading word by word has shown a reduction in awareness of lexical properties of words. The second component shows very clear bilateral symmetry in the precuneus. Individuals who mind wander more tended to show a later activation of the posterior precuneus. The left frontal cortex similarly shows a significantly later activation for those who mind wander more. These are more abstract cortical processing regions responsible for executive control and image of self and social emotions. The separation of these regions from the insula which is considered the core of this component may represent a differential in the timed control of noticing and managing emotions during a task.

The sensory motor regions show an earlier activation but this appears to be more prominent in the superior regions. This region typically has to do with the trunk of the body. Perhaps related to breathing and breath for this particular task.

The fifth component shows some positive correlations with the activity in the occipital lobe. If this is associated with cognitive control, then this may affect how rapidly individuals can monitor internal thoughts.

Overall, however, these components are very high level. Considering the complexity of the data an exploration with larger component models is warranted. As we increase the number of components the results are more detailed and so it would be better to do this with a much larger data set. The present reverse inference methods to explain the differences in component structure between individuals who mind wander are weak at best, but, they do offer a number of ideas which can be tested.

Summary

This dissertation began with a theoretical motivation for the current methods. It is clear that if we are looking for persistent representations of knowledge the system dynamics of the brain are the place to look. We then examined two methods of looking at these dynamics with fMRI resting state data finding that traditional 0-lagged analysis comes short of representing the dynamics in ways that our theory development would suggest that knowledge is stored. Settling on a lagged analysis of the data we then examined these dynamics in a group of adolescents. We explored a number of methods settling on Independent Component Analysis. Relying on reverse inference we interpreted these results to be representative of system dynamics in the brain that

represent knowledge in the sense of perceptual skill and neural preparedness for environmental engagement.

Finally, the behavior known as mind wandering was examined. We characterized mind wandering while reading aloud as not correlating with classic cognitive variables. It was discovered that there was some correlation with anxiety but the separation of anxiety while reading aloud and mind wandering may not be actually from different constructs. Attempts were made at a dynamic analysis but no patterns were found. It initially appeared that the debrief included some individual responses which gave us more information; however, this was misleading and it was clear that individuals who experience strong emotion were unable to remember their mind wandering accurately. This last finding was only limited to a few individuals, and while not testable using quantitative method in the current data set suggest a promising idea for future research.

Finally, to understand how mind wandering while oral reading related to existing dynamic knowledge structures in the brain we compared the projection and component maps from Part 2 to this behavioral variable. The most prominent finding was a separation in time of the occipital region and the core processes of a component we earlier associated with visual perception. This finding has not been reported elsewhere, however the current approach is exploratory and thus it may be that it is revealing a level of representation in the data not previously observed with other methods.

Limitations

In regards to the sampling of the cortical tissue. One very clear limitation is the omission of the subcortical structures in the analysis. The main reason for their

elimination was that there is little to no research on waves of activity across the subcortical structures and how to interpret them in fMRI resting state scans. Does slow wave activity in these regions similarly represent neural preparedness? Subcortical structures are essential to higher cognitive function, and they should be included in the analysis. Future simulations with different voxel sizes and surface based methods will have to be done to discover the appropriate comparative weight for each data type. Another approach would be to use the sub cortical structures as seeds as in Mitra et al., (2015).

A second weakness of the current methods is the temporal resolution. Currently most fMRI research is done with a .8 second TR. The current methodologies used a data set from a longitudinal study therefore the TR was matched to earlier data collection procedures. This, however will offer another opportunity to conduct the same analysis across time to examine changes in lag structure as a function of age.

Theoretically there is a larger issue that will involve additional exploratory research. As mentioned in Part 1 the assumption of neural networks as synchronous does not represent what we know about the temporal nature of knowledge in the brain. This paper attempts to fill this gap by proposing a method of analysis which examines neural representations of knowledge across time.

These methods may be particularly useful in deriving resting state evidence of neural models of sensory processing and perception. The multiple waves model proposed by Pessoa, & Adolphs (2010) suggests that vision begins at a course level and then through repeated multiple paths involving the pulvinar and the amygdala which

241

coordinate cortical processing of visual information in emotionally relevant way. The methodology here may be one way to observe these entrained patterns of activity.

Secondly many cognitive processes involve cascade dynamics at both the neuron and the neuronal population level (Fusi, Drew, & Abbott, 2005). These cascades of processes are thought to underlay memory storage that is a dynamic process unfolding and active over time. These methods described here may allow us to observe memory formation processes which use these very dynamics. Furthermore, cascades are also used in metaphor research in grammar to represent the multiple levels of a metaphor simultaneously where processing continues at all levels and interacts between them (David, Lakoff, & Stickles, 2017). These metaphor properties of language organization may be observed in vivo with ICA as described above.

Furthermore, it must be acknowledged that this methodology captures only one direction of the activity. As mentioned in the MEG study of reading described above, the skill involves a sequence which moves information forward in the cortex in a predominantly bottom up fashion followed by a top down process moving backward along similar regions changing the representation in the occipital cortex. While this involves a wave of activity sequentially in both directions, the current methodology would only capture one direction of this activity. There needs to be a development of the ICA methodology to string together the resulting components into systems which allow multiple directions form information flow.

A second more fundamental issue is that while neural signals are not synchronous and time locked, they also do not always show covariance in lagged structure. While the

dominant model is that the timing of one cell is dependent on the input of another, there are cells in the cerebellum which have been shown to have specially trained and differentially pattered response than their input. These cells appear important for the learning differentials of stimulus onsets (Johansson, Jirenhed, Rasmussen, Zucca, & Hesslow, 2014). Using methods proposed here this feature of neural activity would not be captured.

Finally, the reduction of the data using ICA is questionable. While there are reasons to believe this is not coincidental, the methodology has not be used on a larger data set nor has it been repeated.

Another aspect particular to the mind wandering phenomena is understanding the relation between 0-lag and lagged network analysis. Regions of the DMN which have been identified as important in both resting state and task based methodologies did not appear to be significant in this analysis. However, it was assumed that this methodology would reveal a different aspect of knowledge. Findings here are not expected to parallel findings in 0-lagged network analysis. There also were not differences in regions implicated in reading. Instead the major finding was only in the occipital lobe. Perhaps a deeper examination using tens to hundreds of components might allow the representation of more specific skills and the regions implicated in other functional studies listed above may revel themselves. It is likely that the high level of analysis examined here will only pickup large system-wide differences if those exist and thus we found a different in visual regions.

An analysis of the mind wandering behavior during oral reading especially as it pertained to an emotionally charged text reveled a number of interesting complexities. Future studies should seek to give a variety of texts each with specific differences such as charged positive and negative emotion.

<center>**Future Directions**</center>

Extended Neural Studies

The first step is to attempt to repeat the findings of Part 2 with a larger data set with better temporal and spatial resolution. This will be completed using widely available data now available in the Human Connectome Project using thousands of participants instead of the handful used here. If we can reproduce the ICA findings with these larger data sets the current method may prove to be a powerful alternative to the PCA method described by Mitra et al. (2015) allowing for analysis of individual subject variances which correlate with skills in more realistic group sizes.

As part of this approach, the HCP data set also includes limited behavioral data which could be regressed to analyze some of the theoretical ideas present in the current paper.

Further work needs to be conducted to understand how the amplitude of the covariance may be related to the lag structure. This may help identify what is noise and where to limit the lag representation. While lag representations are expected to encompass the entire brain it is also recognized that as signal travels from its origin the signal degrades. When doing traditional connectivity analysis, a threshold is set and this

<center>244</center>

threshold is used to examine network connectivity. Should a similar threshold be set in lag analysis. Is it reasonable to use covariance amplitude to threshold the representation?

Where is Knowledge?

Also, because the current theory suggests that knowledge is buried in these lagged representations, groups of individuals who vary on expertise should be examined, such as chess players, video game players, computer programmers and many other expertise which may influence the way we interact with the world and the basic knowledge structures we use to navigate our lives. Additionally, there is great opportunity to examine knowledge structures in terms of learning and study skills. For example, procrastinators may show different lag structures than non procrastinators.

Concurrent research during this dissertation exercise inspired the author to better understand how the stories we have about our learning, daily experience, and life project may guide our perception and behavior. If these stories are foundational for how we live our daily lives, they would be expected to have persistent neural representations observable during rest. The current methodologies, when coupled with 0-lag analysis may help us understand how these stories bias our internal systems to engage with the world.

It is also well documented that rs-fMRI changes based on the conditions of image acquisition and the events immediately prior to the acquisition. This could be of particular interest in education and learning. After engaging in a task we may continue to mind wander about the task itself. For example, it has been suggested that at a subconscious level we continue to process information and forget our current problem solving approaches. Both this basic level of continual processing and the process of

integrating new ideas into existing systems of thought could be observed during resting state using this methodology.

Questions About Mind Wandering

Finally, in direct relation to Part 3, it would be useful to conduct the same analysis with a larger variation in mind wandering measures. It is accepted that there are great differences in mind wandering such as positive constructive day dreaming, obsessive thinking, ruminating, distractibility and more. What do these types of mind wandering have in common neurologically and behaviorally? The current method was only examining mind wandering during oral reading.

In conclusion, while the current methods continue to show many limitations, they open doorways into new analytical procedures to further understand how we are persistently representing knowledge in neural system dynamics that unfold over time.

Bibliography

Aertsen, A. M., Gerstein, G. L., & Habib, M. K. (1989). Dynamics of neuronal firing correlation: Modulation of "effective connectivity". Journal of Neurophysiology, 61(5), 900-917.

Altman, J. (1962). Are new neurons formed in the brains of adult mammals? Science, 135(3509), 1127-1128.

Alunni, A., & Bally-Cuif, L. (2016). A comparative view of regenerative neurogenesis in vertebrates. Development, 143(5), 741-753.

Anderson, M. L. (2010). Neural reuse: A fundamental organizational principle of the brain. Biological Psychology, 33(4), 245-266.

Anderson, M. L. (2014). After Phrenology: Neural Reuse and the Interactive Brain. Cambridge, MA: MIT Press.

Arieli, A., Shoham, D., Hildesheim, R., & Grinvald, A. (1995). Coherent spatiotemporal patterns of ongoing activity revealed by real-time optical imaging coupled with single-unit recording in the cat visual cortex. Journal of Neurophysiology, 73(5), 2072-2093.

Arieli, A., Sterkin, A., Grinvald, A., & Aertsen, A. D. (1996). Dynamics of ongoing activity: Explanation of the large variability in evoked cortical responses. Science, 273(5283),1868.

Atkins, R. L. (2017). Effects of focus of attention on tone production in trained singers. Journal of Research in Music Education, 64(4), 421-434.

Baird B, Smallwood J, Schooler JW. (2010). I can shake that feeling: Positive mind-wandering prevents the deterioration of mood. Poster presented at Toward a Science of Consciousness conf. Tucson

Baird, B., Smallwood, J., Lutz, A., & Schooler, J. W. (2014). The decoupled mind: Mind-wandering disrupts cortical phase-locking to perceptual events. Journal of Cognitive Neuroscience, 26(11), 2596-2607.

Bal, P. M., & Veltkamp, M. (2013). How does fiction reading influence empathy? An experimental investigation on the role of emotional transportation. PloS one, 8(1), e55341.

Bargmann, C. I., & Marder, E. (2013). From the connectome to brain function. Nature Methods, 10(6), 483-490.

Barron, E., Riby, L. M., Greer, J., & Smallwood, J. (2011). Absorbed in thought: The effect of mind wandering on the processing of relevant and irrelevant events. Psychological Science, 22(5), 596-601.

Bassett, D. S., & Bullmore, E. D. (2006). Small-world brain networks. The Neuroscientist, 12(6), 512-523.

Bassett, D. S., Meyer-Lindenberg, A., Achard, S., Duke, T., & Bullmore, E. (2006). Adaptive reconfiguration of fractal small-world human brain functional networks. Proceedings of the National Academy of Sciences, 103(51), 19518-19523.

Beaty, R. E., Benedek, M., Kaufman, S. B., & Silvia, P. J. (2015). Default and executive network coupling supports creative idea production. Scientific Reports, 5.

Bechara, A., Damasio, H., & Damasio, A. R. (2000). Emotion, decision making and the orbitofrontal cortex. Cerebral Cortex, 10(3), 295-307.

Beckmann, C. F., Mackay, C. E., Filippini, N., & Smith, S. M. (2009). Group comparison of resting-state FMRI data using multi-subject ICA and dual regression. Neuroimage, 47(Suppl 1), S148.

Beer, R. D. (2000). Dynamical approaches to cognitive science. Topics in Cognitive Science, 4(3), 91-99.

Berken, J. A., Chai, X., Chen, J. K., Gracco, V. L., & Klein, D. (2016). Effects of early and late bilingualism on resting-state functional connectivity. Journal of Neuroscience, 36(4), 1165-1172.

Bimler, D. L., Kirkland, J., & Jameson, K. A. (2004). Quantifying variations in personal color spaces: Are there sex differences in color vision? Color Research & Application, 29(2), 128-134.

Binder, K. S., Tighe, E., Jiang, Y., Kaftanski, K., & Qi, C. (2013). Reading expressively and understanding thoroughly: An examination of prosody in adults with low literacy skills. Reading and Writing, 26(5), 665–680.

Birbaumer, N., Elbert, T., Canavan, A. G., & Rockstroh, B. (1990). Slow potentials of the cerebral cortex and behavior. Physiological Reviews, 70(1), 1–41.

Biswal, B. B. (2012). Resting state fMRI: a personal history. Neuroimage, 62(2), 938-944.

Bliss, T. V., & Collingridge, G. L. (1993). A synaptic model of memory: Long-term potentiation in the hippocampus. Nature, 361(6407),31.

Boller, F. (1978). Comprehension disorders in aphasia: A historical review. Brain Connectivity, 5(2), 149-165.

Botteron, K. N., Dierker, D., Todd, R., Alexopolous, J., Seung, D., Han, K., ... & Van Essen, D. C. (2008). Human vs. computer algorithm choices in identifying identical twin pairs based on cortical shape characteristics–Who's better. Organization for Human Brain Mapping Abstract, 533.

Bressler, S. L. (1995). Large-scale cortical networks and cognition. Brain Research Reviews, 20(3), 288–304.

Bunge, M. (1980). The mind–body problem: A psychobiological approach. New York, NY: Pergamon Press Inc.

Buzsáki, G., Anastassiou, C. A., & Koch, C. (2012). The origin of extracellular fields and currents—EEG, ECoG, LFP and spikes. Nature Reviews Neuroscience, 13(6), 407-420.

Caramazza, A., & Berndt, R. S. (1978). Semantic and syntactic processes in aphasia: A review of the literature. Psychological Bulletin, 85(4),898.

Carlo, C. N., & Stevens, C. F. (2013). Structural uniformity of neocortex, revisited. Proceedings of the National Academy of Sciences, 110(4), 1488-1493.

Christianson, S. Å. (1992). Emotional stress and eyewitness memory: a critical review. Psychological bulletin, 112(2), 284.

Christoff K, Gordon AM, Smallwood J, Smith R, Schooler JW. (2009). Experience sampling during fMRI reveals default network and executive system contributions to mind wandering. Proceedings of the National Academy of Sciences, 106(21), 8719-8724.

Clemenson, G. D., Deng, W., & Gage, F. H. (2015). Environmental enrichment and neurogenesis: From mice to humans. Current Opinion in Behavioral Sciences, 4, 56-62.

Cole, D. M., Smith, S. M., & Beckmann, C. F. (2010). Advances and pitfalls in the analysis and interpretation of resting-state FMRI data. Frontiers in Systems Neuroscience, 4, 8.

Cole, M. W., Ito, T., Bassett, D. S., & Schultz, D. H. (2016). Activity flow over resting-state networks shapes cognitive task activations. Brain and Language, 19(12), 1718-1726.

Collins, A. M., & Loftus, E. F. (1975). A spreading-activation theory of semantic processing. Psychological Review, 82(6),407.

Craig AD (2002). How do you feel? Interoception: The sense of the physiological condition of the body. Nature Reviews Neuroscience, 3(8),655–666.

Crispo, E. (2007). The Baldwin effect and genetic assimilation: Revisiting two mechanisms of evolutionary change mediated by phenotypic plasticity. Evolution, 61(11), 2469-2479.

Curci, A., Lanciano, T., Soleti, E., & Rimé, B. (2013). Negative emotional experiences arouse rumination and affect working memory capacity. Emotion, 13(5),867.

Damasio, A. (2010). Self comes to mind: Constructing the conscious brain. New York, NY: Random House.

Damasio, A. R., Grabowski, T. J., Bechara, A., Damasio, H., Ponto, L. L., Parvizi, J., & Hichwa, R. D. (2000). Subcortical and cortical brain activity during the feeling of self-generated emotions. Nature Neuroscience, 3(10),1049.

David, O., Lakoff, G., & Stickles, E. (2017). Cascades in metaphor and grammar. Constructions and Frames, 8(2), 214-255.

Davis, T. S., Wark, H. A. C., Hutchinson, D. T., Warren, D. J., O'Neill, K., Scheinblum, T., ... & Greger, B. (2016). Restoring motor control and sensory feedback in people with upper extremity amputations using arrays of 96 microelectrodes implanted in the median and ulnar nerves. Journal of Neural Engineering, 13(3),36001.

De Carlos, J. A., & Borrell, J. (2007). A historical reflection of the contributions of Cajal and Golgi to the foundations of neuroscience. Brain Structure and Function, 55(1), 8-16.

De Schotten, M. T., Urbanski, M., Valabregue, R., Bayle, D. J., & Volle, E. (2014). Subdivision of the occipital lobes: an anatomical and functional MRI connectivity study. Cortex, 56, 121-137.

Decety, J., Grezes, J., Costes, N., Perani, D., Jeannerod, M., Procyk, E., Grassi, F. & Fazio, F. (1997). Brain activity during observation of actions. Influence of action content and subject's strategy. Brain: a journal of neurology, 120(10), 1763-1777.

Dehaene, S. & Cohen, L. (2007). Cultural recycling of cortical maps. Neuron, 56(2), 384-398.

Dehaene, S., Cohen, L., & Morais, J. (2015). Illiterate to literate: behavioral and cerebral changes induced by reading acquisition. Nature Reviews Neuroscience, 16(4), 234–244.

Delaney, P. F., Sahakyan, L., Kelley, C. M., & Zimmerman, C. A. (2010). Remembering to forget: The amnesic effect of daydreaming. Psychological Science, 21(7), 1036-1042.

Deng, Y. Q., Li, S., & Tang, Y. Y. (2014). The relationship between wandering mind, depression and mindfulness. Mindfulness, 5(2), 124-128.

Descartes, R.(1989). The passions of the soul. (S. Voss, Trans.). Indianapolis, IN: Hackett Publishing. (Original work published 1649)

Desmurget, M., Epstein, C. M., Turner, R. S., Prablanc, C., Alexander, G. E., & Grafton, S. T. (1999). Role of the posterior parietal cortex in updating reaching movements to a visual target. Nature neuroscience, 2(6).

Dhond, R. P., Witzel, T., Dale, A. M., & Halgren, E. (2007). Spatiotemporal cortical dynamics underlying abstract and concrete word reading. Human Brain Mapping, 28(4), 355-362.

Doucet, G., Naveau, M., Petit, L., Zago, L., Crivello, F., Jobard, G., ... & Joliot, M. (2012). Patterns of hemodynamic low-frequency oscillations in the brain are modulated by the nature of free thought during rest. Neuroimage, 59(4), 3194-3200.

Douglas, R. J., & Martin, K. A. (2007). Recurrent neuronal circuits in the neocortex. Current Biology, 17(13), R496-R500.

Edelman, G. M., & Gally, J. A. (2001). Degeneracy and complexity in biological systems. Proceedings of the National Academy of Sciences, 98(24), 13763-13768.

Eisenberger, N. I., Lieberman, M. D., & Williams, K. D. (2003). Does rejection hurt? An fMRI study of social exclusion. Science, 302(5643), 290-292.

Eriksson, P. S., Perfilieva, E., Björk-Eriksson, T., Alborn, A. M., Nordborg, C., Peterson, D. A., & Gage, F. H. (1998). Neurogenesis in the adult human hippocampus. Nature Medicine, 4(11).

Esposito F, Scarabino T, Hyvarinen A, Himberg J, Formisano E, Comani S, Tedeschi G, Goebel R, Seifritz E, Di SF. (2005). Independent component analysis of fMRI group studies by self-organizing clustering. Neuroimage, 25(1),193–205.

Evans, E. F., Ross, H. F. & Whitfield, I. C. (1965). The spatial distribution of unit characteristic frequency in the primary auditory cortex of the cat. The Journal of Physiology, 179(2), 238-247.

Farah, M. J. (1988). Is visual imagery really visual? Overlooked evidence from neuropsychology. Psychological Review, 95(3),307.

Farnè, A., Serino, A., & Làdavas, E. (2007). Dynamic size-change of peri-hand space following tool-use: Determinants and spatial characteristics revealed through cross-modal extinction. Cortex, 43(3), 436-443.

Feng, S., D'Mello, S., & Graesser, A. C. (2013). Mind wandering while reading easy and difficult texts. Psychonomic Bulletin & Review, 20(3), 586-592.

Fischer, K., & Yan, Z. (2002). The development of dynamic skill theory. Conceptions of development: Lessons from the laboratory, 279-312.

Fischer, K.W. & Bidell, T. R. (2006) Dynamic development of action and thought, in: W. Damon & R. M. Lerner (eds), Theoretical Models of Human Development. Handbook of child psychology, 6th edn., Vol. 1 (New York, Wiley), pp. 313–399.

Fischer, S., Hallschmid, M., Elsner, A. L., & Born, J. (2002). Sleep forms memory for finger skills. Proceedings of the National Academy of Sciences, 99(18), 11987-11991.

Fiser, J., Chiu, C., & Weliky, M. (2004). Small modulation of ongoing cortical dynamics by sensory input during natural vision. Nature, 431(7008),573.

Formisano, E., Kim, D. S., Di Salle, F., van de Moortele, P. F., Ugurbil, K., & Goebel, R. (2003). Mirror-symmetric tonotopic maps in human primary auditory cortex. Neuron, 40(4), 859-869.

Forster, S., & Lavie, N. (2009). Harnessing the wandering mind: The role of perceptual load. Cognition, 111(3), 345-355.

Fox, M. D., Zhang, D., Snyder, A. Z., & Raichle, M. E. (2009). The global signal and observed anticorrelated resting state brain networks. Journal of neurophysiology, 101(6), 3270-3283.

Franklin, M. S., Mooneyham, B. W., & Baird, B. (2014). Thinking one thing, saying another: The behavioral correlates of mind-wandering while reading aloud. Psychonomic Bulletin & Review, 21(1), 205–210.

Friston, K. J. (2000). The labile brain. I. Neuronal transients and nonlinear coupling. Philosophical Transactions of the Royal Society of London B: Biological Sciences, 355(1394), 215-236.

Friston, K. J. (2011). Functional and effective connectivity: A review. Brain Research, 1(1), 13-36.

Friston, K. J., Kahan, J., Razi, A., Stephan, K. E., & Sporns, O. (2014). On nodes and modes in resting state fMRI. NeuroImage, 99(C), 533–547.

Fusi, S., Drew, P. J., & Abbott, L. F. (2005). Cascade models of synaptically stored memories. Neuron, 45(4), 599-611.

Gaillard, A. (1977). The late CNV wave: Preparation versus expectancy. Psychophysiology, 14(6), 563-568.

Gallistel, C. R. (March 2017). Big Ideas in Cognitive Neuroscience: On Memory. Symposium Session Presented at Cognitive Neuroscience Society Annual Meeting. San Francisco.

Ganis, G., Thompson, W. L., & Kosslyn, S. M. (2004). Brain areas underlying visual mental imagery and visual perception: an fMRI study. Cognitive Brain Research, 20(2), 226-241.

Gardner, J. L., Merriam, E. P., Movshon, J. A., & Heeger, D. J. (2008). Maps of visual space in human occipital cortex are retinotopic, not spatiotopic. Journal of Neuroscience, 28(15), 3988-3999.

Germana, J. (1968). Psychophysiological correlates of conditioned response formation. Psychological Bulletin, 70(2), 105.

Glasser, M. F., Sotiropoulos, S. N., Wilson, J. A., Coalson, T. S., Fischl, B., Andersson, J. L., ... & Van Essen, D. C. (2013). The minimal preprocessing pipelines for the Human Connectome Project. Neuroimage, 80, 105-124.

Goldman-Rakic, P. S. (1995). Cellular basis of working memory. Neuron, 14(3), 477-485.

Goodale, M. A., & Milner, A. D. (1992). Separate visual pathways for perception and action. Trends in neurosciences, 15(1), 20-25.

Gottlieb, G. (1991). Experiential canalization of behavioral development: Theory. Developmental Psychology, 27(1), 1–10.

Grady, C. L., Luk, G., Craik, F. I., & Bialystok, E. (2015). Brain network activity in monolingual and bilingual older adults. Neuropsychologia, 66, 170-181.

Gray, C. R., & Gummerman, K. (1975). The enigmatic eidetic image: A critical examination of methods, data, and theories. Psychological Bulletin, 82(3),383.

Gregory, M. D., Agam, Y., Selvadurai, C., Nagy, A., Vangel, M., Tucker, M., ... & Manoach, D. S. (2014). Resting state connectivity immediately following learning correlates with subsequent sleep-dependent enhancement of motor task performance. NeuroImage, 102, 666-673.

Greicius, M. D., Krasnow, B., Reiss, A. L., & Menon, V. (2003). Functional connectivity in the resting brain: a network analysis of the default mode hypothesis. Proceedings of the National Academy of Sciences, 100(1), 253-258.

Grigorenko, E. L., Kornilov, S. A., & Naumova, O. Y. (2016). Epigenetic regulation of cognition: A circumscribed review of the field. Development and Psychopathology, 28(4pt2), 1285-1304.

Grill-Spector, K., Knouf, N., & Kanwisher, N. (2004). The fusiform face area subserves face perception, not generic within-category identification. Nature neuroscience, 7(5), 555.

Harris, K. D. (2005). Neural signatures of cell assembly organization. Nature reviews Neuroscience, 6(5),399.

Harris, K. D., Csicsvari, J., Hirase, H., Dragoi, G., & Buzsaki, G. (2003). Organization of cell assemblies in the hippocampus. Nature, 424(6948),552.

Häusser, M., Spruston, N., & Stuart, G. J. (2000). Diversity and dynamics of dendritic signaling. Science, 290(5492), 739-744.

Hebb, D. (1949). The Organization of Human Behavior. New York, NY: John Wiley and Sons.

Helmstaedter, M. (2013). Cellular-resolution connectomics: Challenges of dense neural circuit reconstruction. Nature Methods, 10(6), 501-507.

Hirst, W., Phelps, E. A., Buckner, R. L., Budson, A. E., Cuc, A., Gabrieli, J. D., ... & Meksin, R. (2009). Long-term memory for the terrorist attack of September 11: Flashbulb memories, event memories, and the factors that influence their retention. Journal of Experimental Psychology: General, 138(2),161.

Hoaglin DC. John W. (2003). Tukey and data analysis. Statistical Science, 18(3),311-318.

Holtmaat, A. J., Trachtenberg, J. T., Wilbrecht, L., Shepherd, G. M., Zhang, X., Knott, G. W., & Svoboda, K. (2005). Transient and persistent dendritic spines in the neocortex in vivo. Neuron, 45(2), 279-291.

Hua, J. Y., & Smith, S. J. (2004). Neural activity and the dynamics of central nervous system development. Nature Neuroscience, 7(4),327.

Hubbard, E. M., Arman, A. C., Ramachandran, V. S., & Boynton, G. M. (2005). Individual differences among grapheme-color synesthetes: Brain-behavior correlations. Neuron, 45(6), 975-985.

Hubel, D. H., & Wiesel, T. N. (1962). Receptive fields, binocular interaction and functional architecture in the cat's visual cortex. The Journal of Physiology, 160(1), 106-154.

Hyvärinen, A. (2013). Independent component analysis of images. Encyclopedia of Computational Neuroscience, 1-5.

Hyvärinen, A., Karhunen, J., & Oja, E. (2004). Independent component analysis. New York, NY: John Wiley & Sons.

Hyviirinen, A. (2001). Fast ICA by a fixed-point algorithm that maximizes non-Gaussianity. Independent component analysis: principles and practice, 71.

Iijima, Y., & Tanno, Y. (2012). The effect of cognitive load on the temporal focus of mind wandering. Shinrigaku kenkyu: The Japanese journal of psychology, 83(3), 232-236.

Ikegaya, Y., Aaron, G., Cossart, R., Aronov, D., Lampl, I., Ferster, D., & Yuste, R. (2004). Synfire chains and cortical songs: Temporal modules of cortical activity. Science, 304(5670), 559-564.

Immordino-Yang, M. H., & Yang, X. F. (2017). Cultural differences in the neural correlates of social–emotional feelings: an interdisciplinary, developmental perspective. Current Opinion in Psychology, 17, 34-40.

Immordino-Yang, M. H., Christodoulou, J. A., & Singh, V. (2012). Rest is not idleness: Implications of the brain's default mode for human development and education. Perspectives on Psychological Science, 7(4), 352-364.

Immordino-Yang, M. H., McColl, A., Damasio, H., & Damasio, A. (2009). Neural correlates of admiration and compassion. Proceedings of the National Academy of Sciences, 106(19), 8021-8026.

Immordino-Yang, M. H., Yang, X. F., & Damasio, H. (2014). Correlations between social-emotional feelings and anterior insula activity are independent from visceral states but influenced by culture. Frontiers in human neuroscience, 8.

Immordino- Yang, M. H. (2007). A tale of two cases: Lessons for education from the study of two boys living with half their brains. Mind, Brain, and Education, 1(2), 66-83.

Ji, D., & Wilson, M. A. (2007). Coordinated memory replay in the visual cortex and hippocampus during sleep. Nature Neuroscience, 10(1),100.

Johansson, F., Jirenhed, D. A., Rasmussen, A., Zucca, R., & Hesslow, G. (2014). Memory trace and timing mechanism localized to cerebellar Purkinje cells. Proceedings of the National Academy of Sciences, 111(41), 14930-14934.

Jones, Richard H. (2000). Reductionism: Analysis and the fullness of reality. Lewisburg, PA: Bucknell University Press.

Kane, M. J., & McVay, J. C. (2012). What mind wandering reveals about executive-control abilities and failures. Current Directions in Psychological Science, 21(5), 348–354.

Kane, M. J., Brown, L. H., McVay, J. C., Silvia, P. J., Myin-Germeys, I., & Kwapil, T. R. (2007). For whom the mind wanders, and when an experience-sampling study of working memory and executive control in daily life. Psychological Science, 18(7), 614–621.

Kay, P., & McDaniel, C. K. (1978). The linguistic significance of the meanings of basic color terms. Language, 54(3), 610–646.

Kenet, T., Bibitchkov, D., Tsodyks, M., Grinvald, A., & Arieli, A. (2003). Spontaneously emerging cortical representations of visual attributes. Nature, 425(6961),954.

Kerns, J. G., Cohen, J. D., MacDonald, A. W., Cho, R. Y., Stenger, V. A., & Carter, C. S. (2004). Anterior cingulate conflict monitoring and adjustments in control. Science, 303(5660), 1023-1026.

King, J., & Just, M. A. (1991). Individual differences in syntactic processing: The role of working memory. Journal of memory and language, 30(5), 580-602.

Klinger E. (1984). A consciousness-sampling analysis of test anxiety and performance. Journal of Personality and Social Psychology, 47(6),1376.

Klinger E. (2013). Goal commitments and the content of thoughts and dreams: Basic principles. Frontiers in Psychology, 4, 415.

Koechlin, E., Basso, G., Pietrini, P., Panzer, S., & Grafman, J. (1999). The role of the anterior prefrontal cortex in human cognition. Nature, 399(6732), 148-151.

Koenigs, M., Barbey, A. K., Postle, B. R., & Grafman, J. (2009). Superior parietal cortex is critical for the manipulation of information in working memory. Journal of Neuroscience, 29(47), 14980-14986.

Kosslyn, S. M., Ganis, G., & Thompson, W. L. (2001). Neural foundations of imagery. Nature Reviews Neuroscience, 2(9),635.

Kucyi, A., & Davis, K. D. (2014). Dynamic functional connectivity of the default mode network tracks daydreaming. Neuroimage, 100(15), 471-480.

Kuhn, M. R., & Schwanenflugel, P. J. (2010). Aligning theory and assessment of reading fluency: Automaticity, prosody, and definitions of fluency. Reading Research Quarterly, 45(2), 230–251.

Lakoff, G. (2012). Explaining embodied cognition results. Topics in Cognitive Science, 4(4), 773-785.

Lashley, K.S. (1929). Brain mechanisms and intellgence. Chicago, IL: University of Chicago Press.

Lazar, R. M., & Mohr, J. P. (2011). Revisiting the contributions of Paul Broca to the study of aphasia. Neuropsychology Review, 21(3),236.

Lenartowicz, A., Simpson, G. V., & Cohen, M. S. (2013). Perspective: Causes and functional significance of temporal variations in attention control. Frontiers in Human Neuroscience, 7, 381.

LePort, A. K. R., Mattfeld, A. T., Dickinson-Anson, H., Fallon, J. H., Stark, C. E. L., Kruggel, F., . . . McGaugh, J. L. (2012). Behavioral and neuroanatomical investigation of Highly Superior Autobiographical Memory (HSAM). Neurobiology of Learning and Memory, 98(1), 78–92.

Levinson, D. B., Smallwood, J., & Davidson, R. J. (2012). The persistence of thought: Evidence for a role of working memory in the maintenance of task-unrelated thinking. Psychological Science, 23(4), 375-380.

Ley, P., & Florio, T. (1996). The use of readability formulas in health care. Psychology, Health & Medicine, 1(1), 7-28.

Lichtheim, L. (1885). On aphasia. Brain, 7, 433-484.

Lindenberg, R., Fangerau, H., & Seitz, R. J. (2007). "Broca's area" as a collective term?. Brain and Language, 102(1), 22-29.

Loftus, E. F., & Loftus, G. R. (1980). On the permanence of stored information in the human brain. American Psychologist, 35(5),409.

Loftus, E. F., & Palmer, J. C. (1996). Eyewitness testimony. In Introducing Psychological Research (pp. 305-309). UK: Macmillan Education.

Loftus, E. F., & Pickrell, J. E. (1995). The formation of false memories. Psychiatric Annals, 25(12), 720-725.

Lorenz, E. N. (1969). Atmospheric predictability as revealed by naturally occurring analogues. Journal of the Atmospheric Sciences, 26(4), 636-646.

Loveless, N. E., & Sanford, A. J. (1973). Slow potential correlates of preparatory set. Nature Neuroscience, 1(4), 303-314.

Lübke, J., & Feldmeyer, D. (2007). Excitatory signal flow and connectivity in a cortical column: focus on barrel cortex. Brain Topography, 212(1), 3-17.

Luczak, A., Barthó, P., & Harris, K. D. (2009). Spontaneous events outline the realm of possible sensory responses in neocortical populations. Neuron, 62(3), 413-425.

Luczak, A., Bartho, P., & Harris, K. D. (2013). Gating of sensory input by spontaneous cortical activity. Journal of Neuroscience, 33(4), 1684-1695.

Luczak, A., Barthó, P., & Marguet, S. L. (2007). Sequential structure of neocortical spontaneous activity in vivo. Proceedings of the National Academy of Sciences, 104(1), 347-352.

Luczak, A., Hackett, T. A., Kajikawa, Y., & Laubach, M. (2004). Multivariate receptive field mapping in marmoset auditory cortex. Journal of Neuroscience Methods, 136(1), 77-85.

Lynch, G., Deadwyler, S., & Cotman, C. (1973). Postlesion axonal growth produces permanent functional connections. Science, 180(4093), 1364-1366.

MacDonald G, Leary MR (2005). Why does social exclusion hurt? The relationship between social and physical pain. Psychological Bulletin, 131(2),202–223.

Majeed, W., & Magnuson, M. (2009). Spatiotemporal dynamics of low frequency fluctuations in BOLD fMRI of the rat. Journal of Magnetic Resonance Imaging, 30(2), 384-393.

Mao, B. Q., Hamzei-Sichani, F., Aronov, D., Froemke, R. C., & Yuste, R. (2001). Dynamics of spontaneous activity in neocortical slices. Neuron, 32(5), 883-898.

Marcus, D. S., Harms, M. P., Snyder, A. Z., Jenkinson, M., Wilson, J. A., Glasser, M. F., ... & Hodge, M. (2013). Human Connectome Project informatics: Quality control, database services, and data visualization. Neuroimage, 80(15), 202-219.

Maret, S., Faraguna, U., Nelson, A. B., Cirelli, C., & Tononi, G. (2011). Sleep and waking modulate spine turnover in the adolescent mouse cortex. Nature Neuroscience, 14(11), 1418-1420.

Marinkovic, K., Dhond, R. P., Dale, A. M., Glessner, M., & Carr, V. (2003). Spatiotemporal dynamics of modality-specific and supramodal word processing. Neuron, 38(3), 487-497.

Markram, H., Toledo-Rodriguez, M., & Wang, Y. (2004). Interneurons of the neocortical inhibitory system. Nature Reviews Neuroscience, 5(10), 793–807.

Mason, A., & Larkman, A. (1990). Correlations between morphology and electrophysiology of pyramidal neurons in slices of rat visual cortex. II. Electrophysiology. Journal of Neuroscience, 10(5), 1415-1428.

Mason, M. F., Norton, M. I., Van Horn, J. D., Wegner, D. M., Grafton, S. T., & Macrae, C. N. (2007). Wandering minds: The default network and stimulus-independent thought. Science, 315(5810), 393-395.

McCormick, D. A., & Bal, T. (1997). Sleep and arousal: Thalamocortical mechanisms. Annual Review of Neuroscience, 20(1), 185-215.

McGhie, A., & Chapman, J. (1961). Disorders of attention and perception in early schizophrenia. Psychology and Psychotherapy: Theory, Research and Practice, 34(2), 103-116.

McKay, L. C., Evans, K. C., Frackowiak, R. S., & Corfield, D. R. (2003). Neural correlates of voluntary breathing in humans. Journal of Applied Physiology, 95(3), 1170-1178.

McMillan, R. L., Kaufman, S. B., & Singer, J. L. (2013). Ode to positive constructive daydreaming. Frontiers in Psychology, 4, 626.

McVay JC, Kane MJ. (2009). Conducting the train of thought: Working memory capacity, goal neglect, and mind wandering in an executive-control task. Journal of Experimental Psychology: Learning, Memory, and Cognition, 35(1),196.

McVay, J. C., & Kane, M. J. (2012). Drifting from slow to "d'oh!": Working memory capacity and mind wandering predict extreme reaction times and executive control errors. Journal of Experimental Psychology: Learning, Memory, and Cognition, 38(3),525.

McVay, J. C., & Kane, M. J. (2012). Why does working memory capacity predict variation in reading comprehension? On the influence of mind wandering and executive attention. Journal of Experimental Psychology: general, 141(2),302.

259

Mechelli, A., Price, C. J., Friston, K. J., & Ishai, A. (2004). Where bottom-up meets top-down: Neuronal interactions during perception and imagery. Cerebral Cortex, 14(11), 1256-1265.

Merleau-Ponty, M. (1996). Phenomenology of perception. Motilal Banarsidass Publishers: India.

Mesulam, M. M. (2015, October). Revisiting Wernicke's Area. Presented at the seventh annual meeting of the Society for the Neurobiology of Language. Chicago: Illinois. Chicago

Mesulam, M. M., Thompson, C. K., Weintraub, S., & Rogalski, E. J. (2015). The Wernicke conundrum and the anatomy of language comprehension in primary progressive aphasia. Brain, 138(8), 2423-2437.

Mesulam, M. M., Wieneke, C., Hurley, R., Rademaker, A., Thompson, C. K., Weintraub, S., & Rogalski, E. J. (2013). Words and objects at the tip of the left temporal lobe in primary progressive aphasia. Brain, 136(2), 601-618.

Metman, L. V., Bellevich, J. S., Jones, S. M., Barber, M. D., & Streletz, L. J. (1993). Topographic mapping of human motor cortex with transcranial magnetic stimulation: Homunculus revisited. Brain, 6(1), 13-19.

Migueles, M., & Garcia-Bajos, E. (1999). Recall, recognition, and confidence patterns in eyewitness testimony. Applied Cognitive Psychology, 13(3), 257-268.

Mitra, A., & Raichle, M. E. (2016). How networks communicate: Propagation patterns in spontaneous brain activity. Philosophical Transactions B, 371(1705),20150546.

Mitra, A., Snyder, A. Z., & Blazey, T. (2015). Lag threads organize the brain's intrinsic activity. National Academy of Sciences, 112(17), E2235-E2244.

Mitra, A., Snyder, A. Z., & Hacker, C. D. (2014). Lag structure in resting-state fMRI. Journal of Neurophysiology, 111(11), 2374–2391.

Mitra, A., Snyder, A. Z., Blazey, T., & Raichle, M. E. (2015). Lag threads organize the brain's intrinsic activity. Proceedings of the National Academy of Sciences, 112(17), E2235-E2244.

Mitra, A., Snyder, A. Z., Constantino, J. N., & Raichle, M. E. (2015). The lag structure of intrinsic activity is focally altered in high functioning adults with autism. Cerebral cortex, 27(2), 1083–1093.

Miyake, A., Friedman, N. P., Emerson, M. J., Witzki, A. H., Howerter, A., & Wager, T. D. (2000). The unity and diversity of executive functions and their contributions to

complex "frontal lobe" tasks: A latent variable analysis. Cognitive psychology, 41(1), 49-100.

Mohajerani MH, McVea DA, Fingas M, Murphy T.H. (2010). Mirrored bilateral slow-wave cortical activity within local circuits revealed by fast bihemispheric voltage-sensitive dye imaging in anesthetized and awake mice. Journal of Neuroscience, 30(10), 3745-3751.

Moore RY, Bjorklund A, Stenevi U (1971). Plastic changes in the adrenergic innervation of the rat septal area in response to denervation. Brain Research Reviews, 33(1), 13-35.

Mottron, L., Dawson, M., Soulieres, I., Hubert, B., & Burack, J. (2006). Enhanced perceptual functioning in autism: An update, and eight principles of autistic perception. Journal of Autism and Developmental Disorders, 36(1), 27-43.

Mountcastle, V. B. (1997). The columnar organization of the neocortex. Cerebral Cortex, 120(4), 701-722.

Mrazek MD, Smallwood J, Franklin MS, Chin JM, Baird B, Schooler J.W. (2012). The role of mind-wandering in measurements of general aptitude. Journal of Experimental Psychology: General, 141(4),788.

Mrazek, M. D., Chin, J. M., Schmader, T., Hartson, K. A., Smallwood, J., & Schooler, J. W. (2011). Threatened to distraction: Mind-wandering as a consequence of stereotype threat. Journal of Experimental Social Psychology, 47(6), 1243-1248.

Mrazek, M. D., Franklin, M. S., Phillips, D. T., Baird, B., & Schooler, J. W. (2013). Mindfulness training improves working memory capacity and GRE performance while reducing mind wandering. Psychological science, 24(5), 776-781.

Mrazek, M. D., Smallwood, J., & Schooler, J. W. (2012). Mindfulness and mind-wandering: finding convergence through opposing constructs. Emotion, 12(3), 442.

Nishitani, N., Schurmann, M., Amunts K. & Hari, R. (2005). Broca's region: From action to language. Physiology, 20(1), 60-69.

Obayashi, S., Suhara, T., Kawabe, K., Okauchi, T., Maeda, J., Akine, Y., ... & Iriki, A. (2001). Functional brain mapping of monkey tool use. Neuroimage, 14(4), 853-861.

Ogawa, S., Lee, T. M., Kay, A. R., & Tank, D. W. (1990). Brain magnetic resonance imaging with contrast dependent on blood oxygenation. Proceedings of the National Academy of Sciences, 87(24), 9868-9872.

Ottaviani, C., Shahabi, L., Tarvainen, M., Cook, I., Abrams, M., & Shapiro, D. (2015). Cognitive, behavioral, and autonomic correlates of mind wandering and perseverative cognition in major depression. Frontiers in Neuroscience, 8, 433.

Pan, W. J., Thompson, G. J., Magnuson, M. E., & Jaeger, D. (2013). Infraslow LFP correlates to resting-state fMRI BOLD signals. NeuroImage, 74(1), 288–297.

Parent, J. M., Vexler, Z. S., Gong, C., Derugin, N., & Ferriero, D. M. (2002). Rat forebrain neurogenesis and striatal neuron replacement after focal stroke. Annual review of neuroscience, 52(6), 802-813.

Park, H. J., & Friston, K. (2013). Structural and functional brain networks: From connections to cognition. Science, 342(6158),1238411.

Parsons, L. M. (2003). Superior parietal cortices and varieties of mental rotation. Trends in cognitive sciences, 7(12), 515-517.

Patihis, L., Frenda, S. J., LePort, A. K. R., Petersen, N., Nichols, R. M., Stark, C. E. L., . . . Loftus, E. F. (2013). False memories in highly superior autobiographical memory individuals. Proceedings of the National Academy of Sciences, 110(52), 20947-20952.

Pavlov, I. P. (1927). Conditioned reflexes: An investigation of the physiological activity of the cerebral cortex. Book 17.

Penfield, W. and Boldrey, E. (1937). Somatic motor and sensory representation in the cerebral cortex of man as studied by electrical stimulation. Brain: a journal of neurology, LX, 389-443.

Penrose, R. (1955, July). A generalized inverse for matrices. In Mathematical proceedings of the Cambridge philosophical society (Vol. 51, No. 3, pp. 406-413). Cambridge University Press.

Pessoa, L. (2009). How do emotion and motivation direct executive control? Trends in cognitive sciences, 13(4), 160-166.

Pessoa, L. (2012). Beyond brain regions: Network perspective of cognition–emotion interactions. Behavioral and Brain Sciences, 35(3), 158-159.

Pessoa, L. (2013). The cognitive-emotional brain: From interactions to integration. Boston, MA: MIT press.

Pessoa, L., & Adolphs, R. (2010). Emotion processing and the amygdala: From a 'low road'to 'many roads' of evaluating biological significance. Nature Reviews Neuroscience, 11(11),773.

Poerio, G. L., Totterdell, P., & Miles, E. (2013). Mind-wandering and negative mood: Does one thing really lead to another? Consciousness and Cognition, 22(4), 1412-1421.

Polanyi, M. (2009). The tacit dimension. Chicago, IL: University of Chicago Press.

Price, C. J., & Friston, K. J. (2002). Degeneracy and cognitive anatomy. Trends in Cognitive Science, 6(10), 416-421.

Pysh, J. J., & Weiss, G. M. (1979). Exercise during development induces an increase in Purkinje cell dendritic tree size. Science, 206(4415), 230-232.

Radley, J. J., Rocher, A. B., Miller, M., Janssen, W. G., Liston, C., Hof, P. R., ... & Morrison, J. H. (2005). Repeated stress induces dendritic spine loss in the rat medial prefrontal cortex. Cerebral Cortex, 16(3), 313-320.

Raichle, M. E. (2006). The brain's dark energy. Science-New York Then Washington-, 314(5803), 1249.

Raichle, M. E. (2009). A paradigm shift in functional brain imaging. The Journal of Neuroscience, 29(41), 12729–12734.

Raichle, M. E. (2010). The brain's dark energy. Scientific American, 302(3), 44–49.

Raichle, M. E. (2015). The brain's default mode network. Annual Review of Psychology, 38(1), 433–447.

Raichle, M. E. (2015). The restless brain: how intrinsic activity organizes brain function. Philosophical Transactions B, 370(1668),20140172.

Raichle, M. E., & Gusnard, D. A. (2002). Appraising the brain's energy budget. Proceedings of the National Academy of Sciences, 99(16), 10237–10239.

Raichle, M. E., MacLeod, A. M., Snyder, A. Z., Powers, W. J., Gusnard, D. A., & Shulman, G. L. (2001). A default mode of brain function. Proceedings of the National Academy of Sciences, 98(2), 676-682.

Ramachandran, V. S., Rogers-Ramachandran, D., & Cobb, S. (1995). Touching the phantom limb. Nature, 377(6549),489.

Ramachandran, V. S., Stewart, M., & Rogers-Ramachandran, D. C. (1992). Perceptual correlates of massive cortical reorganization. Neuroreport, 3(7), 583-586.

Rasinski, T. V., Padak, N. D., McKeon, C. A., Wilfong, L. G., Friedauer, J. A., & Heim, P. (2011). Is reading fluency a key for successful high school reading? Journal of Adolescent & Adult Literacy, 49(1), 22–27.

Rasinski, T.V. (2004). Assessing reading fluency. Honolulu, HI: Pacific Resources for Education and Learning.

Rasinski, T.V., & Hoffman, T.V. (2003). Theory and research into practice: Oral reading in the school literacy curriculum. Reading Research Quarterly, 38, 510–522.

Reichle, E. D., Reineberg, A. E., & Schooler, J. W. (2010). Eye movements during mindless reading. Psychological Science, 21(9), 1300-1310.

Ridley, R. M., Frith, C. D., Crow, T. J., & Conneally, P. M. (1988). Anticipation in Huntington's disease is inherited through the male line but may originate in the female. Journal of Medical Genetics, 25(9), 589-595.

Rock, I. (1985). Perception and knowledge. Acta Psychologica, 59(1), 3-22.

Rubinov, M., & Sporns, O. (2010). Complex network measures of brain connectivity: Uses and interpretations. NeuroImage, 52(3), 1059–1069.

Schmithorst VJ, Holland SK. (2004). Comparison of three methods for generating group statistical inferences from independent component analysis of functional magnetic resonance imaging data. Journal of Magnetic Resonance Imaging, 19(3), 365-368.

Schneider, G., Havenith, M. N., & Nikolić, D. (2006). Spatiotemporal structure in large neuronal networks detected from cross-correlation. Neural Computation, 18(10), 2387-2413.

Schüz, A., & Palm, G. (1989). Density of neurons and synapses in the cerebral cortex of the mouse. Journal of Comparative Neurology, 286(4), 442-455.

Scoville, W. B., & Milner, B. (1957). Loss of recent memory after bilateral hippocampal lesions. Journal of Neurology, Neurosurgery, and Psychiatry, 20(1),11.

Segal, M. (2005). Dendritic spines and long-term plasticity. Nature reviews Neuroscience, 6(4),277.

Sejnowski, T. J. (1999). The book of Hebb. Neuron, 24(4), 773-776.

Serniclaes, W., Van Heghe, S., Mousty, P., Carré, R., & Sprenger-Charolles, L. (2004). Allophonic mode of speech perception in dyslexia. Journal of Experimental Child Psychology, 87(4), 336-361.

Shepherd, G. M. (Ed.). (2003). The synaptic organization of the brain. Oxford, UK: Oxford University Press.

Shuell, T. J. (1986). Cognitive conceptions of learning. Review of educational research, 56(4), 411-436.

Shulley, L. J., & Shake, M. C. (2016). Investigating the relationship between bilingualism, cognitive control, and mind wandering. Journal of Cognitive Psychology, 28(3), 257-274.

Singer, W. (1999). Neuronal synchrony: A versatile code for the definition of relations? . Neuron, 24(1), 49–65.

Skinner, B. F. (1950). Are theories of learning necessary? Psychological Review, 57(4),193.

Skinner, B. F. (1974). About behaviorism. New York, NY: Vintage Books.

Smallwood, J. (2011). Mind-wandering while reading: Attentional decoupling, mindless reading and the cascade model of inattention. Language and Linguistics Compass, 5(2), 63–77.

Smallwood, J., & O'Connor, R. C. (2011). Imprisoned by the past: Unhappy moods lead to a retrospective bias to mind wandering. Cognition & Emotion, 25(8), 1481-1490.

Smallwood, J., & Schooler, J. W. (2015). The science of mind wandering: Empirically navigating the stream of consciousness. Annual Review of Psychology, 66, 487-518.

Smallwood, J., Beach, E., Schooler, J. W., & Handy, T. C. (2008). Going AWOL in the brain: Mind wandering reduces cortical analysis of external events. Journal of Cognitive Neuroscience, 20(3), 458-469.

Smallwood, J., Fitzgerald, A., Miles, L. K., & Phillips, L. H. (2009). Shifting moods, wandering minds: Negative moods lead the mind to wander. Emotion, 9(2),271.

Smallwood, J., Fitzgerald, A., Miles, L. K., & Phillips, L. H. (2009). Shifting moods, wandering minds: negative moods lead the mind to wander. Emotion, 9(2), 271.

Smallwood, J., Gorgolewski, K. J., Golchert, J., Ruby, F. J., Engen, H., Baird, B., ... & Margulies, D. S. (2013). The default modes of reading: Modulation of posterior cingulate and medial prefrontal cortex connectivity associated with comprehension and task focus while reading. Frontiers in Human Neuroscience, 7, 734.

Smilek, D., Carriere, J. S., & Cheyne, J. A. (2010). Out of mind, out of sight: eye blinking as indicator and embodiment of mind wandering. Psychological Science, 21(6), 786-789.

Smith, A. M., Lewis, B. K., Ruttimann, U. E., Frank, Q. Y., Sinnwell, T. M., Yang, Y., ...
&, Frank, J. A. (1999). Investigation of low frequency drift in fMRI signal.
Neuroimage, 9(5), 526-533.

Smith, E., & Delargy, M. (2005). Locked-in syndrome. Bmj, 330(7488), 406-409.

Sporns, O. (2010). Networks of the brain. Boston, MA: MIT press.

Sporns, O., & Betzel, R. F. (2016). Modular brain networks. Behavioral and Brain
Sciences, 67(1), 613–640.

Spreng, R. N., & Grady, C. L. (2010). Patterns of brain activity supporting
autobiographical memory, prospection, and theory of mind, and their relationship
to the default mode network. Journal of cognitive neuroscience, 22(6), 1112-1123.

Spreng, R. N., Stevens, W. D., Chamberlain, J. P., Gilmore, A. W., & Schacter, D. L.
(2010). Default network activity, coupled with the frontoparietal control network,
supports goal-directed cognition. Neuroimage, 53(1), 303-317.

Spruston, N., Stuart, G., & Häusser, M. (1999). Dendritic integration. In Dendrites (pp.
231-271). Oxford UK: Oxford University Press.

Stevens, W. D., Buckner, R. L., & Schacter, D. L. (2009). Correlated low-frequency
BOLD fluctuations in the resting human brain are modulated by recent experience
in category-preferential visual regions. Cerebral cortex, 20(8), 1997-2006.

Straube, T., & Miltner, W. H. (2011). Attention to aversive emotion and specific
activation of the right insula and right somatosensory cortex. Neuroimage, 54(3),
2534-2538.

Strogatz, S. H. (2014). Nonlinear dynamics and chaos: With applications to physics,
biology, chemistry, and engineering. Philadelphia, PA: Westview press.

Stuart, G.J., Sprutson, N., and Hauser, M. (Eds) (1999). Dendrites. Oxford, UK: Oxford
University Press.

Svensén M, Kruggel F, Benali H. (2002). ICA of fMRI group study data. NeuroImage,
16(3PA),551–563.

Takahashi, T., Suzuki, M., Zhou, S. Y., Tanino, R., Hagino, H., Kawasaki, Y., ... &
Kurachi, M. (2006). Morphologic alterations of the parcellated superior temporal
gyrus in schizophrenia spectrum. Schizophrenia research, 83(2), 131-143.

Takahashi, T., Wood, S. J., Yung, A. R., Soulsby, B., McGorry, P. D., Suzuki, M., ... &
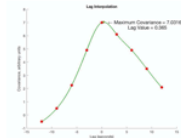Pantelis, C. (2009). Progressive gray matter reduction of the superior temporal

gyrus during transition to psychosis. Archives of general psychiatry, 66(4), 366-376.

Tambini, A., Ketz, N., & Davachi, L. (2010). Enhanced brain correlations during rest are related to memory for recent experiences. Neuron, 65(2), 280-290.

Taylor, C. P., & Dudek, F. E. (1984). Excitation of hippocampal pyramidal cells by an electrical field effect. Journal of Neurophysiology, 52(1), 126-142.

Teigen, K. H. (1994). Yerkes-Dodson: A law for all seasons. Theory & Psychology, 4(4), 525-547.

Thaler, R. H., & Sunstein, C. R. (2008). Nudge: Improving Decisions About Health, Wealth, and Happiness. New Haven, CT: Yale University Press.

Thoenissen, D., Zilles, K. & Toni, I. (2002). Differential involvement of parietal and precentral regions in movement preparation and motor intention. Journal of Neuroscience, 22(20),9024–34.

Thorndike, E. L. (1914). Educational psychology: Briefer course. New York, NY: Teachers College, Columbia University.

Tomás, R. (March 2017). Big Ideas in Cognitive Neuroscience: On Memory. Symposium Session Presented at Cognitive Neuroscience Society Annual Meeting. San Francisco.

Tonegawa, S., Pignatelli, M., Roy, D. S., & Ryan, T. J. (2015). Memory engram storage and retrieval. Current Opinion in Neurobiology, 35, 101-109.

Traub, R. D., & Wong, R. K. (1982). Cellular mechanism of neuronal synchronization in epilepsy. Science, 216(4547), 745-747.

Tukey, J. W. (1977). Exploratory data analysis. Boston, MA: Addison-Wesley.

Uddin, L. Q., Clare Kelly, A. M., Biswal, B. B., Xavier Castellanos, F., & Milham, M. P. (2009). Functional connectivity of default mode network components: correlation, anticorrelation, and causality. Human brain mapping, 30(2), 625-637.

Unsworth N, McMillan BD. (2013). Mind wandering and reading comprehension: examining the roles of working memory capacity, interest, motivation, and topic experience. Journal of Experimental Psychology: Learning, Memory, and Cognition, 39(3),832.

Van den Heuvel, M. P., & Hulshoff Pol, H. E. (2010). Exploring the brain network: A review on resting-state fMRI functional connectivity. European Neuropsychopharmacology, 20(8), 519–534.

Van Den Heuvel, M. P., Mandl, R. C., Kahn, R. S., Pol, H., & Hilleke, E. (2009). Functionally linked resting- state networks reflect the underlying structural connectivity architecture of the human brain. Human Brain Mapping, 30(10), 3127-3141.

Van Dijk, K. R., Hedden, T., Venkataraman, A., Evans, K. C., Lazar, S. W., & Buckner, R. L. (2010). Intrinsic functional connectivity as a tool for human connectomics: theory, properties, and optimization. Journal of neurophysiology, 103(1), 297-321.

Van Dijk, T. A., & Kintsch, W. (1983). Strategies of discourse comprehension. New York, NY: Academic Press.

Van Essen DC, Drury HA, Joshi S, Miller MI. (1998). Functional and structural mapping of human cerebral cortex: Solutions are in the surfaces, Proc Natl Acad Sci U S A , vol. Proceedings of the National Academy of Sciences, 95(3), 788-795.

Van Essen DC. (2002). Windows on the brain: The emerging role of atlases and databases in neuroscience. Current Opinion in Neurobiology, 12(5), 574-579.

Van Essen, D. C. (1997). A tension-based theory of morphogenesis and compact wiring in the central nervous system. Nature, 385(6614),313.

Van Essen, D. C., Glasser, M. F., Dierker, D. L., Harwell, J., & Coalson, T. (2011). Parcellations and hemispheric asymmetries of human cerebral cortex analyzed on surface-based atlases. Cerebral Cortex, 22(10), 2241-2262.

Van Essen, D. C., Smith, S. M., Barch, D. M., Behrens, T. E., Yacoub, E., Ugurbil, K., & Wu-Minn HCP Consortium. (2013). The WU-Minn human connectome project: An overview. Neuroimage, 80(15), 62-79.

Veenendaal, N. J., Groen, M. A., & Verhoeven, L. (2015). What oral text reading fluency can reveal about reading comprehension. Journal of Research in Reading, 38(3), 213–225.

Vygotsky, L. S. (1997). The collected works of LS Vygotsky: Problems of the theory and history of psychology (Vol 3). (N. Swanson, L. W. Swanson Trans), New York, NY: Plenum Press. (Original work published 1987).

Waddington, C. H. (1942). Canalization of development and the inheritance of acquired characters. Nature, 150(3811), 563-565.

Wainwright, P. E., Bulman-Fleming, M. B., Levesque, S., Mutsaers, L., & McCutcheon, D. (1998). A saturated-fat diet during development alters dendritic growth in mouse brain. Nutritional Neuroscience, 1(1), 49-58.

Wall, M. E., Rechtsteiner, A., & Rocha, L. M. (2003). Singular value decomposition and principal component analysis. In A practical approach to microarray data analysis (pp. 91-109). Springer US.

Walter, W., Cooper, R., Aldridge, V. J., & McCallum, W. C. (1964). Contingent negative variation: An electric sign of sensori-motor association and expectancy in the human brain. Nature, 203(4943), 380-384.

Watson, J. B. (1930). Behaviorism, revised edition. Chicago, IL: University of Chicago Press.

Watters, P. A., Martin, F., & Schreter, Z. (1997). Caffeine and cognitive performance: The nonlinear Yerkes–Dodson Law. Human Psychopharmacology: Clinical and Experimental, 12(3), 249-257.

Watts, D. J., & Strogatz, S. H. (1998). Collective dynamics of 'small-world' networks. Nature, 393(6684),440.

Wessinger, C. M., Buonocore, M. H., Kussmaul, C. L., & Mangun, G. R. (1997). Tonotopy in human auditory cortex examined with functional magnetic resonance imaging. Human Brain Mapping, 5(1), 18-25.

White, N. P. (1976). Plato on knowledge and reality. Indianapolis, IN: Hackett Publishing.

Witherington, D.C.(2014, January). Embodiment in the Psychological Science and the Psychology of Embodiment [Video File]. https://www.youtube.com/watch?v=SZon3BYnXpw&t=2584s.

Woldorff, M. G., Liotti, M., Seabolt, M., Busse, L., Lancaster, J. L., & Fox, P. T. (2002). The temporal dynamics of the effects in occipital cortex of visual-spatial selective attention. Cognitive Brain Research, 15(1), 1-15.

Wolpert, D. M., Goodbody, S. J., & Husain, M. (1998). Maintaining internal representations: the role of the human superior parietal lobe. Nature neuroscience, 1(6), 529-533.

Woodhead, Z. V. J., Barnes, G. R., Penny, W., Moran, R., Teki, S., Price, C. J., & Leff, A. P. (2012). Reading front to back: MEG evidence for early feedback effects during word recognition. Cerebral Cortex, 24(3), 817-825.

Woolley, C. S., & McEwen, B. S. (1993). Roles of estradiol and progesterone in regulation of hippocampal dendritic spine density during the estrous cycle in the rat. Journal of Comparative Neurology, 336(2), 293-306.
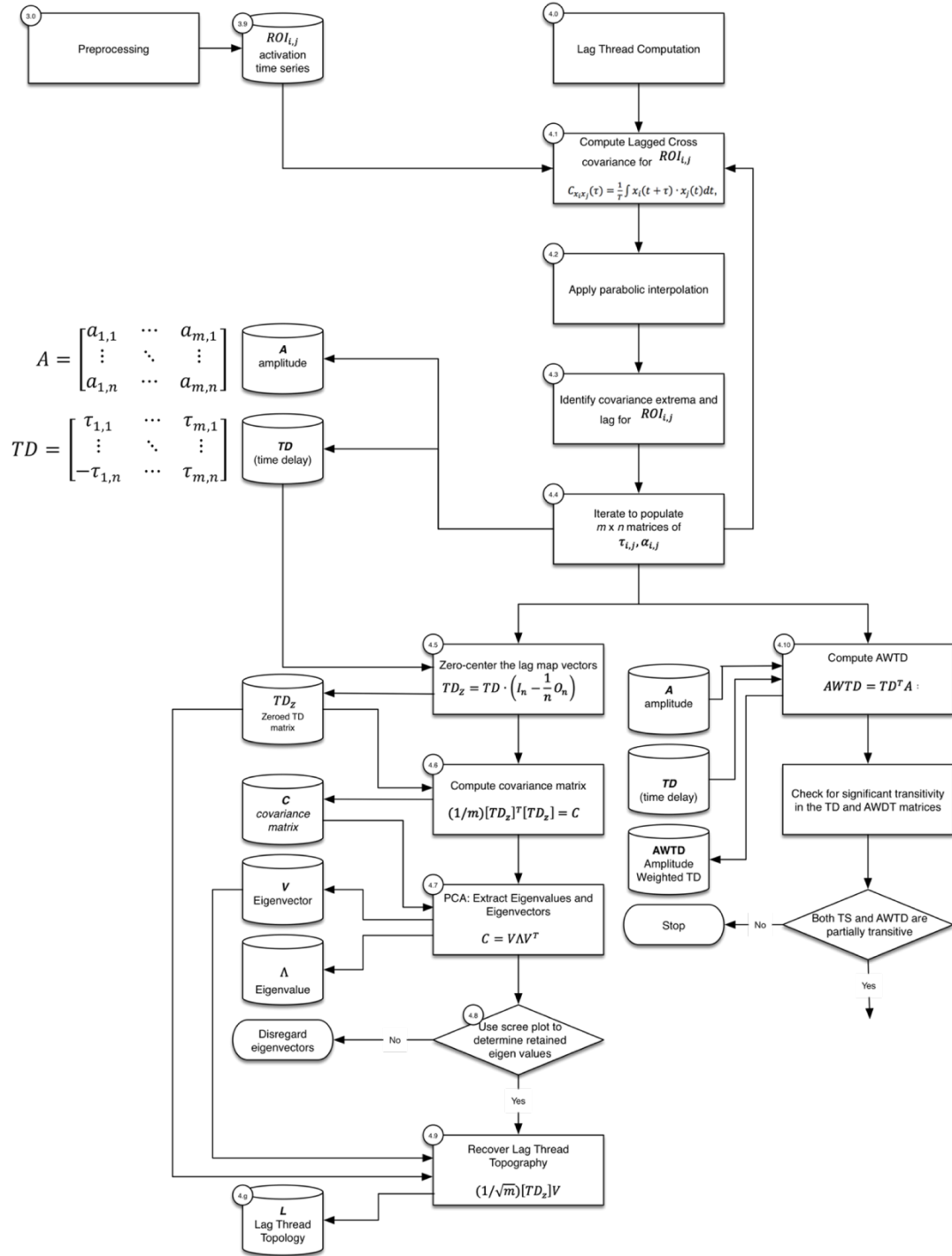
Wulf, G., McNevin, N., & Shea, C. H. (2001). The automaticity of complex motor skill learning as a function of attentional focus. The Quarterly Journal of Experimental Psychology: Section A, 54(4), 1143-1154.

Xiong, J., Parsons, L. M., Gao, J. H., & Fox, P. T. (1999). Interregional connectivity to primary motor cortex revealed using MRI resting state images. Human Brain Mapping, 8(2- 3), 151-156.

Y Cajal, S. R. (1995). Histology of the nervous system. New York, NY: Oxford University Press.

Yang, G., Pan, F., & Gan, W. B. (2009). Stably maintained dendritic spines are associated with lifelong memories. Nature, 462(7275),920.

Yang, T. T., Gallen, C. C., Schwartz, B., Bloom, F. E., Ramachandran, V. S., & Cobb, S. (1994). Sensory maps in the human brain. Nature, 368(6472), 592-593.

Yang, X. F., Bossmann, J., Schiffhauer, B., Jordan, M., & Immordino-Yang, M. H. (2012). Intrinsic default mode network connectivity predicts spontaneous verbal descriptions of autobiographical memories during social processing. Frontiers in psychology, 3.

Yeh, S. R., Musolf, B. E., & Edwards, D. H. (1997). Neuronal adaptations to changes in the social dominance status of crayfish. Journal of Neuroscience, 17(2), 697-708.

Yeo, B. T., Krienen, F. M., Sepulcre, J., Sabuncu, M. R., Lashkari, D., Hollinshead, M., ... & Fischl, B. (2011). The organization of the human cerebral cortex estimated by intrinsic functional connectivity. Journal of neurophysiology, 106(3), 1125-1165.

Yuste, R. (2010). Dendritic spines. Boston, MA: MIT press.

Zhang, M., Li, J., Chen, C., Xue, G., Lu, Z., Mei, L., ... & Wei, M. (2014). Resting-state functional connectivity and reading abilities in first and second languages. Neuroimage, 84, 546-553.

Appendix A: Workflow

Stop	Description		Input		Output
				Artefacts	
4.0	Lag Thread Computation (Mitra et al., 2014; Mitra, Snyder, & Blazey, 2015a)				
4.1	**Compute Lagged Cross covariance for** $ROI_{i,j}$ **:** All remaining time points after preprocessing in ROI time course are compared using a cross covariance function. This results in a covariance value for each lag value as the time course data between the two ROIs are compared.	3.z	3.z: ROI time course BOLD Response		
4.2	**Apply parabolic interpolation** To estimate values of lag less than the TR of 2 seconds parabolic interpolation is applied to the covariance function.				
4.3	**Identify covariance extrema and lag for** $ROI_{i,j}$ Using this interpolated data, the maximum covariance is identified between the two time courses. In essence, the activation sequence is compared at different time points until a maximum covariance is identified. Because the bold signal is aperiodic there is only one such extremum for each comparison. These values are represented by $\tau_{i,j}, \alpha_{i,j}$				
4.4	**Iterate to populate** m **x** n **matrices of** $\tau_{i,j}, \alpha_{i,j}$**:** The extrema values are then entered into two matrices. The Time Delay (TD) matrix represents the pairing of all ROIs and in the case of ROIs is a square matrix (although it is not necessarily square). Each item in TD represents the time shift where the two regions of interest are at maximum covariance amplitude (note that this is not the maximum BOLD response, but the maximum covariance from 4.3. The amplitudes of the covariance function at these extrema are entered into an identical matrix of covariance amplitude (A). For the TD matrix the diagonal will be populated with zeroes because the activation sequence for an ROI maximally covaries with itself with no lag in time. Across the diagonal, the magnitude of the values are equal because if ROI_x lags after ROI_y by t seconds, then ROI_y lags after ROI_x by −t seconds.			4.a 4.b	A amplitude $$A = \begin{bmatrix} a_{1,1} & \cdots & a_{m,1} \\ \vdots & \ddots & \vdots \\ a_{1,n} & \cdots & a_{m,n} \end{bmatrix}$$ T Time Delay matrix $$TD = \begin{bmatrix} \tau_{1,1} & \cdots & \tau_{m,1} \\ \vdots & \ddots & \vdots \\ -\tau_{1,n} & \cdots & \tau_{m,n} \end{bmatrix}$$
4.5	**Zero-center the lag map vectors** (Mitra, Snyder, & Blazey, 2015a) Each column vector of TD is forced to average to zero by dividing each element in the vector by the vector's mean. This is done in matrix notation by pre-multiplying the centering matrix by TD. (double check this reasoning) This gives a standard measure of variance for each time delay vector. In essence this tells us how much each lag deviates from the mean. $$TD_z = TD \cdot \left(I_n - \frac{1}{n}O_n\right)$$ $$TD_z = TD \cdot \left(I_n - \frac{1}{n}O_n\right) = \begin{bmatrix} \tau_{1,1} & \cdots & \tau_{n,1} \\ \vdots & \ddots & \vdots \\ -\tau_{1,n} & \cdots & \tau_{m,n} \end{bmatrix} \cdot \left(\begin{bmatrix} 1_{1,1} & \cdots & 0_{n,1} \\ \vdots & \ddots & \vdots \\ 0_{1,n} & \cdots & 1_{m,n} \end{bmatrix} - \frac{1}{n}\begin{bmatrix} 1_{1,1} & \cdots & 1_{n,1} \\ \vdots & \ddots & \vdots \\ 1_{1,n} & \cdots & 1_{m,n} \end{bmatrix} \right)$$	4.a 4.b	4.a: A amplitude TD Time Delay matrix	4.c	TD_z
4.6	**Compute covariance matrix** Before applying PCA, to the matrix is is converted to a covariance matrix (C) representing the standardized variance of lag times within TD. $$C = (1/m)[TD_z]^T[TD_z]$$	4.c	TD_z	4.d	C
4.7	**PCA: Extract Eigenvalues and Eigenvectors** PCA is applied to C giving us the eigenvalues and eigenvectors of the covariance matrix. Each column in TD represents one possible ordinal sequence of lag values. PCA is applied to find out which sequence represents the maximum amount of variance in the data set. I other words, we are attempting to identify which sequence of lag threads accounts for the maximum amount of information in the data by minimizing the variance using the Eigen vector. The eigenvalue tells us the approximate amount of variation that is accounted for by the lag sequence. The sequences are also orthogonal in this analysis. $$C = V\Lambda V^T$$	4.d	C	4.e 4.f	Eigenvector V Eigenvalue Λ
4.8	**Dimension Reduction** Utilizing a scree plot approach, we identify which eigenvalues represent most of the variance in the data and thus reduce the number of dimensions. In other words, we are asking which sequences account for most of the variance in the				

	data set. $\Lambda > 0$, this is an ideal, however, to reduce the number of dimensions we simply identify the eigenvalues that account for most of the variation in the data. In most cases, this division is clear.				
4.9	**Recover Lag Thread Topography** To recover the lag thread topographies, we obtain the eigenvector weighted sums using the zeroed time delay matrix. *The columns of L are mutually orthogonal and ordered according to variance explained.* $$L = (1/\sqrt{m})[TD_z]V$$	4.c 4.e	TD_z Eigenvector V	4.g	L Lag Thread Topology
4.10	**Compute AWTD** (Mitra et al., 2014) This is the amplitude weighted time delay matrix which can be used to recover signal magnitude information lost in the *TD*. In this matrix each lag is weighted by the corresponding covariance amplitude at that time point. Using this data we can recover signal amplitudes from which the cross-covariance functions were derived. $$AWTD = TD^T A = \begin{bmatrix} \tau_{1,1} \cdot a_{1,1} & \cdots & \tau_{1,1} \cdot a_{m,1} \\ \vdots & \ddots & \vdots \\ -\tau_{1,1} \cdot a_{1,n} & \cdots & \tau_{1,1} \cdot a_{m,n} \end{bmatrix}$$	4.a 4.b	A TD	4.h	AWTD
4.11	**Are TD and AWTD are significantly transitive?** This means that the loops (vectors of TD and AWTD) should equal zero. This is not possible if selecting ROIs that do not represent all regions of the brain. It is also not possible to make it exactly equal zero, so, we are checking for partial transitivity (Nikolic 2007). Significant transitivity is present if the number of all possible triples exhibiting transitivity exceeds the number of those expected by chance alone (P<.05).				
4.12	**Computations of Latency projections** (Nikolic 2007; Schneider et al. 2006) The latency projection from the multidimensional maps in TD and AWTD are reduced into a single one dimensional maps. These resulting row vectors represent latency and amplitude weighted latency at each ROI.		$AWTD_{mxn}$ TD_{mxn}		$AWTD_{p\,1xn}$ $TD_{p,1xn}$
4.13	**Estimate BOLD percent signal change *Amp*** Amp is also referred to as the latency process amplitude image (LPA); this terminology will not be used here. To get Amp we divide $AWTD_p$ by TD_p element-wise. The result is an estimate of regional amplitudes of BOLD percent signal change. $Amp = AWTD_p ./ TD_p$		$AWTD_{p\,1xn}$ $TD_{p,1xn}$		Amp
4.14	PCA is applied to complete set of BOLD time series, which assigns a percentage of variance in the BOLD time series to each PC.				
4.15	Amp is projected onto each principal component to find a weight for each ROI. $$w_i^{Amp} i = Proj\left(Amp, PC_i^{BOLD}\right), i = 1 \dots n$$				

Appendix B: Pipeline for Lag Structure Analysis

$$A = \begin{bmatrix} a_{1,1} & \cdots & a_{m,1} \\ \vdots & \ddots & \vdots \\ a_{1,n} & \cdots & a_{m,n} \end{bmatrix}$$

$$TD = \begin{bmatrix} \tau_{1,1} & \cdots & \tau_{m,1} \\ \vdots & \ddots & \vdots \\ -\tau_{1,n} & \cdots & \tau_{m,n} \end{bmatrix}$$

Appendix C: Reading Comprehension Questions

Reading Comprehension Questions

1) What was wrong with Owen?

2) What was unique about Owen's disorder?

3) What word was Owen's only word he regressed to?

4) What kind of job did his parents have?

5) Did Owen have a brother or a sister?

6) What did Owen and his sibling do?

7) Did doctors think TV was bad for Owen?

8) What movie did Owen respond to with juciferous?

9) What was Owen saying?

10) How did the therapist explain this?

11) Who did Owen ride with at Disneyland?

12) How did Owen act at Disneyland?

13) Did Owen pull out the sword?

14) Did Walter pull out the sword?

15) Who gets sad on Walter's birthdays?

16) Did Owen speak in complex sentences as he got older?

17) What was special about Owen's sentence?

Appendix D: Anxiety Questions

Rating Scale

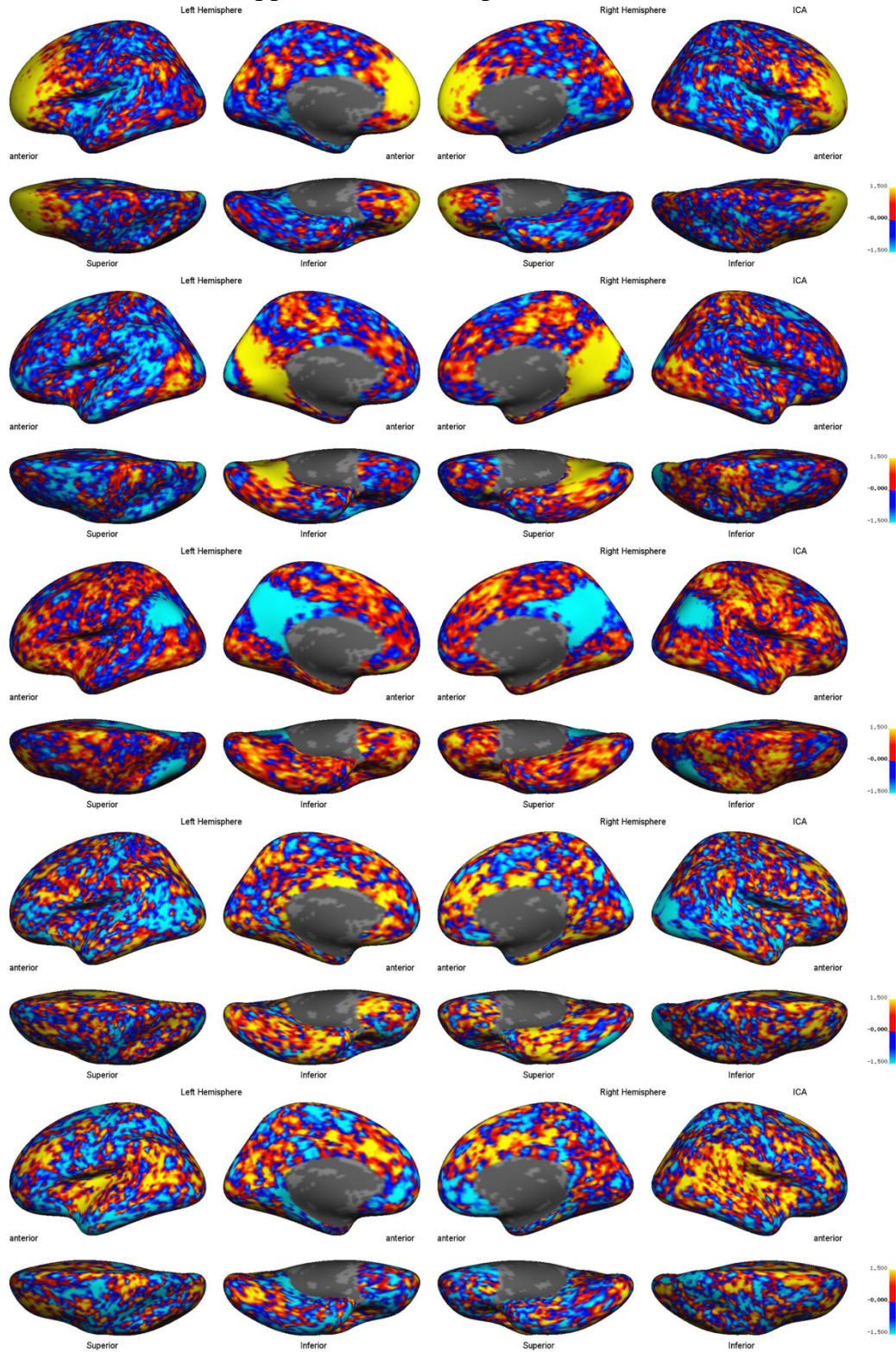| Strongly agree	Agree	Neither agree nor disagree	Disagree	Strongly Disagree

1. I start to panic when I have to read aloud without preparation.

2. I can feel my heart pounding when I'm reading aloud.

3. I feel very self-conscious about reading aloud.
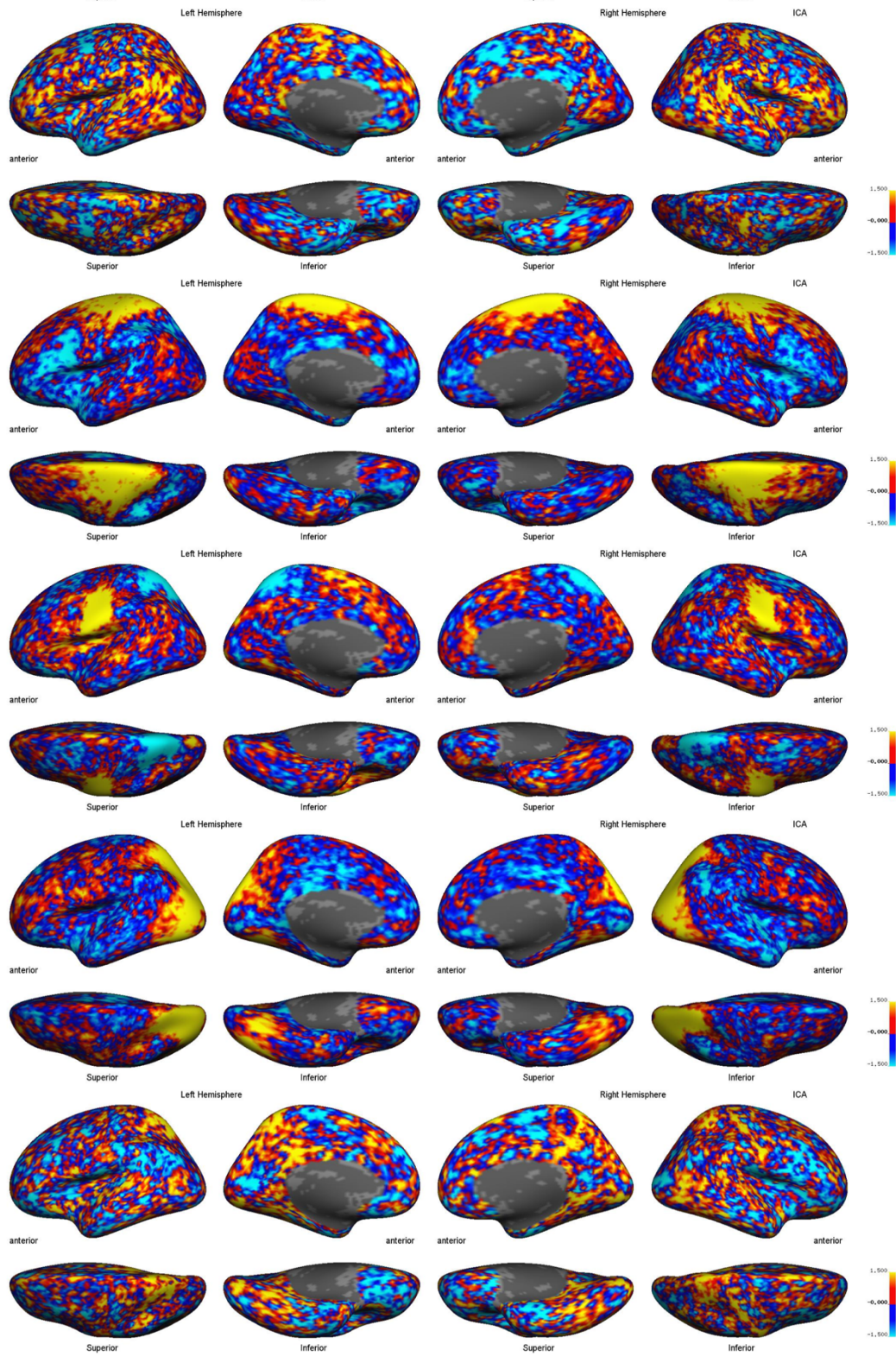
4. I get nervous and confused when I am reading aloud.
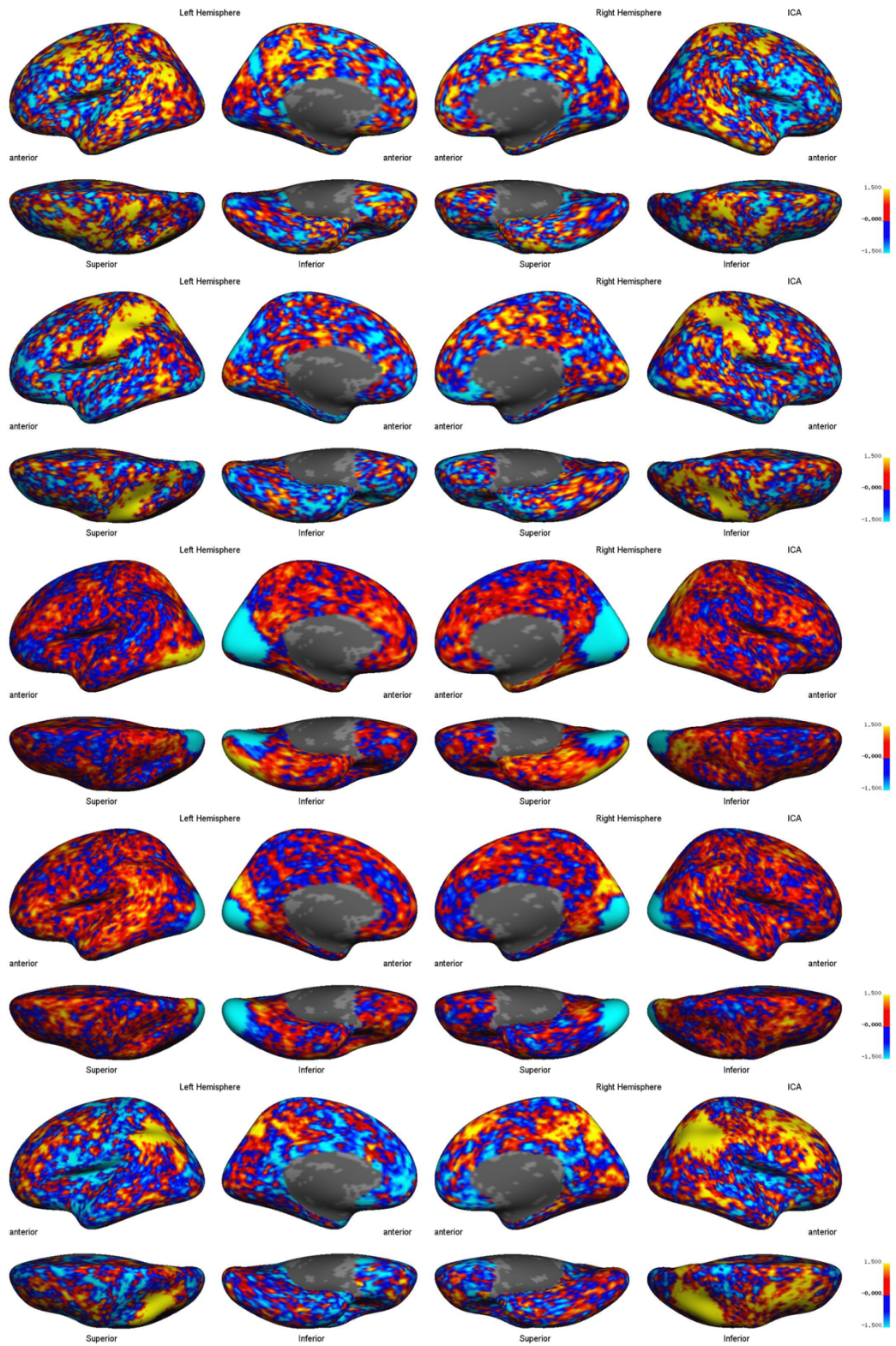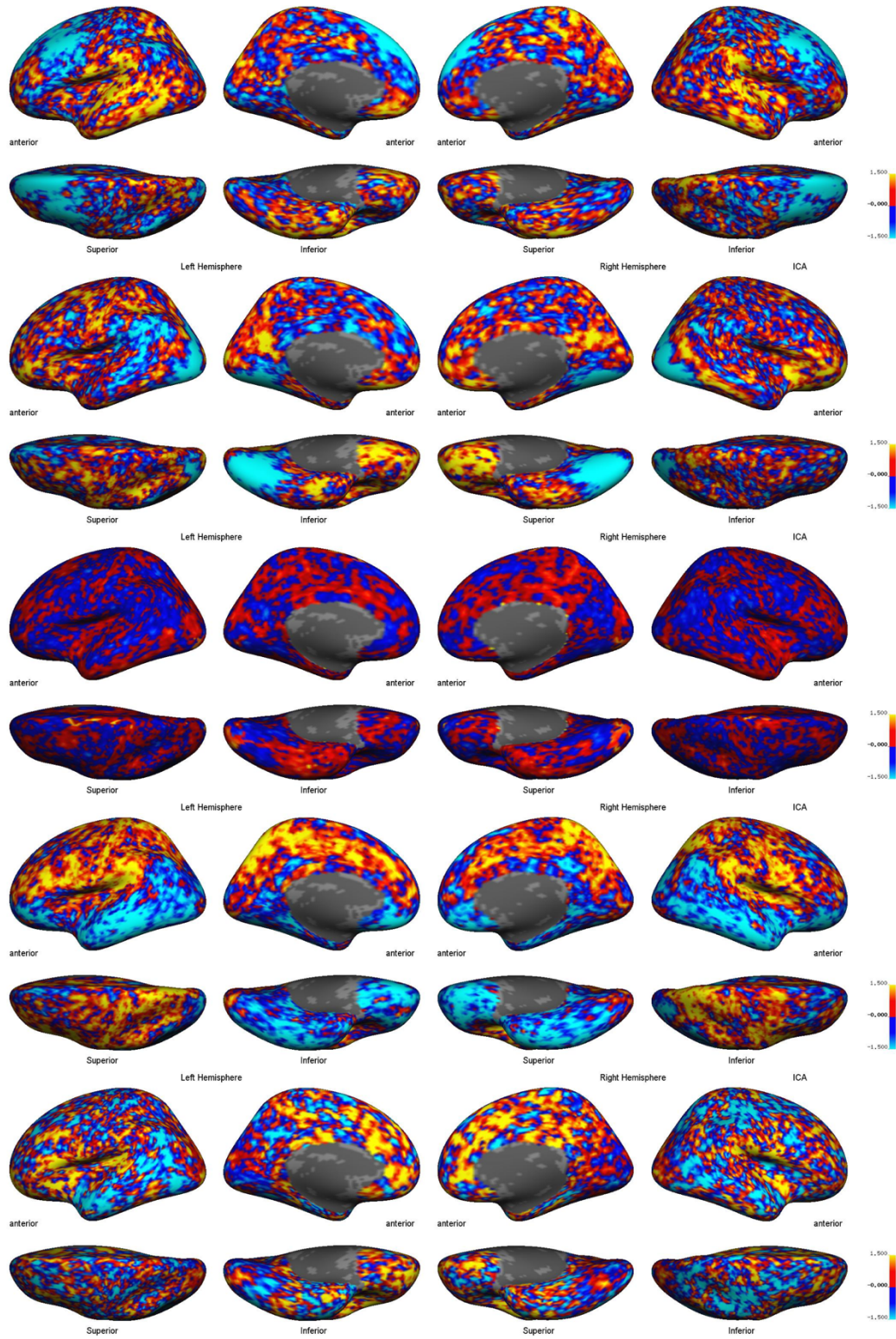
Appendix E: 10 Component Model
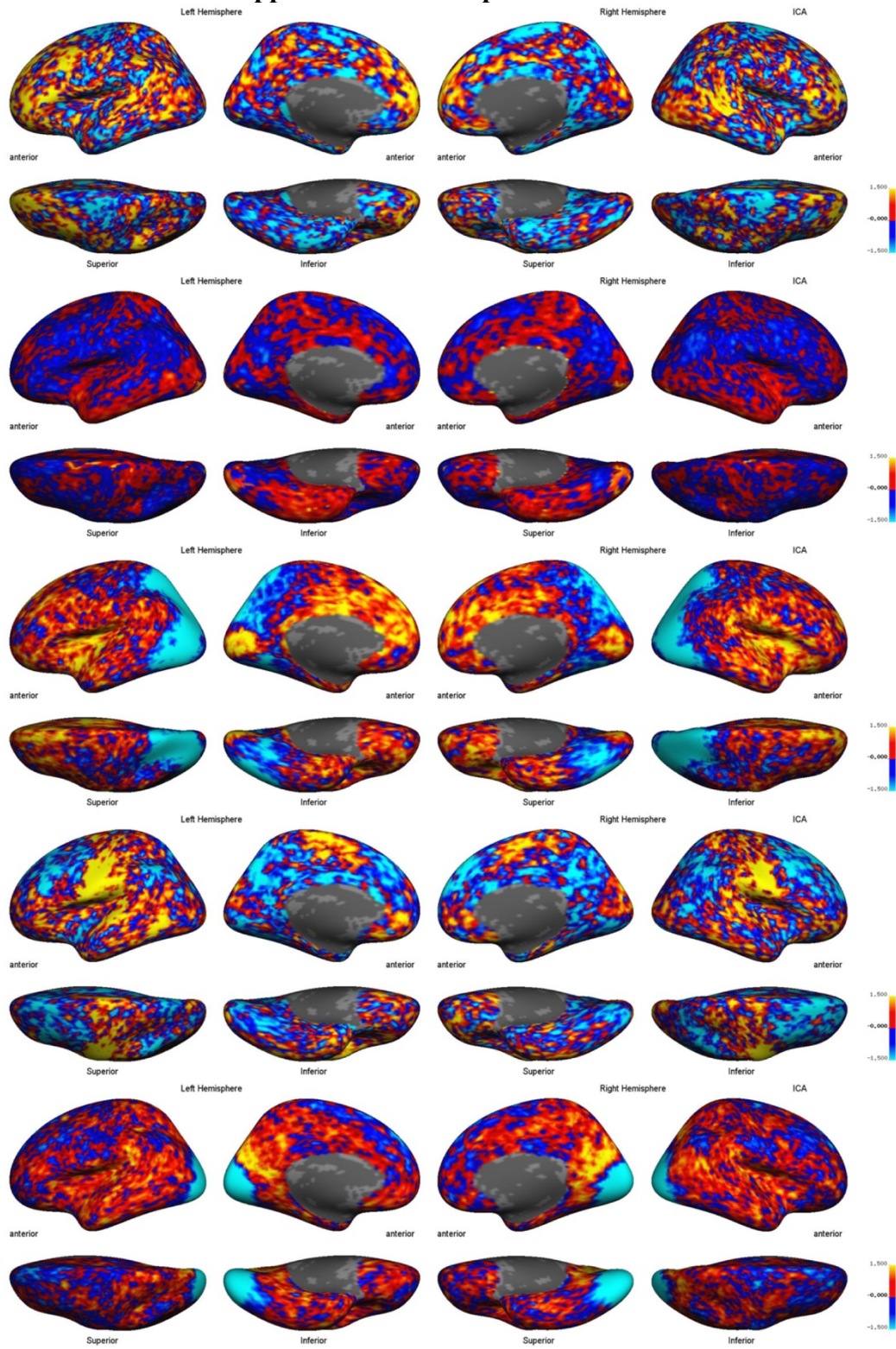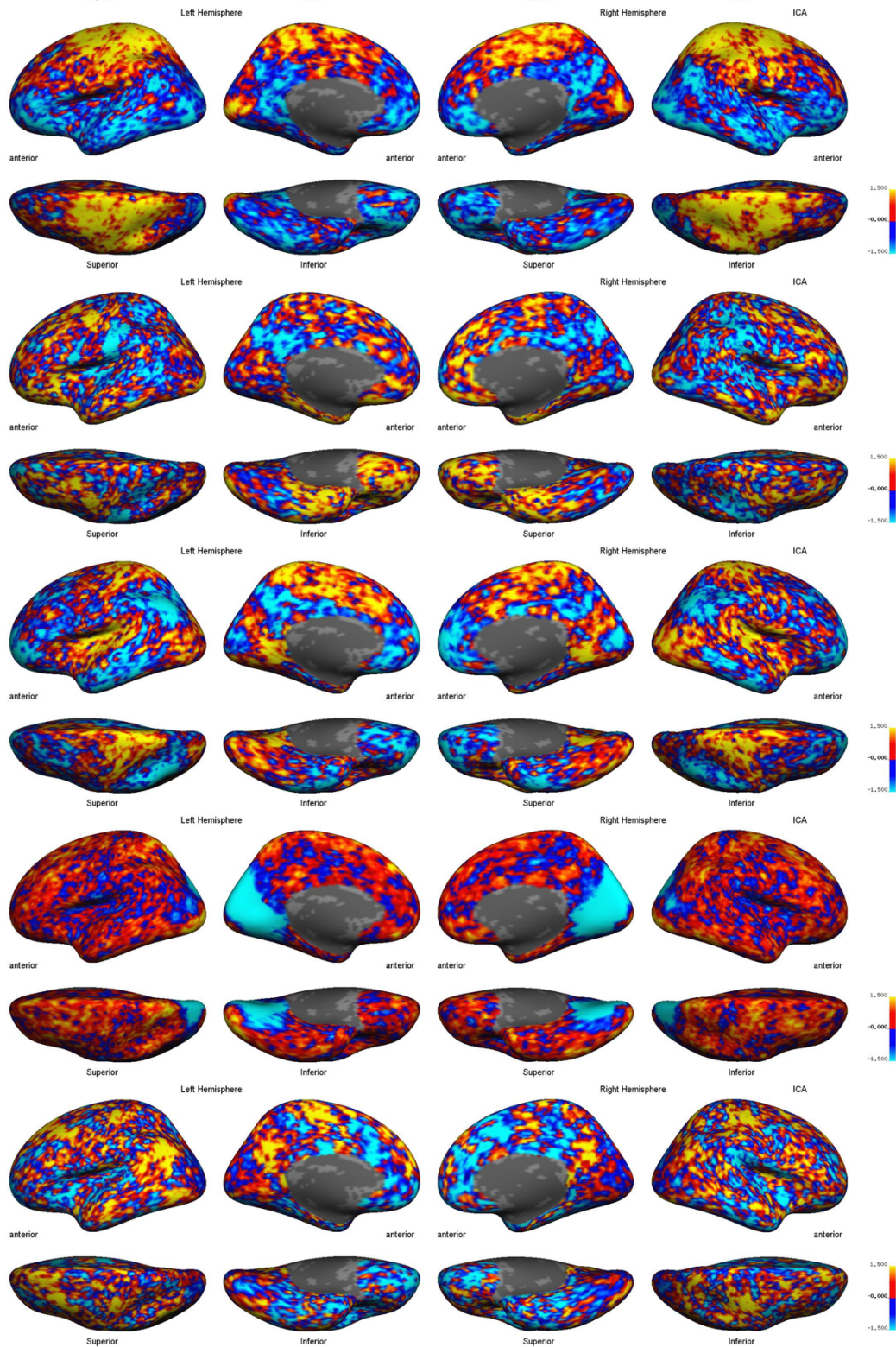
Appendix F: 20 Component Model

Appendix G: 40 Component Model