Quantifying the diversity of neural activations in individual brain regions

Michael L. Anderson (michael.anderson@fandm.edu)
Department of Psychology, Franklin & Marshall College
Lancaster, PA 17604 USA

Luiz Pessoa (pessoa@umd.edu)
Department of Psychology, University of Maryland
College Park, MD 20742 USA

Abstract

This paper offers the first comprehensive characterization of the cognitive diversity of individual brain regions. The results suggest that individual brain regions—even fairly small regions—contribute to multiple tasks across different cognitive-emotional domains, and moreover that there is little difference in diversity between cortical and sub-cortical circuits.

Keywords: neuroscience, selectivity, modularity, philosophical issues.

Introduction

A common view in the cognitive neurosciences is that brain areas are highly selective and exhibit considerable specialization, with each neural region responding to a restricted class of inputs and contributing primarily to a single cognitive domain, such as language or motor control. However, over the past several years this principle has come under increasing critical scrutiny. For instance, although Broca's area is associated with language processing, it turns out to also be involved in many different action- and imagery-related tasks, including movement preparation (Thoenissen et al. 2002), action sequencing (Nishitani et al. 2005), action recognition (Decety et al. 1997; Hamzei et al. 2003; Nishitani et al. 2005), imagery of human motion (Binkofski et al. 2000), and action imitation (Nishitani et al. 2005; for reviews, see Hagoort 2005; Tettamanti & Weniger 2006). Similarly, visual and motor areas—long presumed to be among the most highly specialized in the brain—have been shown to be active in various sorts of language processing and other higher cognitive tasks (Damasio & Tranel 1993; Damasio et al. 1996; Glenberg & Kaschak 2002; Hanakawa et al. 2002; Martin et al. 1995; 1996; 2000; Pulvermüller 2005). In light of such results, researchers have started to question the boundaries between cognitive domains once thought separate and distinct, such as perception and cognition (Barsalou 1999; 2008) and cognition and emotion (Pessoa 2008; 2010).

Recent meta-analyses of imaging results have tended to support this emerging challenge. For example, Russell Poldrack (2006) estimated the selectivity of Broca's area by performing a Bayesian analysis of 3,222 imaging studies from the BrainMap database (Laird et al. 2005). He concludes that current evidence for the notion that Broca's area is a "language" region is fairly weak, in part because it was more frequently activated by non-language tasks than by language-related ones. Similarly, a statistical analysis of 1,469 experiments from the NICAM database (Anderson et al. 2010) demonstrates that most regions of the brain—even fairly small regions—appear to be activated by multiple tasks across diverse task categories (Anderson 2010). The meta-results reported in that study also suggest that the brain achieves its variety of function by putting the same regions together in different patterns of functional cooperation, a finding that appears also to question the long-standing belief in the brain's anatomical modularity (Coltheart 2001).

Such results suggest several novel research directions for the cognitive sciences. For instance, if regions of the brain are indeed put to many different cognitive uses, this suggests that cortical parcellation and function-to-structure mapping should be approached via multiple or cross-domain investigations (Penner-Wilger & Anderson 2008; 2011). This would be a contrast to current practice, in which cortical regions are assigned visual functions by vision researchers, memory functions by memory researchers, attention functions by attention researchers, and so on (Cabeza & Nyberg 2000). In addition, as we come to realize which brain regions, in what combinations, contribute to what tasks, the vocabulary of cognition—the way we categorize and label experiments and mental operations—is likely to need significant revision (Poldrack 2010).

These are big projects that will occupy the attentions of many researchers for years to come. But the first, necessary, and crucial step is to begin to get some sense of the actual, specific diversity of various structures in the brain. Which regions are more, and which less specialized? Are there differences in diversity between large cortical regions, or between cortical and sub-cortical structures? The current paper begins to answer these questions by performing a meta-analysis of 1,138 neuroimaging experiments taken from 11 different task domains.

Methods

Materials

The NICAM database (Anderson et al. 2010) currently contains information from 2,603 fMRI studies reported in 824 journal articles. All the studies involve healthy adults and use a within-subjects, subtraction-based, whole-brain design. That is, for all the studies in the database, brain activity during an experimental task was observed over the whole brain (not just a region of interest), and then compared to and subtracted from activity observed in the same participant during a control task. The logic of subtraction method is such that it should uncover only the regions of activation that support the specific mental function that best captures the difference between the experimental and control task. The neural activations supporting the mental operation that the two tasks have in

common—the visual process allowing one to see the stimuli in a language task, for example—should be subtracted out. The database lists, among other things, the cognitive domain investigated in each study, using the BrainMap ontology (Fox & Lancaster 2002), and the locations in Talairach (Talairach & Torneau, 1988) and MNI (Evans, Collins & Milner, 1992) space of the 21,553 post-subtraction fMRI activation peaks observed during those 2,603 studies.

Procedure

The general methodology for this sort of study is simple and straightforward. First, choose a spatial subdivision of the brain, then choose a subset of experimental domains to investigate, and finally assign activations to each of the spatial regions according to whether the activation peak fell within the boundaries of that region. Spatial binning of activations offers some of the advantages of spatial smoothing, as well as providing orientation to accepted anatomical structures. See (Wager et al. 2009; Wager et al. 2007) for further discussion. At this point the diversity of activity in each region can be calculated, as described below.

The analysis was performed at two levels of spatial granularity. First, the brain was divided into 78 standard anatomical regions based on Freesurfer data (Fischl et al. 2004). These regions are listed in table 1. Then these regions were further sub-divided to form 1,052 smaller regions. The cortical regions were sub-divided by breaking the brain into equally spaced spheres with a radius of 10mm by region; while the sub-cortical structures were divided according to known anatomical structures (e.g. basal ganglia was divided into caudate, claustrum, lentiform nucleus, etc.), again according to Freeesurfer data.

The study was restricted to the following eleven task domains: three action domains—execution, inhibition, and observation—two perceptual domains—vision and audition—and six "cognitive" domains—attention, emotion, language (semantics), explicit memory, working memory, and reasoning. The result of this winnowing process left 1,138 experiments collectively reporting 7,408 locations of peak activation falling within the brain regions defined above. The number of activations in each region was normalized to account for differences in the number of experiments per domain in the entire sample.

Activation peaks are only one of many kinds of data that could be used in such a meta-analysis. They have the distinct advantage that large amounts of such data are readily available, and certainly activation peaks contain a great deal of useful information. See (Fox, Parsons & Lancaster 1998; Kober & Wager 2010; Wager et al. 2009; Wager et al. 2007) for further discussion of this and alternate methods.

For each region, the diversity of activations was calculated using a measure of diversity variability, based on standard deviation, commonly used by to measure demographic diversity in populations and neighborhoods (Chang 1999; Byrne & Flaherty 2004). Diversity was only measured for regions activated by 5 or more experiments.

In this equation, Cat_i refers to proportion of activations in each category; *mean* refers to the average proportion (always 0.091 with 11 categories) and *k* equals the number categories. Diversity is (*1-DV*), normalized such that the values range from 0 (all activations in one category) to 1 (activations spread equally across all 11 categories).

$$DV = \sqrt{\frac{\sum_{i=1}^{k}(Cat_i - mean)^2}{k}}$$

The diversity of a region can also be considered from a Bayesian perspective (Poldrack 2006). Given the observation of activity in one of these regions, how confident can we be (what is the posterior probability that) the activation is the result of a task in a domain of interest?

$$P(D_x|A_z) = \frac{P(Az|Dx)P(Dx)}{P(Az|Dx)P(Dx)+P(Az|\sim Dx)P(\sim Dx)}$$

Here A_z means an observation of activity in region *z*, and D_x is the domain of interest. The posterior probability that an observation of activity in region *z* indicates engagement of a task in domain *x* depends on the probability of an activation in z given a task in x, the prior probability that a task in x is being engaged, the probability of an activation in *z* when the brain is engaged in a task *not* in domain *x*, and the general probability of engaging tasks not in *x*. For current purposes, we assume no prior knowledge of the likelihood of region z being activated by any domain, thus the prior probability $P(D_x)$ is set at 1/11 (0.091). The other values are calculated in the standard way from the data. The final number of interest is the Bayes factor, which is the ratio of the posterior to the prior probability. Here we calculate the Bayes factor assuming the domain of interest for each region is the domain having the highest proportion of activations in that region. In other words, we will be calculating the degree of evidence for the *best possible* scenario. By convention, a Bayes factor between 0 and 3 indicates weak evidence; between 3 and 10 moderate evidence, and above 10 strong evidence (Jeffreys, 1961).

All values reported here were *also* calculated using an alternate spatial subdivision of the brain formed by dividing the brain into equally-spaced spheres of 10mm radius based on a randomly seeded initial location. As these results did not differ significantly from those reported here (indicating the results are not an artifact of the subdivision), we report only the results for the subdivision anchored to known anatomical structures.

Results

The overall average diversity of the 78 large anatomical regions was 0.70 (SD 0.12). The overall average diversity of cortical regions was 0.71 (SD 0.11) and of subcortical was 0.63 (SD 0.17). The average Bayes factor for the 78 large anatomical regions was 3.14 (SD 1.38). The average Bayes factor for cortical regions was 3.08 (SD 1.23) and for subcortical regions was 3.57 (SD 2.02). Individual values are listed in table 1, and displayed in figure 1. Numbers in parentheses indicate the number of experiments activating the region.

Table 1: Diversity of some standard anatomical structures in the brain.

Structure	Diversity		Bayes Factor	
	Right	Left	Right	Left
Occipital Lobe				
cuneus	0.71 (19)	0.71 (47)	3.28	3.44
lateral occipital cortex	0.76 (135)	0.85 (161)	2.49	2.19
lingual gyrus	0.77 (87)	0.80 (122)	2.21	1.82
Temporal Lobe				
bank of the superior temporal sulcus	0.70 (32)	0.72 (74)	2.61	2.91
inferior temporal cortex	0.82 (52)	0.70 (278)	2.02	3.74
fusiform gyrus	0.81 (174)	0.78 (219)	1.65	2.36
middle temporal cortex	0.80 (80)	0.75 (84)	2.03	2.54
superior temporal cortex	0.67 (164)	0.57 (159)	4	4.64
temporal pole	0.62 (13)	0.38 (7)	2.98	6.57
transverse temporal cortex	0.36 (23)	0.44 (26)	6.46	5.8
Parietal Lobe				
entorhinal cortex	0.63 (18)	0.63 (6)	2.82	3.33
inferior parietal cortex	0.89 (192)	0.81 (243)	1.62	2.61
paracentral lobule	0.75 (27)	0.65 (73)	2.33	3.69
parahippocampal cortex	0.71 (42)	0.76 (63)	3.16	2.12
pericalcarine cortex	0.58 (58)	0.68 (44)	4.24	3.3
postcentral gyrus	0.68 (110)	0.65 (200)	4.09	4.36
superior parietal cortex	0.70 (222)	0.70 (344)	3.83	3.82
supramarginal gyrus	0.69 (130)	0.63 (113)	4.05	4.44
Frontal Lobe				
caudal middle frontal cortex	0.79 (132)	0.84 (144)	2.75	1.63
rostral middle frontal cortex	0.78 (164)	0.86 (208)	2.68	1.78
lateral orbitofrontal cortex	0.81 (76)	0.78 (69)	2.39	2.15
medial orbitofrontal cortex	0.71 (15)	0.56 (23)	2.06	3.61
precentral gyrus	0.78 (270)	0.76 (389)	2.98	2.7
frontal pole	n/a (1)	n/a (0)	n/a	n/a
pars opercularis	0.80 (65)	0.80 (133)	2.7	2.49
pars orbitalis	0.78 (14)	0.53 (19)	2.73	6.01
pars triangularis	0.69 (49)	0.76 (82)	3.2	2.41
superior frontal cortex	0.79 (353)	0.88 (400)	2.73	1.52
Cingulate				
caudal anterior cingulate cortex	0.78 (50)	0.67 (48)	2.23	2.34
isthmus of the cingulate cortex	0.72 (46)	0.62 (43)	2.58	2.79
posterior cingulate cortex	0.53 (41)	0.69 (47)	4.92	2.35
precuneus	0.78 (135)	0.74 (146)	3.11	3.36
rostral anterior cingulate cortex	0.66 (34)	0.68 (28)	2.96	3.05
Subcortical				
basal ganglia	0.86 (134)	0.83 (120)	1.68	2.19
hippocampus	0.44 (6)	0.61 (14)	4.1	3.39
hypothalamus	0.49 (8)	n/a (3)	4.1	n/a
amygdala	0.50 (12)	0.42 (25)	4.99	6.64
midbrain	n/a (2)	n/a (2)	n/a	n/a
thalamus	0.73 (66)	0.75 (72)	2.52	2.42

To better evaluate these numbers, consider left inferior temporal cortex, with a diversity of 0.70, equal to the overall average. The proportion of activations in each of the task domains is shown in table 2.

The overall average diversity of the 574 small cortical and 21 small subcortical regions activated by 5 or more experiments was 0.52 (SD 0.13). Those 595 regions were activated by an average of 10.67 experiments. The overall average diversity of the cortical regions was 0.52 (SD 0.13) and of the subcortical regions was 0.59 (SD 0.12). The average Bayes factor for the 595 regions is 4.45 (SD 1.67). The average Bayes factor for cortical regions is 4.43 (SD 1.68) and for subcortical regions is 3.68 (SD 1.11). With 595 regions, it is not possible to provide individual data here. However, the full results will be posted at http://www.agcognition.org/diversity.html

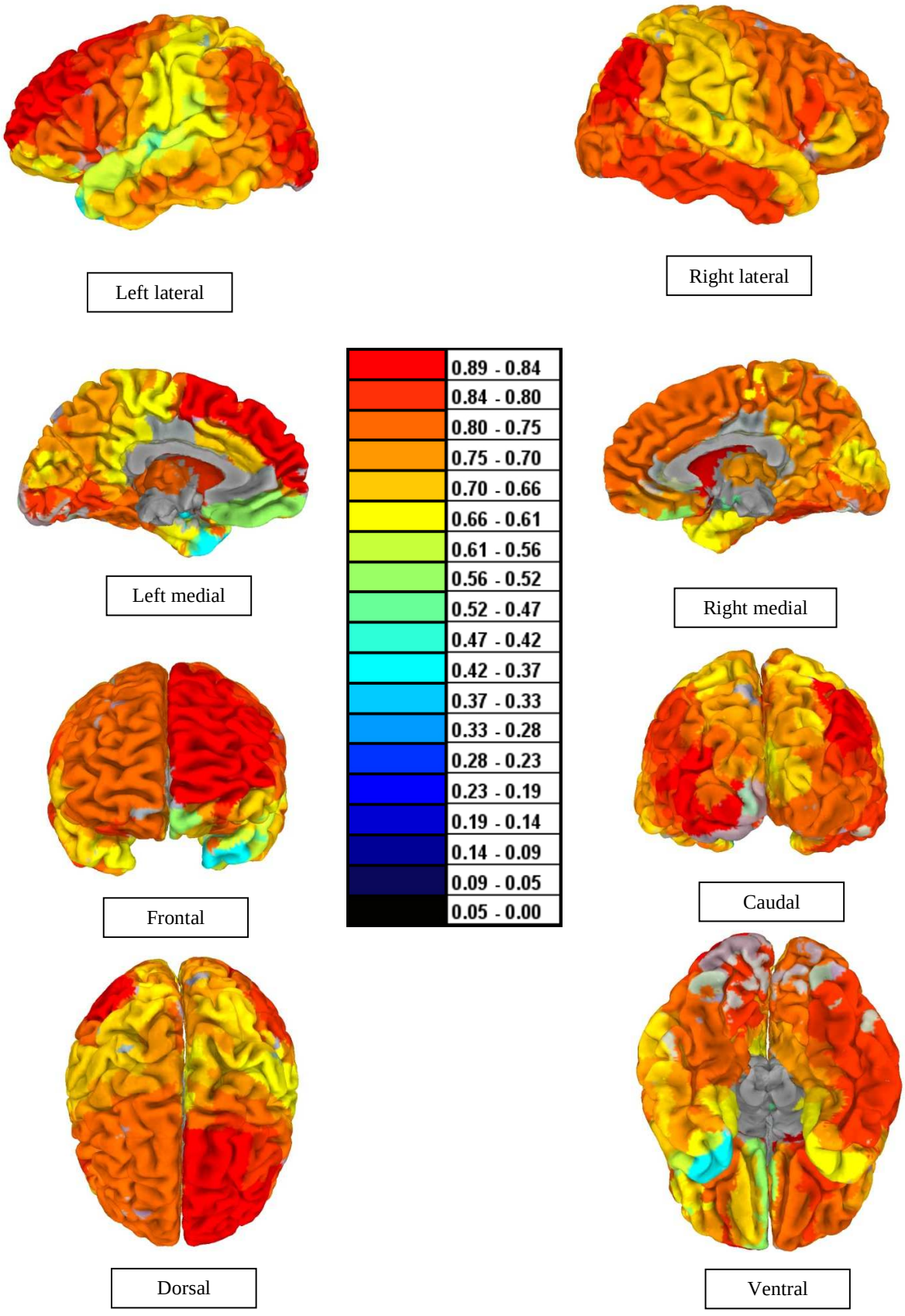

Figure 1: Depiction of the diversity of activations for large anatomical regions. Grey indicates no information. Image prepared by Josh Kinnison and Srikanth Padmala, Indiana University.

Interestingly, only two of the 595 small regions had a diversity of zero: a sub-region of right precentral gyrus centered on Talairach coordinates [26, -22, 60] that was active only in five action execution tasks; and a sub-region of left postcentral gyrus centered on [-38, -31, 50] that was active only in nine action execution tasks. The most diverse small region, at 0.79, was a sub-region of left pars triangularis, centered on [-41, 27, 8], that was active in 15 tasks across 8 of the cognitive domains (all except action execution, action inhibition, and vision).

Table 2: Diversity of activations in left inferior temporal cortex.

Domain	Proportion of activations
Action execution	0.06
Action imagination	0.06
Action inhibition	0.00
Attention	0.02
Language	0.34
Explicit memory	0.12
Working memory	0.12
Reasoning	0.12
Emotion	0.06
Vision	0.07
Audition	0.02

To get some better sense of typical small region diversity, consider a sub-region of the right supramarginal gyrus, centered at Talairach coordinates [44, -35, 39], that was activated in nine experiments and had a diversity of 0.52. Action imagination accounted for 42% of the activations; 27% were in action execution, 20% in reasoning and 11% in working memory.

Although there do appear to be some interesting regional asymmetries in diversity, there is no significant difference between the average regional diversity of the left and right hemispheres. There is a significant positive correlation between diversity and the number of experiments activating a region ($r=0.50$, $p<.001$ for large regions; $r=0.46$, $p<.001$ for small regions).

Discussion

Although there have been prior studies investigating the selectivity of individual brain regions (Poldrack, 2006; Tettamanti & Weniger, 2006; Gauthier et al., 2000) this is the first study to offer a comprehensive survey of regional selectivity in the brain. Overall, the results suggest that most regions of the brain—even fairly small regions—typically contribute to tasks across multiple cognitive-emotional domains.

This reinforces the growing realization that reverse inference—inferring what class of mental operation is being engaged from observation of regional brain activity, e.g. inferring an emotional process from observation of amygdala activation—is an extremely uncertain practice (Poldrack 2006). As we see from the Bayesian results, even in the best case scenario where we assume no prior knowledge, and consider only the strongest possible evidence, such observations typically offer only fairly weak to moderate support for such conclusions (Jeffreys, 1961).

Nevertheless, there does appear to be variability in regional selectivity, and the full results will begin to allow us to differentiate between regions for which reverse inference might be appropriate, and those for which it is clearly not. However, there is also considerable variation in the amount of *evidence* for diversity in each region, especially for the smaller regions. The positive correlation between diversity and number of observed activations is not surprising, as diverse areas will naturally be active more often. What is not known is whether further observations will tend to increase the measured diversity across the brain, thus decreasing regional variability and hemispheric asymmetries. Such matters deserve increased attention.

Although most regions of the brain do not appear to be domain-selective, the current evidence is compatible with the possibility that brain regions each perform a single, specific mental operation that is used in performing many different tasks (Anderson, 2010). Knowing the set of tasks that activate each region will be an important source of information for discovering whether such a possibility obtains, and what the mental operations might be (Penner-Wilger & Anderson, 2011).

It is also possible that while individual regions are not domain-selective, specific *networks* of regions are domain-selective (Anderson et al. 2010; Sporns 2011). This possibility, and the complementary possibility that it may be possible to predict general mental states from observations of network activation, will be one focus of future work.

However, these are, as they say, empirical questions. For many researchers, the most natural interpretation of these results will be that local neural circuits and distributed networks can perform different operations under different circumstances (Lloyd 2000; Hardcastle & Stewart 2002). The cumulative results of years of functional neuroimaging invite us to (cautiously) revisit some fundamental questions about the functional organization of the brain.

References

Anderson, M. L. (2010). Neural reuse: A fundamental organizational principle of the brain. *Behavioral and Brain Sciences*, 33: 245–313.

Anderson, M. L., Brumbaugh, J. & Suben, A. (2010). Investigating functional cooperation in the human brain using simple graph-theoretic methods. In A. Chaovalitwongse, P.M. Pardalos, V. and P. Xanthopoulos, (Eds.) *Computational Neuroscience*, pp 31-42. New York: Springer.

Barsalou, L. W. (1999). Perceptual symbol systems. *Behavioral and Brain Sciences*, 22:577–660.

Barsalou, L. W. (2008). Grounded cognition. *Annual Review of Psychology*, 59:617–45.

Byrne, J. & Glaherty, J. (2004). Measuring diversity in Australian residential property. *Proceedings of the 10th Annual Conference of the Pacific Rim Real Estate Society.*

Cabeza, R. & Nyberg, L. (2000). Imaging cognition II: An empirical review of 275 PET and fMRI studies. *Journal of Cognitive Neuroscience*, 12:1–47.

Chang, M. J. (1999). Does racial diversity matter?: The

educational impact of a racially diverse undergraduate population. *Journal of College Student Development*, 40(4): 377-395.

Coltheart, M. (2001) Assumptions and methods in cognitive neuropsychology. In: B. Rapp (ed). *The handbook of cognitive neuropsychology*, pp. 3–21. New York: Psychology Press.

Damasio, A. & Tranel, D. (1993). Nouns and verbs are retrieved with differently distributed neural systems. *Proceedings of the National Academy of Sciences, USA*, 90:4957–60.

Damasio, H., Grabowski,T. J., Tranel, D., Hichwa, R. D. & Damasio, A. R. (1996). A neural basis for lexical retrieval. *Nature*, 380:499–505.

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*, 120:1763–77.

Evans, A.C., Collins, D. L. & Milner, B. (1992). An MRI-based stereotactic atlas from 250 young normal subjects. *Journal of the Society for Neuroscience Abstracts*, 18:408.

B. Fischl, A. van der Kouwe, C. Destrieux, E. Halgren, F. Segonne, D. H. Salat, E. Busa, L. J. Seidman, J. Goldstein, D. Kennedy, V. Caviness, N. Makris, B. Rosen, and A. M. Dale. (2004). Automatically parcellating the human cerebral cortex. *Cerebral Cortex*, 14:11–22.

Fox, P.T. & Lancaster, J. L. (2002). Mapping context and content: The BrainMap model. *Nature Reviews Neuroscience*, 3:319–321.

Fox, P. T., Parsons, L. M. & Lancaster, J. L. (1998). Beyond the single study: Function-location meta-analysis in cognitive neuroimaging. *Current Opinions in Neurobiology*, 8:178–187.

Gauthier, I., Skudlarski, P., Gore, J.C., & Anderson, A.W. (2000). Expertise for cars and birds recruits brain areas involved in face recognition. *Nature Neuroscience*, 3 (2): 191–197.

Glenberg, A. M. & Kaschak, M. P. (2002). Grounding language in action. *Psychonomic Bulletin and Review*, 9:558–65.

Hagoort, P. (2005). On Broca, brain and binding. *Trends in Cognitive Sciences*, 9(9): 416-423.

Hamzei, F., Rijntjes, M., Dettmers, C., Glauche, V., Weiller, C. & Büchel (2003). The human action recognition system and its relationship to Broca's area: An fMRI study. *Neuroimage*, 19:637–644.

Hanakawa, T., Honda, M., Sawamoto, N., Okada, T., Yonekura, Y., Fukuyama, H. & Shibasaki, H. (2002). The role of rostral Brodmann area 6 in mental-operation tasks: An integrative neuroimaging approach. *Cerebral Cortex*, 12:1157–70.

Hardcastle, V.G. & Stewart, C.M. (2002). What do brain data really show? *Philosophy of Science*, 9(S3): S72-S82

Jeffreys, H. (1961). *Theory of Probability*, Clarendon Press.

Kober, H. & Wager, T. D. (2010). Meta-analysis of neuroimaging data. *WIREs Cognitive Science*, 41: 293–300.

Laird, A., Lancaster, J. L. & Fox, P. T. (2005). BrainMap: The social evolution of a human brain mapping database. *NeuroInformatics*, 3:65–77.

Lloyd, D. (2000). Terra cognita: From functional neuroimaging to the map of the mind. *Brain and Mind* 1(1): 93-116.

Martin, A., Haxby, J. V., Lalonde, F. M., Wiggs, C. L. & Ungerleider, L. G. (1995) Discrete cortical regions associated with knowledge of color and knowledge of action. *Science*, 270:102–105.

Martin, A., Ungerleider, L. G. & Haxby, J. V. (2000) Category-specificity and the brain: the sensorymotor model of semantic representations of objects. In: M. S. Gazzaniga (Ed.) *The new cognitive neurosciences*, 2nd edition, pp. 1023–36. Cambridge, MA: MIT Press.

Martin, A., Wiggs, C. L., Ungerleider, L. G. & Haxby, J. V. (1996). Neural correlates of category-specific knowledge. *Nature*, 379:649–652.

Nishitani, N., Schürmann, M., Amunts K. & Hari, R. (2005). Broca's region: From action to language. *Physiology*, 20:60–69.

Penner-Wilger, M., & Anderson, M.L. (2011). The relation between finger gnosis and mathematical ability: Can we attribute function to cortical structure with cross-domain modeling? *Proceedings of the 33rd Annual Conference of the Cognitive Science Society*.

Pessoa, L. (2010). Emergent processes in cognitive-emotional interactions. *Dialogues in Clinical Neuroscience*, 12(4):433-448.

Pessoa, L. (2008). On the relationship between emotion and cognition. *Nature Reviews Neuroscience*, 9:148–158.

Poldrack, R. A. (2006). Can cognitive processes be inferred from neuroimaging data? *Trends in Cognitive Sciences*, 10:59–63.

Poldrack, R. A. (2010). Mapping mental function to brain structure: How can cognitive neuroimaging succeed? *Perspectives on Psychological Science*, 5:753–761.

Pulvermüller, F. (2005). Brain mechanisms linking language and action. *Nature Reviews Neuroscience*, 6:576–82.

Sporns, O. (2011). *Networks of the Brain*. Cambridge, MA: MIT Press.

Talairach, J. & Tornaux, P. (1988). *Co-planar Sterortactic Atlas of the Human Brain*. Paris: Thieme.

Tettamanti, M. & Weniger, D. (2006). Broca's area: A supramodal hierarchical processor? *Cortex*, 42:491–94.

Thoenissen, D., Zilles, K. & Toni, I. (2002). Differential involvement of parietal and precentral regions in movement preparation and motor intention. *Journal of Neuroscience*, 22:9024–9034.

Wager, T. D., Lindquist, M., Nichols, T., Kober, H. & Snellenberg, J. (2009). Evaluating the consistency and specificity of neuroimaging data using meta-analysis. *NeuroImage*, 24:S210–S220.

Wager, T. D., Lindquist, M., & Kaplan, L. (2007). Meta-analysis of functional neuroimaging data: Current and future directions. *Scan*, 2:150–158.

Yarkoni, T., Poldrack, R. A., Van Essen, D. C. & Wager, T. D. (2010). Cognitive neuroscience 2.0: Building a cumulative science of human brain function. *Trends in Cognitive Sciences*, 14:489–496.