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Task Switching, Executive Control, and Neural Mechanisms

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by

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ABSTRACT

Task Switching, Executive Control, and Neural Mechanisms

by

Yi-Wen Wang

Performance in task switching (TS) is an important measure of cognitive flexibility. However, multiple debates in this field remain unresolved after decades of research, which prevents the development of a coherent TS theory, and limits the application of insights from TS to other fields. One of the reasons is that many TS studies included only rule-based (RB) tasks with shared sets of stimuli, responses, or both, which may lead to overlapping task sets and obscure the interpretation. In order to unravel the puzzle, the current study used distinct sets of stimuli and responses, and compared task switching across two conditions: switching between RB and procedural tasks versus between two RB tasks, and used functional Magnetic Resonance Imaging (fMRI) to observe the brain activity during task switching. Furthermore, general linear model analysis, multivariate pattern analysis and dynamic causal modeling were conducted on fMRI data to identify key features of TS neural mechanisms. The results suggested that activations in the orbitofrontal cortex showed multitask-specific patterns that can be used to identify TS components in general fMRI studies. Furthermore, a set of TS principles was proposed for building TS neural computational models for future research.

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Chapter 1. Introduction

The effect of task switching is ubiquitous in our daily life. Safe drivers avoid using their phone while driving, because they know that would slow down their reactions when something comes up unexpectedly. Some speakers ask their audience to postpone their questions till the end, because that often disrupts their flow of thinking. Busy workers often find it difficult to switch back to what they were planning to do after being interrupted. Clinically, levels of inflexibility of task switching is an important indication of brain injuries or neuropsychological disorders, and many neuropsychological tests include components of task switching, such as WCST, CANTAB, TEA, and D-KEFS (Das & Wylie, 2014; Strauss et al., 2006), just to give some widely used examples. Therefore, it is not surprising that task switching has been intensively studied in humans and animals with all kinds of approaches that researchers have access to, including but not limited to brain lesions, manipulation of neurotransmitters, transcranial magnetic stimulation (TMS), electroencephalogram (EEG), and brain imaging studies such as positron emission tomography (PET) and functional magnetic resonance imaging (fMRI). What is somewhat surprising, then, is that so many debates about the underlying mechanisms of task switching remain unresolved over the decades.

Based on our introspection, task switching appears to require maintaining relevant task sets active and inhibiting interference from irrelevant task sets, which is managed by a

cognitive control center. However, this seemingly intuitive assumption has provoked controversies that obscured our understanding of task-switching mechanisms. For example, researchers do not agree on whether or not there is a TS control center that is separate from the task sets, little consensus about the dynamics of TS-control process has been achieved among theorists, and discrepancies between fMRI and lesion studies certainly do not help. Some of the unsettled debates may be caused by experimental designs. Therefore, the goal of my work is to untangle the puzzle by avoiding some of the drawbacks in typical TS studies and applying new approaches of data analysis.

Questions and challenges

Of course, researchers have achieved much progress in associating neuroscientific observations with task-switching impairments. Take the intensively studied WCST as an example. Lesion studies in humans and animals have identified many brain regions that are involved in WCST, such as anterior cingulate cortex (ACC), orbitofrontal cortex (OFC), and basal ganglia (BG) (Buckley et al., 2009; Lombardi et al., 1999), whereas changing dopamine levels (DA) in prefrontal cortex (PFC) led to paradoxical effects (Roberts et al., 1994; McDowell et al., 1998). Many other task-switching tests also showed associations with frontal lobe damages and are therefore classified as assessments of Frontal Lobe Syndrome (Stuss &

Alexander, 2009). These observations, however, revealed a problem: as studies typically show that any local disruption to the extensive frontal-striatal network is sufficient to disrupt performance in WCST and other task-switching tests, the precise targets in the brain for treatments remain unclear when precision medicine is to be developed.

Lacking a solid understanding of task switching mechanisms also troubles the design of behavioral studies. Many experiments include task switching components to study cognitive functions other than task switching. For example, Maddox et al. (2004) asked participants to quickly switch between memory scanning and category learning tasks with a simple assumption: a secondary declarative task disrupts feedback processing with declarative systems, but not with procedural systems. However, this type of behavioral manipulation often faces challenges to their effectiveness on the targeted underlying neural processes. Another well-known but mysterious phenomenon is the spacing effect in learning: switching between two types of learning often leads to better performance than blocked learning of each task separately (e.g. Carvalho & Goldstone, 2014; Cross, Schmitt, &Grafton, 2007). However, it is reported to be extremely hard for participants to learn intermixed declarative and procedural categorization tasks, while no difficulties are found for blocked training of each task separately (Ashby and Crossley, 2010; Erickson, 2008). To my knowledge, no task-switching theories can be used to address these challenges.

What is particularly important but is often overlooked is that, in event-related fMRI studies, the task-switching paradigm is sometimes used for adding control trials (as specific examples of potential impacts to fMRI studies, Chapter 6 will discuss Simons et al., 2005 and Konishi et al., 2000). Specifically, trials with and without experimental manipulations are intermixed randomly in a block so that their related blood-oxygen-level-dependent (BOLD) response can be contrasted. However, if different types of trials are processed as different tasks in our brain, the contrast analysis that is meant to reveal experimental effects might actually reveal task-switching related activities. Meanwhile, refuting this possibility would pose severe challenges to the effectiveness of revealing task-switching mechanisms using event-related fMRI studies.

In addition, fMRI studies of task switching are facing other issues. First, there are discrepancies between findings of fMRI studies and lesion studies. Despite the strong evidence from lesion studies, many fMRI studies have failed to find consistent switch-related activations in orbital frontal cortex (OFC; Richter & Yeung, 2014; Ruge et al., 2013; see also Rogers et al., 2000 and Monchi et al., 2001 for possible explanations). Similarly, the involvement of subthalamic nucleus (STN) in task switching has been supported by lesion studies in animals (Isoda& Hikosaka, 2008) and local field potential (LFP) recording in Parkinson's disease (PD) patients (see Jahanshahi et al., 2015 for a review), but virtually no

fMRI studies have reported switch-related activations in this region. This may be explained by the fact that analysis of brain imaging data often relies on contrasts, which would fail to show differences in these regions when they are persistently active under multitask context.

Second, while task switching is considered a window to executive control functions, no regions have been found to selectively respond to switch trials (see Ruge et al., 2013 for a review). Furthermore, regions that are active in task-switching studies are often found to be also active in single-task studies. Lacking evidence for distinct switch-related brain regions obscures the interpretation of executive control mechanisms. Chapter 5 discusses several plausible explanations for it, such as performance under the experimental context might require executive control circuits to stay active.

Third, some regions that are regularly reported to have switch-related activations, such as superior parietal lobe (SPL), intraparietal sulcus (IPS), and pre-supplementary motor area (preSMA) (Kim et al., 2012; Ruge et al., 2013), are also associated with more down-stream functions rather than executive control, such as motor functions (see discussions in Chapter 4). Concluding that these regions are recruited in task switching does not help much to understand executive functions, because task-switching related activities in those regions may simply reflect the updates of task sets (defined here as the necessary neural processes for

implementing stimulus-to-response transformations), which may or may not be consciously controlled.

Furthermore, the lack of consensus on task-switching mechanisms is shown obviously on the theoretical level. Reviews of task switching (e.g. Ruge et al., 2013; Richter & Yeung, 2014; Kiesel et al., 2010) have posed questions to the fundamental assumptions of task-switching theories, such as whether or not the processes of task reconfiguration and inhibitory control are involved at certain time points. The following section reviews some of the key concepts and questions about task switching.

Task switching basics

Single-task vs. multitask

The premise of task switching is that there are multiple tasks to switch between. However, what defines a task may be more controversial than intuition suggests. Take the current study as an example. Participants were trained with two category sets separately, where each category set contains two categories. Later when being presented figures one at a time, with each one randomly drawn from one of the two category sets, participants were asked to determine which category each figure belongs to. In this period of time, how do we know

whether they were behaving as if it was a single categorization task with four categories, or were switching between the two categorization tasks?

The answer has to be related to how task switching is defined. Since the early discussions of task switching, the existence of switch costs has been the defining measure. In addition, it has been reported that by manipulating the instructions, switch costs can appear or disappear as participants view it as a combination of multiple tasks or a single task (Dreisbach, Goschke, & Haider, 2006, 2007; Dreisbach & Haider, 2008). Therefore, the existence of switch costs was taken as a justification that this study did probe task switching. As a stronger support, whether or not performance was affected by other factors that have been regularly shown to affect switch costs (discussed in Chapter 3) was also examined.

Task set

Task switching involves changes of task sets. However, there is no consensus for the definition of task set in the task switching literature. Some examples of the definitions include: representation of cognitive and motor requirements of a task (Koch et al., 2018), a control system that provides top-down configuration signals (Dosenbach et al., 2006), task rules (Wisniewski et al., 2014), a set of executive control parameters to complete the task (Witt et al., 2012; Mayr and Kliegl, 2000), the internal representation of the task goal and implemental procedures (Forstmann et al., 2005; Whitmer and Banich, 2012), or most formally, "a set of

parameters in a computational model that is sufficient to program the model to perform particular task-relevant computations" (Logan and Schneider, 2010). As can be seen in this small sample of definitions, some define task-set units as a seemingly centralized control system, while others imply a more distributed network with parameters. Without attempting to resolve the debates of levels of awareness, voluntariness or cognition in task sets, I adopt a more inclusive definition that contains the lower systems -- i.e., the whole network from receiving perceptual input to generating behavior output in the brain, and define task set as the necessary neural processes for carrying out a stimulus-response (S-R) transformation task. Note that for a well-practiced procedural behavior, the task set may not involve much executive control, which makes this definition different from the “task-set units” (defined as the control center) in some task switching models (e.g. Gilbert & Shallice, 2001; Brown et al., 2007).

To illustrate the idea of task set defined here, consider a simple task: see the red light and step on the brake. Before the S-R transformation can be done, one has to attend to relevant features of the stimulus (color, but not the size, of the light), and pass the extracted perceptual information to relevant stimulus-action (S-A) mapping (A stands for an abstract action decision, such as “stop”), then the actual motor response (step on the brake pedal) can be planned based on relevant action-response (A-R) mapping. Task set can be considered as the

configuration of "relevant" activations for all of these steps. Note that this conceptual scheme does not make any assumptions about brain regions or networks, and nor does it assume that the three steps have to be processed separately or controlled cognitively. As an extreme example, reflexes are hard-wired (configured) concatenation of the three steps that may not recruit the cerebrum, and their configuration can be altered by top-down influence when one tries to resist reflex, for example.

In most cognitive tasks, the configuration is believed to be managed by executive control or cognitive control (although, again, these terms are often used without being formally defined). Researchers who use task-switching paradigms to study executive control believe that the decreased efficiency of configurations under multitask context helps to reveal how the executive system works. Here, multitask context is defined as a narrow time-window when multiple tasks are to be carried out concurrently or switching sequentially (Koch et al., 2018). Note that while multitask context poses more challenges (e.g. mutual interference from tasks), it does not imply that the executive circuits that work for overcoming those challenges are only activated in multitask context, given that most tasks are much more complicated than a reflex. As discussed in the next section, the major differences among theories of task switching are assumptions about configurations of task sets and how the multitask challenges are handled.

TS theories and models

As aforementioned, multitask challenges are assumed to be managed by executive control. It is the top-down influence that directs us to say "yellow" instead of "green" when seeing a line of yellow text "green" in the Stroop task. Intuitively (but not without debates), such executive control seems to be separate from, for example, memory retrieval processes of color naming and text reading. Assuming that our brain works differently when having to select among multiple behavioral options, such as in the Stroop task versus single-task scenarios, such as always interpreting the text “green” as “green” while ignoring text color in normal reading, it is possible to identify executive control by capturing the nature of the differences between the two scenarios. Indeed, various theories have been developed and backed with empirical data.

Two conceptual task switching theories dating back to the1990s provide a good starting point to this topic. One of them is the task reconfiguration theory proposed by Rogers and Monsell (1995), which emphasizes active control on switch trials. Namely, the task set parameters of the previous, irrelevant trial need to be removed and replaced on switch trials. Based on their theory, this process is not required on stay trials, which leads to the relatively increased response times (RTs) on switch trials. However, we now know that the cause of switch costs (increased RT and/or error rate) is not as crystal clear as they proposed. For

example, performance on stay trials in multitask contexts are worse than in single-task contexts, and the costs are greater in PD patients and older adults than in healthy controls (Marí-beffa & Kirkham, 2014; Kray & Lindenberger 2000, Mayr & Liebscher 2001, Meiran &Gotler 2001), which indicates that task execution is affected by some global factors in multitask contexts even on stay trials.

The other is the task-set inertia theory by Allport and colleagues (Allport, Styles, & Hsieh, 1994; Allport & Wylie, 2000), which suggests that switch costs do not measure active control; rather, switch costs can be simply explained by the interference from persisting activation of the irrelevant task from the previous trial, along with persisting inhibition to the current task under multitask contexts. However, this simple model cannot explain why variable and fixed cueing intervals have different influence on performance: the effect that switch costs decrease as the response-stimulus interval increases is only evident with fixed but not variable cueing intervals (Rogers and Monsell, 1995).

While over-simplified, both theories pointed out how two founding elements of executive control -- initiating task sets and overcoming interference -- may work in task switching. Outside the field of task switching, much evidence shows that stimulus-response (S-R) transformations can be initiated in both bottom-up and top-down fashion. For example, many patients with Parkinson's disease have difficulties with initiating voluntary movements, but are

able to perform fluent movements upon receiving external sensory cues (Snijders et al., 2011); action slip (making unintentional errors) signifies the failure of top-down control (Norman, 1981); we also know that some behaviors can be stopped by inhibitory circuits (e.g. Hikosaka & Isoda, 2010). Therefore, it is reasonable to assume that task switching also recruits these control mechanisms. However, there is little consensus among task-switching theories about whether or not each type of control happens at certain timing, such as when a cue is presented on the stay trial.

Some researchers have developed mathematical models to address these issues more formally. For example, Schneider and Logan (Schneider & Logan, 2005; Schneider & Logan, 2009) developed the compound cue model to capture the features of switch costs without any task-switching control component. They proposed that cues and stimuli are encoded to retrieve a response from long-term memory; therefore, the switch costs reflect repetition benefit ("priming" effect) on stay trials when memory has been loaded from long-term storage (on switch trial) and kept in short-term storage for ready access. However, this model is purely mathematical, and its equivocation becomes evident when the whole process is to be implemented in a neural model. For example, are there separate long-term and short-term storages, or is short-term storage actually an activated portion of long-term storage (Eriksson et al., 2015 proposed a detailed scheme for the latter)? In addition, S-R mappings in task

switching are often flexible, which means perceptual information cannot be automatically transformed into actions or decisions. In other words, while the model looks purely stimulus-driven, an unspecified control process of selecting relevant transformation must exist in between the input encoding and memory retrieval phases, and the effect of this process (most likely top-down) may be absorbed in some terms with different names in their model.

Computational models contain more detailed assumptions about executive control. For example, the CARIS model (Meiran et al., 2008) assumes that task set can be separated into input set and response set, which are controlled by task decision process (activated by cue) and rule implementation; the input-set biasing happens during the cueing interval, whereas the response set is biased by the rule implementation process after response selection. ACT-R models (e.g. Sohn & Anderson, 2001; Altmann & Gray, 2008) and neural computational models (e.g. Gilbert & Shallice, 2001; Brown et al., 2007) also provide details for the mechanisms in between input set and response set. The basic assumptions of these models are listed in Table 1-1.

Surprisingly, only one of these models includes inhibitory control, despite strong evidence for its existence (Gade et al., 2014). Since the explanatory power for enhancing relevant activation and inhibiting irrelevant activation is the same for overcoming interference,

even to verify or falsify the basic assumption of inhibitory control becomes extremely difficult, if not impossible.

Table 1-1

Basic assumptions of computational models of task switching.

Model	Conflict handling	Configuration of S-R transformation
Altmann & Gray, 2008	Winner takes all	Bottom-up driven memory retrieval
Brown et al., 2007	ACC detects the conflict and enhances relevant task set	Set by PFC, ACC, and a plan layer
Gilbert & Shallice, 2001	Winner takes all	Set by a control unit and a task-demand unit (including excitatory and inhibitory control)
Meiran et al., 2008	Winner takes all	Set by top-down control and a perceptual filtering mechanism
Sohn & Anderson, 2001	Winner takes all	Set by the control rules

A similar issue is that these models often account for basic task-switching phenomena equally well, and each model is supported by empirical data. Many of those data are collected from paradigms designed for verifying these theories (see Grange & Houghton, 2014 for a brief review of task-switching paradigms). Of course, diverse mechanisms proposed by these models may simultaneously exist in task switching. Along with the refinements of these theories, such as dividing task reconfiguration into multiple components, perplexity has come with open possibilities. Nonetheless, these models have provided many potential mechanisms to investigate, along with various ways of measuring switch costs using diverse paradigms that

may help to understand how task sets are influenced in task switching. Chapter 3 contains further discussions on some of those measures.

Identify the executive control circuits

An extensive frontal-parietal network is regularly reported in task switching fMRI studies, including dorsal lateral PFC (DLPFC), ACC, inferior frontal junction (IFJ), BG, preSMA, SPL, and precuneus (e.g. Richter & Yeung, 2014; Ruge et al., 2013). For the purpose of identifying executive control circuits, such an extensive network may lead to more opacity than clarification. The inclusion problem is not just from correlational brain imaging studies, but also from causal studies. Specifically, when any findings of that disruptions to a single spot in the brain leading impairments in task switching are taken as evidence that the spot is involved in executive control, many non-executive control regions are meant to be included.

The problem can be illustrated by the following thought experiment: Consider a task switching experiment where participants have to move their hands on different sets of response buttons for corresponding tasks. In the control condition, they are allowed to see the buttons, and in the experimental condition, their sight is blocked so that they have to fumble for the relevant sets of buttons. The disruption to visual guidance towards the buttons, while nothing to do with controlling task switching (but definitely contributing to the response set), will certainly impair the performance in the experimental condition. The same is true for any task

set regions: these regions have to work for updates (just like participants can use visual input for guiding their hands when reaching relevant button sets), and when disrupted (as their sights are blocked), response time and error rate will increase. Obviously, only when taking the basic function of visual guidance into consideration can we determine its role in task switching appropriately. Therefore, in Chapters 4 and 5, task set identification are supported by evidence from causal studies.

To identify task set regions, multiple fMRI contrasts were conducted to identify all the regions responsive to specific events (see Chapter 2 for details). Then, lesion studies with special focus on impairments in task-switching and S-R behavior were reviewed for each region. Since categorization requires S-R transformation, convergent evidence for a region being associated with S-R impairments was taken as the evidence for that region being part of the task set (see Chapter 4 for details). As discussed earlier, task-set regions can also show switch-related activation. Only regions that cannot be classified as part of the task sets are entered into my consideration for its involvement in task-switching control, because as long as their involvements in task switching can be well accounted by more basic functions, there is no need to assign higher cognitive features to them. Note that not all researchers agree with this view; for example, Kim et al. (2012) considered SPL one of the regions that guide task

switches, whereas in Chapter 4, I infer that SPL is more involved in task preparation than switch control, which is close to the view of Bunge et al. (2003; see also Bunge 2004).

On top of the above issues, most task-switching studies use only declarative tasks, and many use multivalent stimulus sets and response sets (multivalent means these sets are shared by tasks). This not only restricts the generalizability of conclusions drawn from these studies, but may also lead to indistinguishable activations due to overlapping task sets.

Introducing between-system task switching

The goal of the current study is to add some clarification to the task-switching mechanisms. Specifically, I will try to identify the executive control circuits, and reveal neural activities of executive control from brain imaging data. To address the challenges mentioned above, the current study contains two tasks that depend on different systems; namely, rule-based categorization (RB) tasks that depend on declarative systems, and information-integration categorization (II) tasks that depend on procedural systems. It has been demonstrated in Maddox et al. (2004) that switching within declarative systems and switching between declarative and procedural systems have different interference patterns behaviorally. Specifically, performance dropped when switching between RB categorization learning and memory-scanning tasks, but not when switching between II categorization learning and

memory-scanning tasks. And theoretically, RB and II categorization tasks may recruit different task sets. The interaction between executive control circuits and task sets of different systems may induce distinct BOLD patterns and help to untangle the executive control activities.

The design

The current study requires participants to switch between two tasks. One of the two conditions contains RB and II tasks, and the other contains two RB tasks. However, previous research showed that switching between RB and II tasks is extremely difficult to learn (Ashby and Crossley, 2010; Erickson, 2008). Fortunately, in more recent studies, Crossley et al. (2016) and Turner et al. (2017) showed that people could be trained to switch reliably between the two tasks when preceding cues for each task are provided. In these studies, participants learned the two tasks separately, and later were asked to switch between the two tasks on a trial-by-trial basis. Therefore, the current study adopted this approach. In the task-switching literature, using preceding cues to inform the upcoming tasks is called an explicit cueing paradigm.

Note that the design of the current study is very similar to Turner et al. (2017), and the aforementioned issues of brain imaging studies also occurred in theirs. For example, they did not find switch-related activations in previously implicated regions such as ACC, BG, and STN, but instead reported SPL and supramarginal gyrus (SMG). The focus of their study was on the difference between within-system and between-system switching, and they did report

different patterns for II to RB versus RB to II switch trials. However, this finding may be confounded because the difficulties of their II and RB tasks were different, and there was no control condition of within-system (RB to RB) switching to exclude this confounding factor.

Therefore, several improvements were added to the current study:

(a) The difficulty of one-dimensional rule-based categorization task was raised to match difficulties of tasks as much as possible.

(b) A condition of within-system switching was added. This provides a reasonable contrasting condition for untangling the task sets and the switch control circuits in multitask context, and helps to exclude the confounding of un-even difficulties while attributing distinct BOLD patterns to specific factors.

(c) Time precision of the fMRI scanning protocol was improved from 2 s to 0.72 s, and spatial resolution was improved from 3^3 mm to 2^3 mm, which should be helpful for detecting activities in small regions like STN.

(d) Dynamic causal modeling (DCM; Friston et al., 2019) and multi-variate pattern analysis (MVPA; Etzel et al., 2013) were added to data analysis. As discussed earlier, traditional contrast analysis for fMRI data might not be sufficient for identifying switch systems. MVPA can be used to detect changes of patterns despite the local activation might be

similarly strong to all types of events. And DCM can be useful for identifying changes of functional connectivity on switch trials.

Briefly, each condition of the current study contained three sessions. The first two sessions were purely behavioral and aimed to ensure that participants were trained to reliably switch between two tasks. The results from the second session were also compared with in-scanner behavioral data to examine the consistency of basic task-switching features. Although theoretically no cues are required for switching between univalent stimulus sets (which means stimulus sets for each categorization task were distinct), cues informing the participants about upcoming tasks were provided on each trial in the training sessions, because Erickson (2008) and Crossley et al. (2016) showed that cues are very helpful for people to learn difficult between-system switching. Note that even with cues, both studies only successfully trained about half of the participants, which is similar to the current study. Successful switchers were invited back to the third session where they performed the tasks while receiving fMRI scans at the same time. Details of the design are described in Chapter 2.

II and RB tasks

The current study contains two conditions: one is switching between procedural and declarative tasks (II and RB1), and the other between two declarative tasks (RB1 and RB2). Specifically, each stimulus is a disk with several bars in it, and has two features: spatial

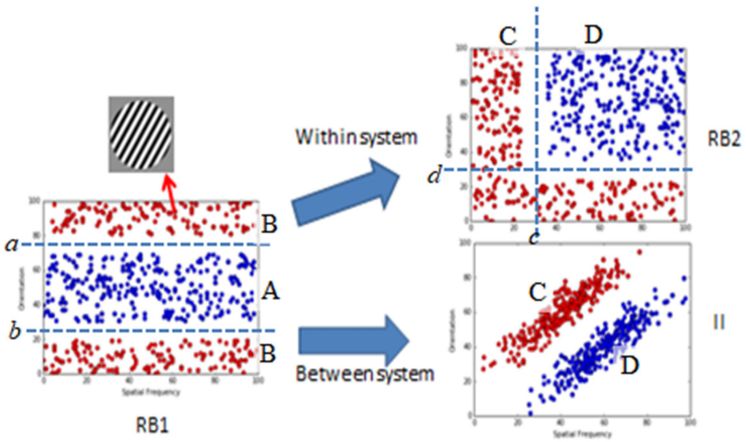
frequency (i.e. bar width, or number of bars in the disk) and orientation (i.e. the angle of bars). By separating the stimulus distribution space with a line, one can create rule-based category structures and information-integration ones.

The definition of an RB task is that the task can be carried out based on some simple rule that can be described as a Boolean expression of the stimulus values on a few stimulus dimensions, such as "category is A when bar angle is greater than 90 degrees". Both of the two RB tasks in the current study require a logical conjunction of two rules.[1] For RB1, only the orientation dimension is relevant, where category A is the conjunction of orientation smaller than a value *a* and orientation greater than another value *b*, and B is A's complement. For RB2, two dimensions are relevant, where D is the conjunction of spatial frequency greater than *c* and orientation greater than *d* (Figure 1-1), and C is D's complement.

[1] Note that in some studies (e.g. Hélie et al., 2010; Spiering & Ashby, 2008), rules of RB1 and RB2 were described as disjunctive and conjunctive, respectively. However, both RB1 and RB2 contain an "AND" and an "OR". Specifically, RB1 contains A = "orientation smaller than *a* AND greater than *b*", B = "orientation greater than *a* OR smaller than *b*", whereas RB2 contains C = "frequency smaller than *c* OR orientation smaller than *d*", D = "frequency greater than *c* AND orientation greater than *d*". In other words, there are two possible strategies participants can use for each category set (some may use AND and its complement while others may use OR and its complement), and the current study did not try to detect which strategy was adopted. The description of "conjunction" is to point out that both RB1 and RB2 require two rules, and that the essential difference between RB1 and RB2 is the number of relevant dimensions.

Figure 1-1

Example stimulus and category structures of RB1, RB2, and II.



Information-integration (II) tasks are those in which accuracy is maximized only if information from two or more incommensurable stimulus dimensions is integrated at some pre-decisional stage (Ashby & Gott, 1988). They are not RB tasks, because optimal performance cannot be achieved by applying Boolean rules. Evidence suggests that learning of II tasks depends on procedural system that is mediated largely within the striatum (Ashby & Ennis2006; Filoteo et al., 2005; Knowlton, Mangels & Squire, 1996; Nomura et al., 2007; Seger & Miller, 2010). The dissociation between RB and II categorization tasks have been shown to reveal key features of declarative system and procedural system (see Ashby & Valentin, 2017 for a review).

Overview of the chapters

As briefly mentioned earlier, more in-depth discussions on each topic are included in Chapters 3 to 6. For easy reading, all the details of methods (including experiment design and data analysis) and general results are put together in Chapter 2. Chapter 3 discusses behavioral results, with particular focus on switch costs and how they are coherent with previous findings and predictions of existing theories of task switching. Chapter 4 discusses brain regions of task sets, which is especially relevant for disentangling the switch control circuits from the whole network if possible. Chapter 5 discusses how the brain might work for task preparation during cue processing and for carrying out the target task in multitask context. Finally, on the basis of evidence from Chapters 3 to 5, Chapter 6 discusses how the current findings can be used to respond to the challenges on task-switching theories, and some of the important implications to fMRI studies and executive control.

Chapter 2. Methods and General Results

This chapter explains the full experimental design of the study, data analysis methods and general results. Post hoc analysis for answering research questions and implications of the results will be discussed in Chapters 3 to 6.

Briefly, the experiment contains 3 sessions, and each was conducted in different days. The first 2 sessions were carried out back to back in a computer lab, and the third session was conducted within 3 days in an MRI scanner. Unlike most task-switching studies that typically contain familiar tasks, the tasks in the current study were newly learned by the participants. Therefore, sessions 1 and 2 aimed to ensure people being trained on both tasks before measuring their abilities of switching between tasks, and only participants whose accuracy achieved 70% or above for both categorization tasks in the last single-task block of session 2 were invited back for session 3.

Sessions 1 & 2: Computerized experiments

Method

Conditions and Stimuli: This experiment used a between-subject design, where each participant only participated in one of the two conditions: RB-II or RB-RB. In the RB-RB condition, participants switched between two different rule-based (RB) categorization tasks

(RB1 and RB2) on a trial-by-trial basis, and in the RB-II condition, participants switched between an RB task (RB1, the same as in the RB-II condition) and an information-integration categorization task (II).

Each categorization task contains stimuli from two categories (A and B for RB1, C and D for RB2 and II). The distributions of the stimuli, defined in an arbitrary 100×100 space, are shown in Figure 2-1. Each sample from the distributions was converted to a round disk containing gray-scale circular sine-wave gratings in orientation×spatial frequency space by the equations shown in Table 2-1.

Figure 2-1

The distribution of categories and corresponding responses.

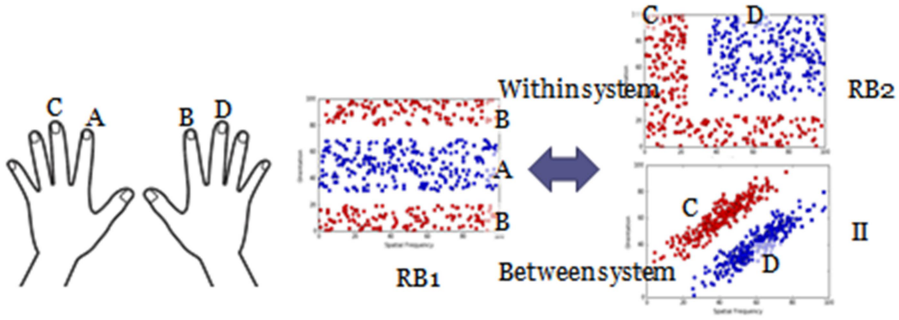


Table 2-1

Formulae for mapping (x, y) to (orientation, spatial frequency).

	Orientation (radian)	Spatial Frequency (cycles per degree)
RB1	$y \times \frac{\pi}{200} + \frac{\pi}{4}$	$2^{(-2.8+x*0.023625)}$
RB2 and II		$2^{(-0.2375+x*0.023625)}$

Each stimulus subtended approximately 10° of visual angle and was displayed against a gray background using routines from Brainard's (1997) Psychophysics Toolbox.

Apparatus: The experiment was controlled using custom MATLAB scripts and functions from Brainard's (1997) Psychophysics Toolbox. Participants were asked to learn to categorize images into 4 categories with both hands on keyboard keys specially labeled "A", "B", "C" and "D". They were asked to use their index fingers for pressing A and B keys, and middle fingers for C and D keys. Stimuli and feedback were presented on an LCD monitor.

Participants: Fifty-seven participants were recruited from UCSB community. All were between age of 20 and 40, right handed, with normal or corrected-to-normal eye sights. All were compensated by monetary rewards. Twenty-five of them were assigned to the RB-II condition, and 31 of them were assigned to the RB-RB condition. The assignment was random for the first 52 participants, and the last 5 participants in the RB-RB condition were recruited to balance the number of successful learners for both conditions. The exact sample sizes of the data sets are reported in the results.

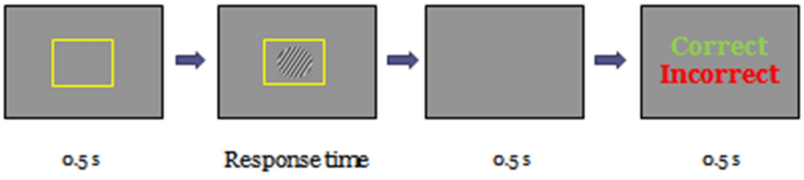
Procedure: The experiment consisted of two sessions, which were conducted back to back in two consecutive days. Each training session consisted of 14 blocks. In day 1, the first 6 blocks were for learning the first category set (RB1), followed by 6 blocks for the second category set (II for between-system condition, and RB2 for within-system condition), and 2 blocks for all categories. In day 2, the sequence of blocks was 3 blocks for the first category set, 3 blocks for the second category set, and 8 blocks for all categories. Participants were

asked to learn to categorize figures by starting out guessing and receiving feedback. They were informed that there were two category sets, and were prompted at the beginning of each block which set(s) they were going to learn. They were allowed to rest as long as they would like in between blocks, and none of their resting periods were more than a minute.

There were 50 trials in each block. On each trial, a crosshair showed on the screen for 0.5 s, followed by a yellow or blue square frame for 0.5 s as the cue for learning RB1 or RB2/II, respectively. After that, a stimulus showed on the screen with the cue surrounding it until the participant pressed a key. Then there was a 0.5 s blank, followed by a string of 'Correct' in green or 'Incorrect' in red at the center of the screen for 0.5 s as the feedback of the correctness of their response (Figure 2-2). If they pressed a key that was not assigned to the category set, the feedback would be 'Wrong key' in white. If no response was given in 5 s, the screen would show 'Too slow' in white, and the trial would end. There was a 1 s blank in between trials.

Figure 2-2

Illustration of a trial in the training sessions.



Results

Learning curves for each session of all the participants are shown in Figure 2-3, and the curves from the successful learners were shown in Figure 2-4, which seems to show a difference between RB-II and RB-RB for the first 6 blocks. However, participants were randomly assigned to the two conditions, and there were no different manipulations of any kind for the two conditions. Therefore, the difference between conditions may happen by chance. The performance of the two groups converged at the end of session 2.

Figure 2-3

Learning curves from session 1 and session 2 from all participants. Session 1: blocks 1 to 6 are task 1 (RB1), blocks 7 to 12 are task 2 (II or RB2), blocks 13 to 14 are for task switching. Session 2: blocks 1 to 3 are task 1, blocks 4 to 6 are task 2, blocks 7 to 14 are for task switching.

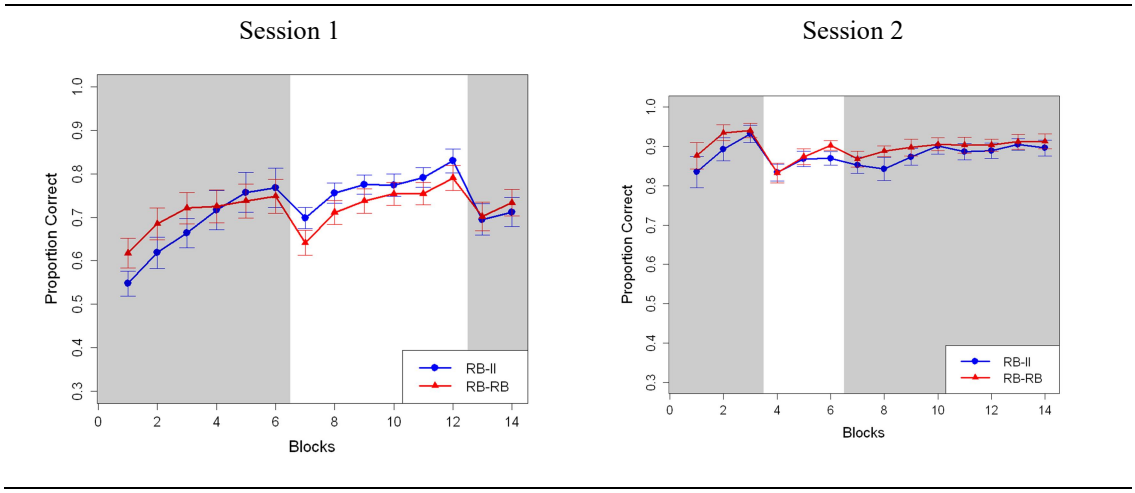
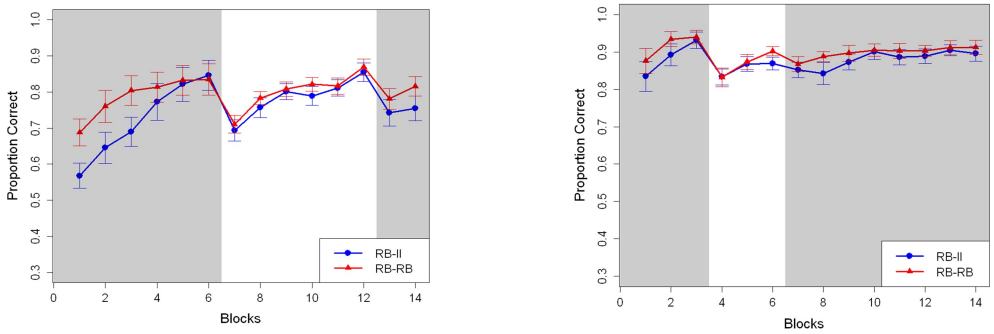


Figure 2-4

Learning curves from session 1 and session 2 from successful switchers. Session 1: blocks 1 to 6 are task 1 (RB1), blocks 7 to 12 are task 2 (II or RB2), blocks 13 to 14 are for task switching. Session 2: blocks 1 to 3 are task 1, blocks 4 to 6 are task 2, blocks 7 to 14 are for task switching. Error bars represent standard errors.

Session 1 Session 2



The following data analysis contains only data from session 2 by participants who were invited back for the fMRI scanning sessions. All the statistical analysis was conducted with the lme4 package in R. Meanings of the variables and notations for expressing a linear model are listed in Table 2-2. Each linear model contains fully crossed factors as specified, and a random factor for the subject effect. ACC and RT from each trial were entered into the models without adjustments unless specified.

Table 2-2

Variables and notations in linear models.

Variable or notations	Variable type	Meaning
A ~ B	Notation	A explained by B
A×B	Notation	Factors A and B are fully crossed
A:B	Notation	Interaction of A and B
ACC	Binary	Accuracy of response (1: correct; 0: incorrect)
RT	Positive real	Response time
Block type	Factor	Single-task or mixed block
Task	Factor	RB1 or RB2/II
Cost	Real	Switch cost in ACC/RT (difference of means on switch and stay trials)
Switch	Factor	Switch or stay trial
Condition	Factor	Condition RB1-II or Condition RB1-RB2

CSI	Integer	Cue-to-stimulus interval (0, 1, 2, 3)
RCI	Integer	Response-to-cue interval (3~7)

For detecting the mixing costs, trials from block 3 and block 6, as well as stay trials from block 13 and block 14 in session 2 were entered into the linear model of "Response (ACC or RT) ~ Block Type (single or mixed)". The effect of Block Type (i.e. mixing costs) was significant on RT ($p < .001$), but was absent on ACC.

For detecting the switch costs in the mix blocks, data from blocks 13 and 14 were entered into the regression model of "Performance (RT or ACC) ~ Switch ×Task×Condition" to examine if Switch has a significant effect. The results showed that the effect of Switch on ACC was significant ($p = .02$), as well as on RT ($p < .001$). The Task effect was found significant only on RT ($p < .001$).

The significant Task effect in RT suggests that RB1 was easier than II/RB2, thus the switch costs were calculated for each participants and entered into the regression model of "Cost~Condition×Task" for detecting asymmetric switch costs, which should be revealed by a significant effect of Task. The results showed that neither effect was significant.

Session 3: fMRI scans

Method

Conditions and Stimuli: They were identical to those in session 1 and 2.

Apparatus: The experiment was controlled using custom MATLAB scripts and functions from Brainard's (1997) Psychophysics Toolbox. Participants were asked to categorize images into 4 categories with both hands using the Cedrus button box. They were asked to use their index fingers for pressing A and B keys, and middle fingers for C and D keys, just as what they did in the training sessions. Stimuli and feedback were presented on a digital projector and screen viewed through a head-coil-mounted mirror.

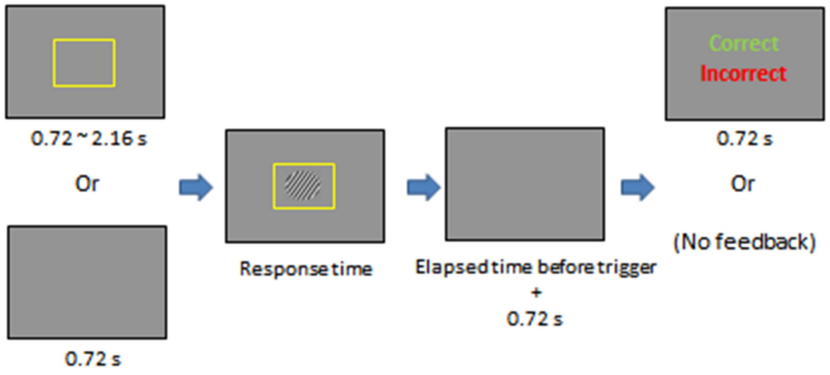
Participants: Participants whose accuracy of RB2/II was 75% or above in block 6 or block 14 in session 2 were invited back for this study within 3 days. As a result, 22 participants in condition RB-II, and 21 participants in condition RB-RB participated in the fMRI sessions.

Procedure: The procedure was identical to the switching portion of sessions 1 and 2, except the number of trials and the timing for cues, feedback and ITIs. Onsets of cues, feedback, and stimuli were synchronized with the scanner TRs. Stimulus was response terminated, as in the training sessions. Feedback was presented for 1 TR (0.72 s). There was a 1-TR blank screen between the first TR trigger signal since the last response and the onset of feedback. In other words, separation between feedback and response was between 1 and 2 TRs. On 50% of the trials, feedback was omitted. The partial trials design was for more accurate estimation of time courses (Ollinger et al., 2001; Serences, 2004). ITI were 3 to 11 TRs (drawn from a truncated geometric distribution) for jittering. On half of the trials, a cue of colored

frame as in sessions 1 and 2 was shown for 1 to 3 TRs (drawn from a truncated geometric distribution) before stimulus onset; for the rest of trials, a white cross hair was shown for 1 TR instead (Figure 2-5).

Figure 2-5

Illustration of a trial in the fMRI session.



Prior to the actual scanning session, participants completed a brief practice block of 40 trials outside the scanner that was matched to the design of the scanning experiment to reacquaint them with the task and to familiarize them with the new timing and pace. In the scanner, each participant completed 5 blocks, each of about 7 minutes. The first 28 TRs of each functional run were left blank to allow adequate time to reach steady-state scanning; the last 30 TRs were left blank to allow the BOLD response to decay from previous trials.

Neuroimaging acquisition: The scanning sessions were conducted at the UCSB Brain Imaging Center using a 3T Siemens Prisma Fit MRI scanner with a 32-channel phased array head coil. Cushions will be placed around the head to minimize head motion. Functional runs

used multi-band gradient echo EPI (echo-planar pulse) sequence (TR: 720 ms; TE: 37 ms; FA: 60^{o}; FOV: 208x208mm^3; voxel size: 2×2×2 mm^3) with generalized auto-calibrating partially parallel acquisitions (GRAPPA). Each volume consisted of 72 slices (interleaved acquisition; 2 mm thick with 0 mm gap; 2 mm×2 mm in-plane resolution; 104×104 matrix) acquired at an angle manually adjusted from the localizer image to minimize in-plane artifact susceptibility near orbitofrontal cortex from sinus cavities (Deichmann, Gottfried, Hutton & Turner, 2003). A localizer, 2 GRE field mapping scans with different TEs (2 mm thick; FOV: 208x208mm^2; voxel size: 2×2×2mm^3; FA=60^{o}; TR= 758ms; TE=4.92 ms and 7.38 ms), a T1-flash structural scan (TR=2500 ms; TE=2.22 ms; FA=7°; FOV: 241 × 241 mm^2; voxel size: 0.94x0.94x0.94mm^3), and a T2 scan (TR=3200 ms; TE=566 ms; FA=120°; FOV: 241×241 mm^2; voxel size: 0.94x0.94x0.94mm^3) were obtained before the EPI scans. Slice orientation were identical for all GRE and EPI sequences. Each scanning session lasted about 60 minutes.

Data screening

This research focused on reliable switching, thus blocks with average ACC of either task $\leq$ 79% in the fMRI sessions were excluded from data analysis. The threshold was to ensure that data from participants applying one-dimensional rules to two-dimensional tasks (RB2 or II) were unlikely to be included. To ensure that MVPA have reasonable size of data for training and testing, data from participants with less than 4 survived blocks were further excluded. As a

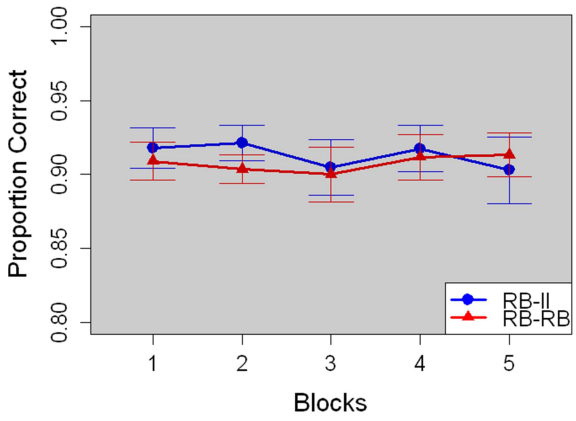
result, the samples sizes of MVPA are 15 participants in the RB-II condition and 16 participants in the RB-RB condition.

Behavioral Results

Accuracy curves of session 3 are shown in Figure 2-6. The curves are pretty much overlapped and showed no difference between two conditions. While feedback were still provided on half of the trials, both curves appear flat, which suggests that the performance of participants may have arrived ceilings.

Figure 2-6

Curves of proportion correct from session 3. Error bars represent standard errors.



As in session 2, statistical analysis was conducted with lme4, and the meanings of factors are listed in Table 2-2.

First, data from all the participants were entered into regression analysis. Regression model fits for ACC and RT on trials followed by and not followed by feedback were conducted

separately (denoted by f/FB and n/FB, respectively), with the performance measures explained by "Task ×Condition×Switch×CSI×RCI" (see Table 2-2 for meanings of abbreviations). The results are summarized in Table 2-3.

Table 2-3

p-value of each factor effect in the linear model of Performance ~ Task ×Condition ×Switch ×CSI ×RCI, where Performance is ACC or RT. For clearness, only p-values less than 0.1 were listed.

	ACC		RT	
	f/FB	n/FB	f/FB	n/FB
Task	< .001	< .001	< .001	< .001
Switch	.074	.003	< .001	< .001
CSI			< .001	< .001
RCI		.086		
Task:Condition	.090	< .001	< .001	< .001
Task:RCI	.072			.057
CSI:Task	.077			
CSI:Switch		.003	< .001	< .001
RCI:Switch			.093	
Switch:Condition			.023	.008
CSI:Switch:Task		.041		.051
CSI:RCI:Condition	< .001			
RSI:Switch:Task:Condition			.079	

The interaction effect of CSI:Switch was significant, thus the regression models of ACC~CSI and RT~CSI was further fitted to data from n/FB trials for each type separately. The results showed that the CSI effect in ACC was only significant on switch trials ($p < .001$) but not stay trials ($p = .17$). The CSI effect in RT was significant for both trial types (switch: $p < .001$; stay: $p = .05$).

Strictly speaking, when feedback was given, the mental processes may have entered into another "task", and thus the following trial could never be purely "stay". This may explain why the switch-related effects to ACC on f/FB trials were weaker than that on n/FB. In contrast, the switch-related effects on RT were mostly consistent for both types.

Second, the same analysis was conducted on data excluding blocks with accuracy less than 79% on at least one of the tasks, and the results are shown in Table 2-4. Similar to the results above, main effects of Task, Switch, and CSI are significant in RTs. The regression models of ACC~CSI and RT~CSI were further fitted to data from n/FB trials for of each switch type separately. The results were consistent: the CSI effect in ACC was only significant on switch trials ($p = .007$) but not stay trials ($p = .954$). The CSI effect in RT was evident for both trial types (switch: $p < .001$; stay: $p = .084$).

Table 2-4

p-values of Performance ~ Task×Condition×Switch×CSI×RCI for ACC and RT from good blocks. For clearness, only p-values less than .1 were listed.

	ACC		RT	
	f/ FB	n/ FB	f/ FB	n/ FB
Task	< .001	< .001	< .001	< .001
Switch	.084	.002	< .001	< .001
CSI			< .001	< .001
Task:Condition		.050	< .001	.001
RCI:Switch			.065	
RCI:Condition				.034
CSI:Switch		.086	< .001	< .001
CSI:Condition				.009

Switch:Condition			< .001	< .001
CSI:Switch:Task		.007		
CSI:RCI:Condition	< .001			
Swtich:Task:Condition	.083			
Switch:Task:RCI:Condition				.075

fMRI Data Analysis: General

Data Preprocessing: The following pre-processing pipeline was conducted before further data analysis: distortion correction, motion correction, and spatial smoothing. Slice-timing correction was not conducted as suggested by the Human Connectome Project, where the multiband technique with the same length of TR (0.72 s) was used (Elam & Harms, 2016). Spatial normalization was only conducted for group-level analysis. All of these steps were conducted using SPM12.

Atlases for labeling brain regions: The following brain atlases were consulted (listed by consulting order): SUIT (Diedrichsen et al., 2009), the probabilistic atlas of the motor cortices by Mayka et al. (2006), the probabilistic atlas of the basal ganglia by Keuken et al. (2015), the atlas by Neuromorphometrics in SPM12 (Ashburner et al., 2016), BioImage Suite by Yale University (2014).

Abbreviations: Since there is going to be a lot of terms of brain regions, events, and contrasts in the following contents, abbreviations will be used without mentioning their full spellings in the text for better readability. All the abbreviations are listed in Table 2-5.

Table 2-5

Abbreviations.

Brain regions	
a (prefix)	anterior (e.g. aIns: anterior insula)
ACC	anterior cingulate cortex
BG	basal ganglia
CD	caudate (CDh: head; CDb: body; CDt: tail)
FO	frontal operculum
IFG	inferior frontal gyrus (opIFG: pars opercularis; orIFG: pars orbitalis; trIFG: pars triangularis)
OFC	orbitofrontal cortex
MFG	middle frontal gyrus
ICC	isthmus of corpus callosum
Ins	insula
l (prefix)	lateral (e.g. lOFC: lateral orbitofrontal cortex)
m (prefix)	medial (e.g. mSFG: medial superior frontal gyrus)
MTG	middle temporal gyrus
PFC	prefrontal cortex
PMd	dorsal premotor cortex
PMv	ventral premotor cortex
Precentral	precentral gyrus
Postcentral	postcentral gyrus
PCu	precuneus
PO	parietal operculum
Put	putamen
RO	rolandic operculum
SFG	superior frontal gyrus
SMA	supplementary motor cortex
preSMA	pre-supplementary motor cortex
SPL	superior parietal gyrus
SMG	supramarginal gyrus
STG	superior temporal gyrus
STN	subthalamic nucleus
Vis	visual cortices
fMRI events	
A, B, C, D	response to category A, B, C, D, respectively

II	C and D in condition 1
RB1	A and B in both conditions
RB2	C and D in condition 2
s11, s22	target interval on stay trials of category 1 (RB1) and category 2 (II/RB2)
s*ij*	target interval on switch trials from category *i* to category *j*
c*i*	cue interval on category *i*
X-Y	SVM classification between events X and Y
Others	
ACC	Accuracy
BA	Brodmann area
Cond	Condition
DBS	deep brain stimulation
DCM	dynamic causal modeling
EDSS	Expanded Disability Status Scale
GLM	general linear model analysis
a-map	association-test map
u-map	uniformity-test map
MVPA	multi-variate pattern analysis
RT	response time
S-R	stimulus-response
SVM	support vector machine
TMS	transcranial magnetic stimulation
TS	task switching
WCST	Wisconsin Card Sorting Test

fMRI GLM Analysis

All of the analysis was conducted in SPM12. Events for GLM analysis were defined by stimulus types (crosshair, cue or target), categories (A, B, C, D, category 1, category 2), and feedback for the convenience of contrast analysis. For example, a contrast of c11 (presentation

of cues on RB1 stay trials) versus c21 (presentation of cues on RB1 switch trials) can be used to identify switch-specific neural activations for RB1 cue processing.

Individual beta-value maps of each event were then normalized to MNI152 space for group-level contrasts. Regions that showed significant activations on the events of cues and target stimuli on all types of trials are listed in Tables 2-6 to 2-8. A full list of contrasts, implications and significant results is shown in Table 2-9.

Table 2-6

Intersect of clusters found in c1 > 0 and c2 > 0 contrasts in condition RB-II ($p_{(unc.)} < .001$), cluster size ≥ 10 voxels). The numeric values are from event c1. Note that BA 9 showed significant activations to c1 and c2 in different clusters, thus is not listed. The coordinates are in MNI space.

Cluster size	Peak voxel				
	t value	x	y	z	Labels
1994	10.68	-12	-96	16	Vis
	8.98	-26	-88	16	Vis
	8.96	-28	-70	-12	Vis
2248	9.42	36	-64	-16	Right occipital fusiform gyrus
	8.76	30	-66	-10	Right Cerebral White Matter
	8.6	28	-72	-18	Right Cerebellum Exterior
45	6.19	-24	-64	44	Left SPL
146	6.18	-24	-6	52	Left SFG
	4.95	-30	-8	46	Left precentral gyrus
	4.43	-24	6	52	Left MFG (BA 6, PMd)
73	6.16	-52	4	20	Left precentral gyrus
	4.64	-52	6	32	Left precentral gyrus
	4.24	-44	4	32	Left precentral gyrus
138	6.16	-6	4	56	Left SMA
	5.43	-4	12	50	Left SMA

	5.03	-4	-4	58	Left SMA
89	6.06	30	-68	28	Right SPL
44	5.98	-30	24	8	Left FO
16	5.85	-8	-76	-18	Left Cerebellum Exterior VI
219	5.78	-40	-30	40	Left postcentral gyrus
	5.48	-50	-20	38	Left Cerebral White Matter
	4.74	-32	-36	42	Left postcentral gyrus
32	5.6	8	10	52	Right SMA/preSMA
43	5.08	24	-64	50	Right SPL
	4.74	28	-50	46	Right SPL
19	4.85	-32	-44	44	Left SPL

Table 2-7

Intersect of clusters found in c1 > 0 and c2 > 0 contrasts in condition RB-RB ($p_{(unc.)} < .001$), cluster size ≥ 10 voxels). The numeric values are from the t-map of event c1. The coordinates are in MNI space.

Cluster Size	Peak voxel				
	t value	x	y	z	Labels
1818	9.08	40	-70	-6	Vis
	8.97	30	-68	-12	Vis
	8.5	34	-54	-16	Right fusiform gyrus
1754	8.44	-6	-98	12	Left occipital pole
	8.3	-30	-62	-14	Left fusiform gyrus
	7.37	-32	-76	-14	Left occipital fusiform gyrus
44	7.66	-4	6	54	Left pre-SMA
404	7.37	-34	-46	50	Left SPL
	6.72	-34	-34	42	Left postcentral gyrus
	6.59	-44	-38	52	Left SPL
21	7.37	-8	18	50	Left SMA/pre-SMA
98	6.68	-22	-4	48	Left SFG (BA6/PMd)
	5.5	-30	-2	52	Left MFG (BA6/PMd)
179	6.44	30	-62	50	Right SPL
	5.39	36	-36	44	Right SPL
	4.96	30	-50	50	Right SPL
99	6.14	-26	-56	46	Left Cerebral White Matter (BA7)

62	5.54	-42	4	28	Left precentral gyrus
25	5.5	32	0	52	Right MFG (BA6/PMd)
44	5.45	50	8	26	Right precentral gyrus
	4.7	42	6	30	Right precentral gyrus
65	5.43	50	-54	2	Right Cerebral White Matter Fusiform
	5.28	42	-58	4	Right Cerebral White Matter
22	5.19	-54	8	20	Left precentral gyrus
32	5.17	-28	-68	32	Left Cerebral White Matter (BA39)
12	4.84	30	-70	28	Right SOG superior occipital gyrus

Table 2-8

Intersect of results of A+B+C+D > 0 from both conditions ($p_{(FWE)}$ < .05, cluster size ≥ 10 voxels). Manual inspections were made to ensure that all of the peak voxels showed significant activations to all types of events (A, B, C, D, stay, switch). The numeric values are from condition RB-RB. The coordinates are in MNI space.

Cluster size	Peak voxel				
	t value	x	y	z	Labels
9317	16.81	-8	-100	12	Occipital pole
	16.06	16	-70	-16	Cerebellum Exterior VI
	14.65	32	-68	-20	Cerebellum Exterior VI
3316	16.44	-44	-42	48	SMG
	16.28	-32	-46	46	SPL
	15.64	-28	-62	50	SPL
2428	16.38	28	-64	38	SPL
	13.68	34	-60	48	AnG
	13.48	52	-32	44	Cerebral White Matter
214	14.22	-38	0	8	aIns
	10.98	-44	-8	10	RO
354	13.08	6	26	46	preSMA
	9.92	6	32	34	mSFG (BA 8)
	8.03	-2	18	50	Pre-SMA
62	13.06	-28	-52	-48	Cerebellum Exterior VIIIa
	8.9	-18	-56	-46	Cerebellum White Matter (VIIIb)
451	12.27	-32	32	-2	Cerebral White Matter
	10.29	-32	14	10	FO

	9.73	-32	18	2	aIns
171	10.76	30	-46	-50	Cerebellum Exterior VIIIa
	9.89	28	-54	-52	Cerebellum Exterior
	7.84	26	-62	-58	Cerebellum Exterior
270	10.68	-48	6	18	opIFG
	9.51	-58	8	18	precentral gyrus
	8.79	-46	6	26	precentral gyrus
23	10.31	50	12	28	opIFG
30	10.18	40	0	14	RO
49	10.14	34	-16	-4	Cerebral White Matter
62	9.99	-26	42	-20	mOFC medial orbital gyrus (BA11)
	7.72	-26	52	-16	BA10
	6.85	-20	36	-18	mOFC (BA11)
10	9.96	-26	-2	54	BA 6
137	9.85	52	10	12	opIFG
	9.83	54	14	20	opIFG
	8.59	48	14	4	Cerebral White Matter
223	9.77	34	30	-4	Cerebral White Matter (BA47)
	9.73	34	24	8	FO
	7.82	38	20	2	aIns
169	9.75	-18	-14	20	Cerebral White Matter
	9.7	-10	-4	8	Thalamus Proper
	9.09	-16	-4	18	Cerebral White Matter
320	9.64	-44	40	22	MFG (BA 10)
	8.2	-38	30	24	Cerebral White Matter
	8.1	-38	44	14	MFG (BA46)
488	9.52	48	34	20	MFG (BA 9)
	9.33	42	48	2	MFG (BA 10)
	9.1	44	42	16	MFG (BA 10)
76	9.47	-22	0	8	Putamen
	8.84	-24	8	8	Putamen
	8.84	-26	-2	-10	Cerebral White Matter (BA34)
78	9.42	26	52	-18	BA 10
	8.13	24	40	-18	mOFC (BA11)
	6.49	20	34	-22	mOFC (BA11)

23	9.02	44	12	-2	FO
	6.61	38	6	2	aIns
32	8.86	-32	-18	-4	CDt
24	8.66	4	-32	26	ICC
35	8.52	-30	0	68	Unknown (BA6)
	7.88	-38	-2	66	Unknown (BA6)
86	8.36	14	-6	16	Right Cerebral White Matter
	7.5	14	4	12	Caudate
	7.42	12	-14	12	Thalamus Proper
15	7.96	12	2	2	Cerebral White Matter
10	7.87	18	-30	-4	Thalamus Proper
15	7.84	28	2	-8	Putamen
28	7.63	46	46	-14	OFC (BA 47)
24	7.1	-8	26	30	ACgG (BA32)
12	6.73	-10	-70	34	PCu

Table 2-9

Brain regions identified by fMRI contrasts. The threshold is $p_{(unc.)} < .001$, cluster size ≥ 10 voxels. Each contrast of X > Y was masked by the t-map of X ($p_{(unc.)} < .001$).

fMRI contrasts	implication	Identified regions
A > B and C > D	Left hand	Cond RB1-II: precentral, postcentral, VIIIa, V, VI Cond RB1-RB2: V, precentral, postcentral
B > A and D > C	Right hand	Cond RB1-II: precentral, postcentral, V Cond RB1-RB2: PO, V, VI, VIIIb
A > C and B > D	RB1 task set (exclude response set)	Both: MTG Cond RB1-RB2: BA10, SCA, MTG, trIFG
C > A and D > B	RB2/II task set (exclude response set)	Cond RB1-II: BA46, BA10, OrIFG, SMG Cond RB1-RB2: PCu, BA9, BA7
s21 > s11	RB1 switch; II/RB2 inertia	Cond RB1-II: precentral Cond RB1-RB2: SMG, SPL
s12 > s22	RB2/II switch; RB1 inertia	PCu

		Cond1: VI, PCC Cond2: PMd, BA4, BA40
s11 > s21	RB1 task set	Cond2: VIIb, BA9
s22 > s12	RB2/II task set	Cond2: VIIb, CrusII, BA10
s11 > s22	RB1 task set	N/A
s22 > s11	RB2/II task set	VI, CrusI, CrusII, PCu, FO, BA10, IFG, SMG, SPL, AnG
s21 Cond 1 > Cond 2	II task inertia; II to RB switch control	N/A
s21 Cond 2 > Cond 1	RB2 task inertia; RB2 to RB1 switch control	V, RO, ACC, PMd, precentral
s12 Cond 1 > Cond 2	RB to II switch control	N/A
s12 Cond 2 > Cond 1	RB1 to RB2 switch control	V, PMd, preSMA
s11 Cond 1 > Cond 2	II task inertia	N/A
s11 Cond 2 > Cond 1	RB2 task inertia	V, PMd, BA40, Put
s22 Cond 1 > Cond 2	RB1 task inertia; II task set	N/A
s22 Cond 2 > Cond 1	RB1 task inertia; RB2 task set	VIIIb, I-IV, V, AnG, SPL, BA6
Cue > crosshair	proactive control	SMG, SPL (switch)
c11 Cond 1 > Cond 2	RB1 task preparation (manage II)	BA9
c11 Cond 2 > Cond 1	RB1 task preparation (manage RB2)	N/A
c22 Cond 1 > Cond 2	II task preparation (manage RB1)	N/A
c22 Cond 2 > Cond 1	RB2 task preparation (manage RB1)	Ins
c21 Cond 1 > Cond 2	RB1 task preparation (manage II), switch control	N/A
c21 Cond 2 > Cond 1	RB1 task preparation (manage RB2), switch control	N/A
c12 Cond 1 > Cond 2	II task preparation (manage RB1), switch control	N/A
c12 Cond 2 > Cond 1	RB2 task preparation (manage RB1), switch control	SMG

DCM

DCM analysis was conducted on regions of interest (ROIs) determined by the purpose of answering research questions (see Chapter 5). Each ROI was a sphere of diameter 5 mm, and the center was selected from Table 2-8 and transformed back to the individual space. Time series were extracted using SPM12 and mean-centered before entering DCM. While slice-time correction was not conducted, it has been shown that DCM can account for slice timing differences up to 1 s (Kiebel et al., 2007). Since the purpose of DCM analysis in the current study was to investigate whether or not a hypothesized influence was significant, but not to compare different hypotheses on neural connectivity, only one model was built for each research question and fitted to all the participants, and Bayesian parameter averaging was used to estimate parameters and their posterior probabilities. Connections in each model were assumed to be modulated by switching. All of these steps were conducted using SPM12.

The first model aimed to examine how the influence from neocortex to cerebellar CrusII is modulated by switching. Since anatomical studies in monkeys reported that CrusII is strongly connected with area 46d (e.g. Kelly & Strick; 2003), the model was set up as BA 46 projecting to CrusII. Activation of BA 46 was assumed to be driven by target stimuli.

The second model was to examine the recruitment of STN, IFG, ACC, preSMA, and OFC in top-down interference control during task switching. All of the cortical ROIs were

found to show task-separable activations (Table 2-10), which supports their involvements in task-specific processing. Since the focus is the influence of top-down control, down-stream regions were assumed to receive influence from upstream regions (Figure 5-2). IFG, ACC and preSMA have been shown to project to STN, and have been regularly implicated in inhibitory control (see Table 4-3), thus the model is built accordingly. Activations in cortical regions were assumed to be driven by target stimuli. The results are shown in Table 5-5.

The third model was to examine the influence of STN (presumably indirect through the thalamus) to task-set regions in PFC, including IFG, MFG (BA 9 and BA 46), and preSMA. These regions are identified as part of the S-R task sets by reviewing lesion studies (see discussions in Chapter 4). Activations in all of the ROIs were assumed to be driven by target stimuli. The set-up is shown in Figure 5-3, and the results are shown in Table 5-6.

MVPA

MVPA searchlight was conducted with a linear support vector machine (SVM) classifier applied on a moving sphere of diameter 5 mm. For each participant, blocks 1, 3 and 5 were used for training the SVM, and blocks 2 and 4 were used for testing. The contrasting classification pairs include: s11-s22, s21-s11, s12-s22, s21-s12, A-B, C-D, A-C, B-D. The analysis was implemented in Matlab scripts with SVM toolbox, which will be posted on GitHub. The same analysis was applied with events being randomly re-assigned (e.g. for

classification of s11 vs. s22, half of the s11 epochs were randomly chosen and assigned as s22 and vice versa) for checking the false alarm rates (results are referred as "false-alarm maps" below).

The individual results were first normalized to MNI152 space using SPM12. The normalized individual maps were then averaged to get the group-mean maps. A threshold of classification accuracy 54% was applied to all the group-mean maps. This threshold was determined by that the classifications of A-B and C-D showed no results in the false-alarm maps, whereas motor cortices were detected in the group-mean maps. Tests with false-alarm maps showed that this approach produced lower false alarm rates than one-sample t-test.

A full list of identified regions is organized in Table 2-10. Since the classification accuracy was generally small (60% or less), to reduce the influence of false alarms to the inferences, only regions that were identified in multiple classifications that shared the same implications (e.g. C-D in both conditions, or intersect of A-C and B-D within condition) or overlapped with GLM results are discussed in the following chapters.

Table 2-10

Regions with classification accuracy ≥ 54%.

Classification pair	Implication	Identified regions
A-B	Motor response or categorization for RB1	N/A
C-D	Motor response or categorization	Both conditions: SPL

	for RB2/II	Cond RB1-II: AnG, SFG, STG, MTG Cond RB1-RB2: frontal pole, pre-SMA
A-C	Task separable; to be compared with s11-s22 and B-D	Cond RB1-II: MFG, STG, SMG Cond RB1-RB2: SFG, PCu, MTG, Vis
B-D	Task separable; to be compared with s11-s22 and A-C	Both conditions: AnG Cond RB1-II: postcentral, SFG, MFG, mSFG, AnG, Vis, STG, trIFG
s11- s21	RB1 switch; II/RB2 inertia	Pre-SMA, SPL
s12-s22	RB2/II switch; RB1 inertia	Cond RB1-RB2: PMd, MFG, SPL, AnG
s11- s22	Task separable; to be compared with A-C and B-D	Both conditions: AnG, pre-SMA, BA 47, Vis, mSFG, OFG, ACC Cond RB1-II: opIFG
s21-s12	Condition RB1-II: Within-system vs. between-system switch Condition RB1-RB2: TS for 1D vs. 2D stimuli	N/A

Chapter 3. Switch Costs

The existence of switch costs arguably defines task switching (TS). In one of the earliest task-switching studies, Jersild (1927) found that the total time that participants took to alternate between addition and subtraction calculations was higher than when they only had to perform a single type of calculation on the same list of numbers. Since then, many theories have been proposed to explain switch costs, and various experimental paradigms have been developed to test these theories. However, consensus about the underlying processes has not been achieved yet. As discussed below, findings are often specific to the designs and the tasks, and other times, theories and models just lead to similar predictions and are hard to differentiate. In this chapter, I will compare my results with observations reported in the task-switching literature, and discuss how much they support some of the important theories and help to settle some of the debates.

Discussion in this chapter is mainly on data from successful learners (participants with ACC > 70% in the last single-task block of either task in session 2); for fMRI sessions, only blocks with good performance are included (ACC of both tasks $\geq$ 80%), and the discussion is mainly on trials that when there was no feedback on the preceding trial (see Chapter 2 for details).

One task, or many?

The premise of task switching is that there are multiple tasks to switch between. As mentioned in Chapter 1, the existence of switch costs, along with the observation that some of the characteristic manipulations known to affect switch costs (discussed later) were significant, are taken as justification that this design did probe task switching. Specifically, switch cost was significant in the last 2 mixing blocks of the training session (RT: $p < .001$, ACC: $p = .021$), as well as in the fMRI session (RT: $p < .001$; and ACC: $p = .002$), and it was reduced when preceding cues were provided (RT: $p = .003$).

However, using the existence of switch costs as evidence of multiple tasks is not without problems. A potential issue can be demonstrated when considering the similarity between switch costs and repetition effect; the latter is regularly observed in almost all kinds of behavior. Specifically, since a switch cost is defined as the relative increase in RT and/or the relative decrease in ACC on switch trials, it can also be interpreted as task-level repetition effect on stay trials. But the similarity between task-level repetition effects and response-level repetition effects has rarely been discussed (if any) in the TS literature, because most of the TS studies have required the same response set for the tasks, and focused on the observation that

conflicts with repetition effects: repeating the same response on switch trials leads to increased RT and higher error rate (Gade et al., 2014).

In the current study, the response-level repetition effect was evident within each category set (RB1, RB2, and II) in the current study (ACC: $p = .059$, RT: $p = .01$). In addition, the response-level repetition benefit, just like the task-level switch costs, was affected by cues. Specifically, preceding cues significantly facilitated the changes of responses within each task (e.g. response 'A' after response 'B'; $p = .008$). In other words, if specific response for corresponding category (e.g. see a member of category A and press the left index finger) is considered a task, the within-task "(response) switch cost" (another way to describe the repetition benefit) was also reduced by cues. The underlying mechanism of response repetition benefits (or within-task "switch costs") may share common features with that of the between-task switch costs, because exerting control over a built-up tendency of repeating an action is one of the key features of cognitive flexibility, which is often studied with single-task design (e.g. Ku et al., 2006 and Hikosaka & Isoda, 2010). In brief, while this similarity may pose challenges to the definition of a task, it does not diminish the value of switch costs as a behavioral marker of executive control. Rather, it has an important implication: the ubiquity of repetition effects suggests that even non-TS designs may recruit TS mechanisms. Similarly,

studies on repetition benefit may also be helpful for understanding TS mechanisms, but including such topic here would be beyond the scope of the current study.

Also note that the term "stay trial" is used here to describe a trial preceded by the same task, although "repeat trial" is more often used in the task-switching literature. In this work, the latter is used to refer to when the correct response is to repeat the previous response. Comparing to "repeat", "stay" better illustrates that the task set stays, while the stimuli and the responses might not repeat on those trials.

Theories and debates

Some of the task-switching theories and models were reviewed in chapter 1. While they disagree in many ways, they all include two features: activation and inhibition of task sets. The disagreements are mainly about how, when, and to what extent the activation and inhibition take place. For example, the task reconfiguration theory advocated by Rogers and Monsell (1995) emphasizes active control on switch trials, whereas the task set inertia (TSI) theory by Allport and colleagues (Allport, Styles, & Hsieh, 1994; Allport & Wylie, 2000) emphasizes passive interference.

The concept of having to update the task set before conducting a task was proposed as early as task switching phenomena were first reported by Jersild (1927). In this example, both

tasks used lists of numbers as stimuli, and the tasks required either addition or subtraction. Jersild observed that RTs in the task-switching blocks were higher than in single-task blocks (note that all the trials were switch trials in his task-switching blocks), and suggested that task switching requires updating of the task set on switch trials, whereas performing a single task requires maintaining the same task set, and thus the former takes longer. The concept of updating task sets is nowadays called task reconfiguration.

To more closely investigate the task reconfiguration theory, Rogers and Monsell (1995) introduced the alternating runs paradigm so that mixed blocks contained both stay and switch trials. They manipulated the response-stimulus interval (RSI) and found that switch cost decreased as RSI increased (the reduction in switch cost is termed RISC below), which is taken as strong evidence for a reconfiguration process: longer RSI provides more time for reconfiguration, which may include proactive activation of relevant task sets and proactive suppression on irrelevant task sets.

On the other hand, Allport and colleagues (Allport, Styles, & Hsieh, 1994; Allport & Wylie, 2000) suggested that switch costs do not measure proactive control; rather, switch costs can be simply explained by the interference from persisting activation of the irrelevant task from the previous trial, along with persisting inhibition to the relevant task under multitask contexts. They hypothesized that RISC was due to decaying interference from the irrelevant

task set and did not have to involve proactive activation (i.e. activation of the task set can occur no earlier than receiving the target stimulus), nor did the onset of activation have to be restricted on switch trials.

However, Rogers and Monsell (1995) defended their view of active control with the observation that RISC was only evident with fixed RSI but not variable RSI, and reasoned that with variable RSI, the timing of target becomes unpredictable and thus proactive control is undermined. Later, this debate was investigated using an explicit task-cueing paradigm that allows independent manipulations of response-cue interval (RCI) and cue-stimulus interval (CSI). Since RCI does not affect task-specific preparation (because the upcoming task remains unknown until a cue is presented), it is a better tool than RSI to untangle whether RISC is due to decay of interference or sufficient time for reconfiguration. By manipulating CSI and RCI, Meiran et al. (2000) inferred that both task set reconfiguration and passive decay of previous tasks take place, along with a residual component that does not disappear with prolonged CSI and RCI. Note that RISC also appears in single-task contexts (e.g. Savine et al., 2010), which indicates that the beneficial effect of cues is not restricted to switch trials. This provides another example of the similarity between switch costs and repetition effect.

Nonetheless, the passive interference effect does play an important role in switch costs. The support for TSI comes from the so-called asymmetric switch cost: the observation that

switch costs are higher when switching from the difficult to the easy task compared with the other way around (Arbuthnott, 2008; Meuter & Allport, 1999; Allport et al., 1994). This can be explained by the stronger activation of the difficult task or stronger inhibition of the easy task. Without considering the interference effect, the task reconfiguration theory predicts the opposite: switching to the easy task requires less effort of task reconfiguration and thus should cause less switch cost. In addition, the aforementioned conflicting repetition effect on switch trials is also strong evidence of interference. In the current study, though, neither the asymmetric switch cost nor the conflicting repetition effect was evident. A possible explanation is that the difference of the difficulty and/or the persisting interference between the two tasks was not large enough. Or, as Yeung and Monsell (2003) suggested, switch asymmetry might depend on high levels of intertask conflict, which is much weaker with univalent stimuli.

However, even if interference exists, it is not necessarily managed by inhibition. A straightforward alternative explanation is an activation difference, which has been adopted by multiple theories (see Table 1-1 for examples). Strong support for inhibitory control comes from the n-2 repetition effect: when there are three tasks (denoted by A, B, C) to switch among, performance on trial n is better when the n-2 trial is a different task (i.e. sequence CBA) than the same task (ABA). This can be explained if task A is more strongly inhibited in the sequence

ABA than in CBA because it is more recently switched from in the former case. This effect has been observed in many studies and across different paradigms (see Koch et al., 2010 for a review), and was suggested to occur during response-related processing (Gade et al., 2014).

Since then, several designs have been proposed to probe inhibitory control, and these studies suggested that there is top-down inhibition that is linked to cues or task preparation (e.g., Mayr & Keele, 2000) and bottom-up inhibition for resolving conflict (e.g., Koch, Gade, Schuch, & Philipp, 2010; Schuch & Koch, 2003). Similarly, the top-down and bottom-up arguments along with diverse theories of mental processing have also been proposed for activation (see Grange and Houghton, 2014 for a review). A plausible scenario is that these mechanisms coexist and temporally overlap with each other. Thus, the following section aims to probe the diverse components of switch costs.

Dissect the switch costs

As briefly mentioned above, there are various manipulations that may affect switch costs. Relevant manipulations in the current study include RCI, CSI, presence of cues, and task difficulty. The current study adopted an explicit cueing paradigm. Specifically, the training session contained single-task blocks and mixed blocks with fixed RCI and CSI, whereas the fMRI session contained mixed blocks with varied RCI and CSI, with only half of the trials

preceded by a cue (colored frame). The stimuli were univalent, which means that task switching was possible even without preceding cues. However, since target stimuli were always presented with a corresponding colored frame, it is possible that even on un-cued trials, the categorization processing was preceded by cue processing. Furthermore, data analysis showed that RB1 was easier than RB2/II for both conditions, but the asymmetric switch cost was not significant, which indicates that the task-difficulty effect may not be evident.

Within-system vs. between-system TS

A key feature of the current study is that it contained both within-system and between-system switching, which allows us to examine whether or not the two types of switching possess different behavioral patterns. The behavioral data showed multiple significant cross-condition interactions (such as Task×Condition and CSI×Switch×Condition in ACC; see Chapter 2 for details). Post hoc analysis found that switch costs in ACC of RB2 were higher than of II, and the absence of a significant difference between ACC of RB2 and II excludes the potential confound of unequal difficulty. This may be an indication that within-system interference was stronger than between-system interference. Other than that, the behavioral data did not show qualitative differences between within-system and between-system task switching. Discussions in the following paragraphs hold for both conditions.

Mixing cost

It is now clear that the RT switch cost found in Jersild (1927) was actually a combination of mixing cost and switching cost. The former is the performance drop found by comparing stay trials across mixed blocks and pure blocks, and the latter comprises the rest of the switch cost. Since mixing cost is found with stay trials, it is strong evidence of persisting interference other than switching control under a multitask context, although alternative explanations have also been proposed, such as that performance in pure blocks benefits from a stronger priming effect (Marí-beffa and Kirkham, 2014). Presumably, mixing costs also exist on switch trials, and thus a switch cost is a combination of mixing cost and switching cost. In the current study, mixing costs in RT were significant for both tasks in both conditions ($p < .001$).

The measurement of mixing costs is important, because high mixing costs could lead to low switch costs and confound the inference, as what was found in PD patients. This finding was interpreted as low repetition benefit (Marí-beffa & Kirkham, 2014). Several hypotheses have been proposed for mixing cost:

1. Failure to engage in task preparation: this hypothesis is supported by the observation that increasing CSI in mixed blocks produces benefits for stay trials as much as for switch trials (Kiesel et al., 2010). However, the same was not found in the current study (see the paragraph about RISC below). Besides, an issue with this hypothesis is that possible

explanations for the failure are lacking. The following two hypotheses may provide good supplements.

2. Additional memory demands for conjunction task rules: this hypothesis is supported by the observation that univalent stimuli do not normally produce mixing costs (Allport & Wylie, 2000; Jersild, 1927; Wylie & Allport, 2000). Note that while using univalent stimuli, a mixing cost was found in the current study. Even so, additional memory demands could still account for this finding, since additional memory for mapping category set to response set was required in the mixed blocks but not in the pure blocks. Specifically, both category sets required choices of left versus right, but RB1 required index fingers, whereas RB2/II required middle fingers, which was found to be a significant source of interference (see the paragraph about sources of interference below).
3. Enhanced inhibition due to negative priming and/or antiperseveration suppression: this hypothesis appears to be against the observation that PD patients typically show stronger perseveration in WCST (e.g. Hélie et al., 2012).

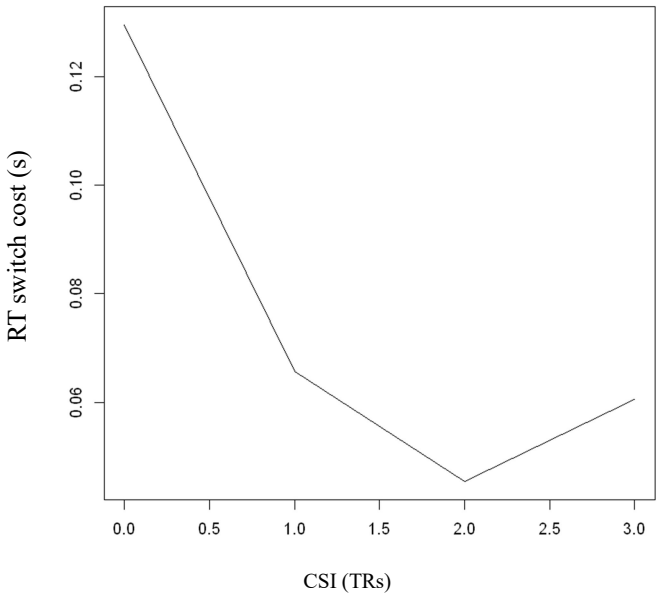
RISC

It is often observed that the reduction in switch cost (RISC) approaches zero with prolonged CSI and RCI, which is also supporting evidence for the existence of persisting interference (residual cost). More importantly, RISC is often taken as support for the decay of

TSI (but see Grange & Houghton, 2014 for challenges on this hypothesis). In the current study, RISC was not evident (Figure 3-1). Several studies have shown that the effect of RCI is not consistent when it varies, which is exactly so because of the jittering design in the current study. For example, Rogers and Monsell (1995) reported that RISC was only observed with fixed RSI (= RCI + CSI); Meiran et al. (2000) found that extending the RCI prolongs task-repetition RTs; and Horoufchin et al. (2011) reported that switch costs were only reduced at long RCIs when the RCI for the previous trial was short. As to the CSI effect, it has been reported that longer cue presentation time could lead to higher switch cost (Verbruggen et al., 2007), which might explain the slightly upward trend when CSI increased from 2 TRs to 3 TRs. In short, the support for decay theory with RISC is lacking in the current study, but it might be due to high variability of CSI and RCI.

Figure 3-1

Mean switch costs in RT vary by CSI.



Benefit from preceding cues

Cues have been reported to benefit task preparation, especially for people with neurobehavioral disorders (e.g. Brown and Marsden, 1988; Hartman et al., 2003; Schmitz et al., 2006; Poljac et al., 2010; Van Eylen et al., 2011). These findings have been taken as strong evidence for active control. Consistently, CSI effect in the current study was significant on within-task response-change costs (e.g. switching between A and B) and between-task switch costs (switching between RB1 and RB2/II), and the benefit was mainly on non-zero CSI relative to zero CSI (i.e. with relative to without preceding cues).

Notably, the beneficial effect of preceding cues on response-change costs (i.e. repetitive effect) was significant on stay trials ($p = .008$). In other words, if response changes are

considered a type of task switching (in this case, a task is defined as seeing a member of a specific category and conducting appropriate finger pressing), the cue also facilitates within-task "(response) switching". This finding has two important implications. First, as mentioned earlier, it indicates that there may be common features (presumably anti-automation) among TS and general tasks. Second, it poses doubt on the effectiveness of measuring task reconfiguration with switch costs, because the task reconfiguration theory assumes that there is no need for reconfiguration on stay trials. More specifically, the higher RT on no-cue within-task "switching" trials (e.g. A to B or B to A) relative to cued trials suggests that some proactive processing for the latter was postponed until the stimulus was presented for the former. Such observation is strong evidence for proactive control during cue interval even on stay trials and against the most strict reconfiguration theory which assumes that proactive control only occurs on switch trials.

Besides, while proactive processing could be activation or inhibition, the repetition effect on stay trials is unlikely to reflect the latter, because if the inhibition effect was applied equally to all the categories, there should be no response repetition benefit; and if the inhibition was specific to the most recent trial, a repetition "cost" rather than "benefit" should be observed. On the contrary, if it is reflecting proactive task-set activation, since cues for the categories in the same set are the same, the induced task-preparation effect should be indifferent for the two

categories. This prediction is supported by the observation that the response-repetition benefit was not significant for stay trials with preceding cues (i.e. no difference between A to A and A to B). If the property of within-task "switch costs" also holds for TS switch costs, it seems to favor the hypothesis of enhancive more than inhibitory proactive control.

Also note that all the no-cue trials were preceded by a crosshair in the current study, but since there are no no-cue trials without a preceding crosshair, there is no way to tell from the behavioral data whether the presence of crosshair introduced additional effects.

Conflicting response-repetition effect in task switching

As discussed earlier, repeating responses usually lead to better performance (decreased RT and higher ACC) in normal tasks. However, task switching studies typically observe response–repetition costs on switch trials and response-repetition benefits on stay trials. Since the current study required separate response sets for tasks (index fingers for RB1, and middle fingers for RB2/II), responses on switch trials could never be repeating. However, when the response is considered in term of left versus right (e.g. A following C is considered a repeating response, because both responses are on the left), the response-repetition benefit was significant on stay trials (RT: $p < .001$; ACC: $p = .027$) but not on switch trials (RT: $p = .762$; ACC: $p = .203$) in the training session. This finding is partially consistent with the typical observation of conflicting response repetition effect in task switching. Unfortunately, it cannot

be taken as strong evidence, since it is seriously confounded by the fact that the stay trials never required switching finger types whereas the switch trials always did.

Sources of interference: response set versus category set

While the conflicting response-repetition effect was absent in the current study, evidence for mutual interference between tasks can still be provided by data of wrong-key presses. What makes the current study special is that each task set is a combination of response set (index fingers or middle fingers) and category set (RB1 or RB2/II). When a mistake is made, it could be due to the interference from the irrelevant response set or category set. To tell which interference source is more possible, I reasoned that when the interference was from the irrelevant response set, participants would press the wrong key on the correct side (e.g. left index finger press for answering category C), otherwise the response side should be random. The ratio of correct sides on wrong-key trials (219 trials in total) was 80.95%, which was significantly higher than chance. To examine the alternative – the interference was from the irrelevant category set, I also examined the ratio that RB2/II responses were according to RB1 rule (only 45 wrong-key trials in total; note that there is no way to apply RB2/II strategies on RB1 stimuli). The ratio was 53.33%, which was not significantly above chance ($p = .655$). Adding correct-key wrong-response trials of RB2/II increased the number of trials to 679, but decreased the ratio to 41.23%, which further repels the possibility that RB1 rules had been

applied. Thus, this analysis did not provide evidence for category-set interference. And for the wrong-key trials, it is more likely that the interference was from irrelevant response sets.

Since wrong key is a strong indication of interference, I also examined the RSI and CSI effects on RT of wrong-key trials, as well as the ratio of wrong keys, but no significant results were found. However, the null results could be due to relatively small sample size. Notably, 40% of the wrong keys occurred on stay trials, which is strong evidence for persisting interference from the other task. Without lingering activation of the irrelevant task, it would be hard to explain why the just activated, relevant task set would be outperformed by an inactive, irrelevant task set. This is consistent with the view of additional memory burden in mixing costs, although their emphases are slightly different (persisting activation here can be passive, whereas additional memory requirement in mixing costs implies it is active).

Note that 91.7% of wrong answers cannot be explained by wrong-key presses for correct answers (97.9% of them were correct-key presses). However, those responses were only on 5.4% of the trials and may simply reflect not properly learned portions. While we cannot exclude the possibility that those errors were caused by disruptions to the category sets, at least part of the disruptions cannot be explained by TSI from the preceding trials, since 46.1% of such errors were on stay trials.

TS on repeat trials

Another interesting finding is that more errors were made on repeat trials (when the correct response should be just repeating the previous keypress). Specifically, if the responses have no tendency, the ratio of repeating and changing responses should be equal regardless of the correctness. However, there were less repeating responses than should be on error trials ($p = .013$; ratios of fail-to-repeat responses in conditions RB-II and RB-RB are 64% and 54%, respectively; no such difference on correct responses), which indicates a tendency of changing responses. For repeating trials, there is no need to reconfigure responses, thus this tendency can serve as evidence for trial-by-trial task-set configuration, the existence of TSI even within tasks, and lessened interference control on TSI.

Conclusion

The current study observed patterns that support the view of proactive control (e.g., the beneficial effect of preceding cues, and the absence of RISC effect with variable RSI) and the additional-memory theory (e.g. mixing costs, and wrong-key presses for correct answers on stay trials), but evidence for inhibitory control (n-2 repetition effect) was not evident. In addition, evidence also suggests that some of the features of cognitive flexibility are shared by TS and normal tasks (e.g. repetition effect, and beneficial effect of preceding cues on response

changes). These patterns were consistent across RB-RB and RB-II switching, although switch costs appeared to be higher for RB-RB switching than for RB-II switching.

So far, behavioral data from the current study has helped to respond to a theoretical question: whether task-set reconfiguration occurs only on switch trials. Several pieces of evidence favor the opposite, such as preceding cues benefited performance on switch trials as well as on stay trials, and similar errors occurred on both types of trials. In the following chapters, brain imaging data will provide supporting evidence for the persistent executive control on stay and switch trials.

Furthermore, the following theoretical questions will be addressed with the supplement of brain imaging data. First, to address the debate about whether or not TS is special, i.e. requires additional executive-control mechanisms comparing to simple tasks. Second, to figure out the timing of proactive control (e.g. whether it occurs before the target stimulus is presented). Third, to figure out how the interference might be managed in the brain – whether it is by enhancing the relevant task set, inhibiting the irrelevant task set, or both. Forth, to figure out if the brain handles TS with a uniform approach: more specifically, whether RB-RB switching and RB-II switching are managed differently. For these purposes, the necessary first step is to identify the activities of basic task sets, which is the main goal of Chapter 4.

Chapter 4. In Search of the Task Sets

When we find a region activates stronger on switch trials than on stay trials, how can we tell if it is controlling the switching of tasks (e.g., detecting the switch needs and inhibiting irrelevant task sets accordingly), or is simply busy updating information upon the request of a switch-control circuit? To understand how our brains work for task switching, the first step would be to identify the task-relevant regions, which compose the so-called "task set" in the task-switching literature (Grange and Houghton, 2014). As introduced in Chapter 1, "task set" in this work is defined as all the necessary neural processes for carrying out an S-R transformation task, which includes the whole network from receiving perceptual input to generating behavior output. In this chapter, this term is used to refer to that network.

Challenges of fMRI inferences

This research used fMRI as the tool to identify relevant neural activities. Since the 1990s, fMRI studies have been providing evidence of how certain brain regions are consistently activated for specific behaviors (Bandettini, 2012). However, controversies have also been introduced, especially when a brain region has been suggested in fMRI literature for a type of task, but damages to it rarely lead to impairment of performing that task. For example, while fMRI studies of episodic retrieval have consistently revealed activations in parietal cortex,

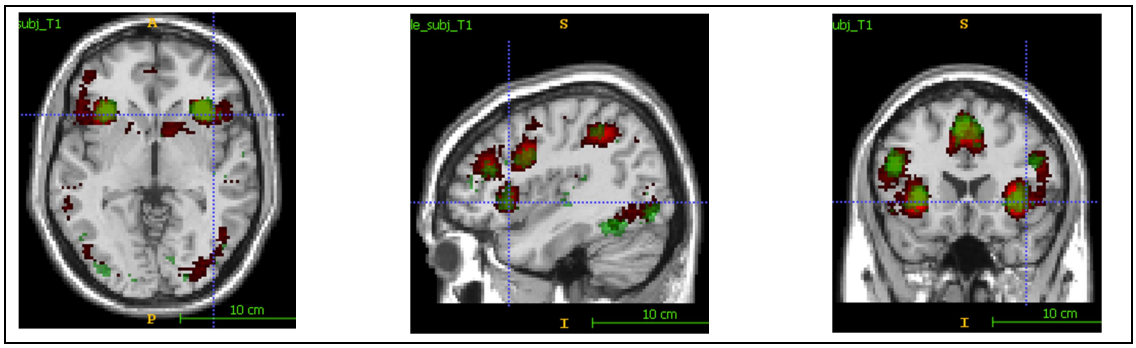
parietal lesions do not typically yield severe episodic-memory deficits (Cabeza et al., 2008); similar issues have obscured the understanding of rostral PFC (Burgess et al., 2006); and sometimes contradictory conclusions were drawn (for example, Faillenot et al., 2001). It is now recognized that carrying out a task never just involves one cognitive function, and some of the involved functions could be differentially critical to the task (Silva et al., 2018). This type of confusion is not rare, especially when conclusions are drawn by reviewing the literature of a relatively narrow topic.

To illustrate how readily this may happen, consider that I tried to identify the circuit of "categorization" using fMRI and found many brain regions activated on target trials, but how relevant would they be to the task? The first step would be to compare my results with previous studies. Typically, this would be done by querying bibliographic databases with names of the brain regions and relevant research terms. Recently, an online database, Neurosynth, has been built to facilitate this process. Neurosynth contains more than fourteen thousand fMRI studies and provides automatic meta-analysis on hundreds of popular research topics. To review if a region is regularly reported in fMRI studies of “categorization” would be similar to consulting the uniformity-test map (u-map) of categorization on Neurosynth for a z-score in that region (https://neurosynth.org/faq/#q18).

So what might be the issue of this confirmatory approach? It can be demonstrated when I also compared the u-map of “categorization” with the u-map of, say, "difficulty". While I found that my results were highly consistent with the u-map of “categorization”, I also found it consistent with the u-map of “difficulty”. In fact, when I compared u-maps of “categorization” and “difficulty”, I found many overlapping regions (Figure 4-1). Since regions appearing in both u-maps are reported in categorization studies as frequently as in difficulty studies, it greatly undermines my confidence that these regions are specialized for categorization.

Figure 4-1

U-maps of categorization (green) and difficulty (red) from Neurosynth, showing clusters consistently activated in studies that use the two terms. Most clusters overlap in the two maps. Images are created by overlaying u-maps on a normalized single-subject T1 image (provided in SPM12) using ITK-SNAP.



Since “difficulty” is more elemental than “categorization” (“A more elemental than B” means that B might involve A, but not the other way around), a way to reconcile is to infer that “these regions were active because the tasks were difficult”. Unfortunately, this would not be very informative. But when I added “switching” to my list and found that brain activation patterns of “categorization” and “switching” were also highly similar, more informative

inferences could be made. For example, this could be an indication that categorization recruited mechanisms of TS. In other words, consulting more maps of elemental functions would allow me to see a broader picture and avoid bias. In discussions later, I will refer to maps of several elemental functions to assist with inference, such as finger movement, maintenance, interference, inhibition, attention, and difficulty.

But the intrinsic limitations of brain imaging methods cause other confusions. Even when the correlation between observed patterns and behavior is valid, causal inference can never be made without causal experiments. While I did not have a chance (and it is not always possible) to conduct causal studies in humans, lesion studies in human patients and animals could provide relevant causal observations. And of course, any inference should be aligned with existing observations. Thus, I consider reviewing the causal literature a critical step for identifying task sets. With the converging evidence from data analysis, meta-analysis and causal studies, I will infer the potential functions for brain regions found during my data analysis, identify regions that are most likely necessary for categorization, and infer their potential functions in the task set.

Before moving on, please be aware that having a similar collection of activated brain regions across tasks should not serve as evidence of homogeneity of neural mechanisms for both tasks, because the requirement of switching between tasks might have forced the brain to

keep a task set active even when it is not needed for the current trial. This is called the "task-set inertia" effect and has been observed in many fMRI studies (Richter and Yeung, 2014). Similarly, the null findings of between-condition contrasts might be because task-set inertia caused the rule-based networks to remain active in both conditions, thereby reducing the overall difference. In other words, the "task set" identified in this chapter might be better viewed as a mixture of sub-task sets. There will be discussions about task-set inertia in Chapter 5.

Since there is going to be a lot of terms of brain regions, events, and contrasts in the following discussion, I will use abbreviations without mentioning their full spellings in the text for better readability. All the abbreviations were listed in Table 2-5.

Potential functions of brain regions

To avoid confirmation bias, I adopted an exploratory approach to identify the task-set regions: list all the possible functions for all the brain regions found in data analysis and causal studies separately, and infer their possible roles based on converging evidence. Meta-analysis maps will be used mainly for confirmation and support. All the relevant brain regions with their potential functions by trial type, data analysis, meta-analysis, and causal studies are

summarized in Table 4-1. Definitions of function types and the logic of inference are explained in the following subsections.

Table 4-1

Activated brain regions and their inferred functions. Regions are from Tables 2-6 to 2-8. Target/cue/both means activation was found during target stimulus/cue/both interval(s). "ext." stands for "extend to".

Region	Respond to	Meta-analysis	Data analysis (on Target)	Causal studies
ACC	Target	N/A (but in switching u-map)	General; Task-separable	Switching
AnG	Target	Attention	General; Task-separable	Response configuration
CDh and CDb	Target	N/A	General, biased to switch	Switching, task-related
CDt	Target	N/A	General	Task-related
FO	Both	Attention	General	Switching, task-related
trIFG	Target	N/A	General; Biased to RB1	
orIFG (BA 47)	Target	N/A	General	Switching, task-related
opIFG (PMv)	Target	Finger, difficulty, interference, maintenance	General; task-separable	Switching, task-related
OFC	Target	N/A	General; task-separable	Switching
aIns (ext. orIFG)	Target	All but finger	General; biased to switch	Switching; other
ICC	Target	Interference, inhibition, maintenance	General	Motor planning: implementation
MFG (BA 9 and 10)	Both	difficulty, interference, maintenance	General; biased to 2D stimuli	Switching, task-related
MTG	Target	N/A (but in categorization u-map)	Category specific	Task-related
Vis	Both	Attention	General, biased to RB1 or 2D (different divisions)	Visual
PMd	Target	All but inhibition	General, biased to switch	Motor planning: implementation

precentral	Both	All but inhibition	General	Motor planning: command
postcentral	Both	Finger	General	Motor planning: somatosensory
PCu	Target	Attention	Biased to 2D stimuli and switch	N/A
PO	Target	N/A	General, biased to switch; motor related	Motor planning: somatosensory
Put	Target	Finger, inhibition	general	Task-related
RO	Both	Finger	General; motor related	Other
SMA	Cue	Finger	General	Switching; Motor planning: implementation
preSMA (ext. mSFG)	Both	All but finger	General; task-separable; biased to switch	Motor planning: implementation; switching
STG	Target	Attention	Category specific (condition 1), biased to RB1 (condition 2)	Task-related
SPL (ext. SMG)	Both	All but inhibition	General; biased to switch; motor related	Motor planning: implementation
SMG	Target	Inhibition	General; Category specific	Response configuration
Cerebellum:VI, CrusI	Both	maintenance (with s22> s11, not with cue), finger	General; biased to 2D; motor related (VI)	Motor planning: implementation; switching
Cerebellum: CrusII	Target	N/A	General; biased to 2D stimuli	switching
Cerebellum: VIIb, VIIIa, VIIIb	Target	Finger	General; motor related (VIIIa, VIIIb)	switching

Reasoning on fMRI data

GLM and SVM classification were used for identifying relevant regions, and details can be found in Chapter 2. All the regions are listed in Table 4-1 and separated into several types: "general", "task separable", "biased to", and "category specific". "General" means the region was activated during the target-stimulus intervals (when the stimulus was on) in both conditions. "Motor-related" means the region was most likely activated for motor planning. "Task separable" means activation patterns of the two tasks were differentiable by SVM classification. "Biased to" means a region showed stronger activation on an event than on its counterpart in a GLM contrast. "Category specific" means this region seems to respond selectively to specific categories.

The inference rules are summarized in Table 4-2. Most of the rules are obvious, except that "motor-related" might need some elaboration. Rules for "motor-related" include:

1. Activations are stronger on the contralateral cerebral hemisphere and the ipsilateral cerebellar hemisphere to the side of motor responses; for example, both A and C responses used the left hand, thus the intersection of the A > B contrast and the C > D contrast should identify motor regions on the right cerebral hemisphere and left cerebellar hemisphere.

2. The intersection of A-B and C-D in SVM analysis, because the only feature of within-category differentiations across category sets is the motor responses (patterns for differentiating left hand and right hand).

3. The intersection of C > D contrasts or D > C contrasts across conditions, because motor representation is more likely to be consistent across conditions than representation of individual categories in RB2 and II. For example, when C > D contrasts in II and RB2 identified a common region, it is not very likely that both the newly formed representations of category C in II and in RB2 happen to be represented in that region, since they are perceptually distinct, and the categorization strategies are different. It cannot be explained by general categorization processes either, because then there would not be a difference between C and D. The most possible explanation is that category C consistently recruits motor planning for pressing the left middle finger.

Table 4-2

Inferred functions and their corresponding rules. Only types that appeared in Table 4-1 are listed.

Function	Rules
General	Intersect of GLM results of sum(A,B,C,D) > 0 in both conditions
Motor-related	Intersect of A > B and C > D; intersect of B > A and D > C; intersect of SVM A-B and C-D; intersect of C > D in condition 1 and 2
Biased to switching	GLM contrasts s21 > s11 and s12 > s22, as well as contrasts between conditions on switch trials
Biased to RB1	GLM s11 > s22 contrasts; intersect A > C and B > D contrasts
Biased to 2D	Intersect of GLM contrasts s22 > s11 from both conditions; intersect of C > A and D > B

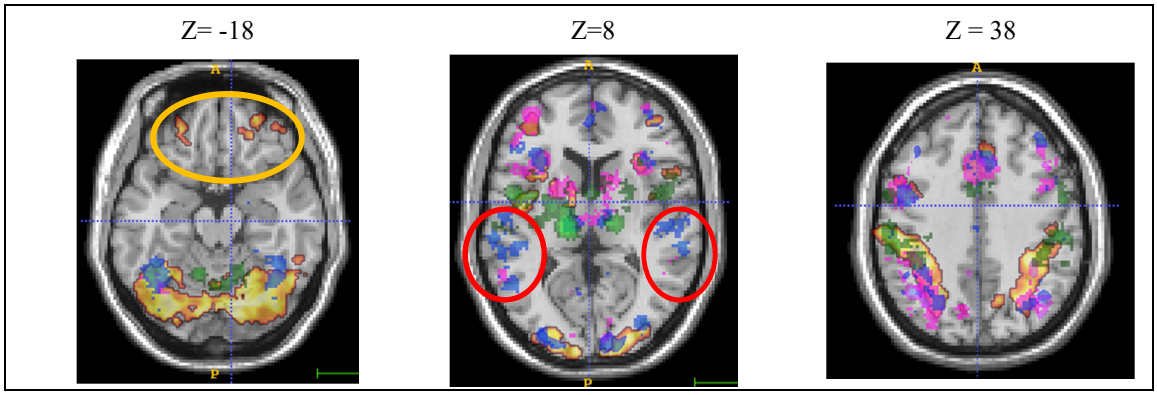
	from both conditions
Task separable	SVM s11-s22
RB2 separable	SVM C-D in condition 2
Category specific	A mixture of multiple contrasts or SVM results. For example, intersect region of SVM C-D, A-C and B-D

Confirmation and support by meta-analysis maps

Meta-analysis maps from Neurosynth were used mainly for confirmation and support. There are two types of maps: uniformity-test maps (u-maps) and association-test maps (a-maps). According to the website (https://neurosynth.org/faq/#q18), z-scores on u-maps show how much a voxel is consistently activated in studies that use a given term, whereas z-scores on a-maps show whether activation in a region occurs more consistently for studies that mention the selected term than not. For comparing my results with previous studies, I consulted the u-maps of "categorization", "switching", and "finger movement" to see how much they were aligned with previous studies of similar topics. As shown in Figure 4-2, most clusters in the results of General overlapped with voxels from at least one of the maps, which indicates that the activation pattern in the current study was highly consistent with similar studies.

Figure 4-2

Data analysis results of General (golden) was highly consistent with u-maps of categorization (blue), switching (pink), and finger movement (green), with just a few non-overlap regions: 1. Frontal orbital lobes (yellow circle) and tails of the caudate (not shown) were only found in the General-activation map. 2. STG and MTG (red circles) were only found in u-maps of categorization and switching, but not in the General-activation map; nonetheless, task-related patterns were found in these regions using GLM contrasts and SVM analysis (see Table 4-1).



In addition, data analysis results were compared with a-maps of finger movement, maintenance, interference, inhibition, attention, and difficulty. The latter five processes are considered elemental for task-switching. Notice that "shifting" and "updating" are also regularly discussed in the task-switching literature but were not included, because their a-maps did not have much overlap with the current results. Regions associated with difficulty are more likely domain general (i.e., not dedicated to a specific type of task), including opIFG, aIns, MFG, PMd, precentral, preSMA, and SPL. Regions associated with attention are likely for visuospatial process, including AnG, FO, Vis, PMd, precentral, PCu, preSMA, STG, and SPL. Regions associated with maintenance might contain the circuits for keeping task sets activated, including opIFG, ICC, MFG, PMd, precentral, preSMA, SPL, cerebellum. Interestingly,

motor-related regions (precentral, PMd, preSMA, and SPL) are found in almost all the selected a-maps. This observation seems to reflect how our brains feature motor preparation when taking actions. All of the associated research topics for each region are listed in the "meta-analysis" column in Table 4-1.

Summarizing results from causal studies

To verify or falsify a theory, scientists have to systematically manipulate factors and collect outcomes in the physical world, and compare the outcomes against what the theory predicts. There are no exceptions for neuroscience. However, while lesions and stimulations can been conducted under proper regulations in animals, mappings from animal brains to human brains are not always clear, not to mention that animals and humans might perform tasks in different ways (for example, see the review by Orban [2016] for a demonstration of this issue in the parietal lobe). Since options for brain stimulation in humans are limited (for example, TMS can only affect brain regions beneath the skull, and DBS can only be used for patients), and there is virtually no way to experimentally conduct brain lesions to humans, examining the dysfunctions in patients who have survived from stroke or head injuries becomes an invaluable source of causal observations in humans. Here, patient studies were used as a major reference for inference, with the supplement of brain stimulation studies in humans, as well as lesion and stimulation studies in animals. Special focus is on motor,

task-switching, inhibition, working memory, decision-making, and Apraxia (especially on tool use) for the literature review.

How might categorization, or more generally, a stimulus-response (S-R) task be carried out in our brains? The literature survey shows that disruptions along the S-R transformation can appear in many qualitatively different ways, which suggests that there are multiple stages in the process. Presumably, information would be extracted from perceptual input. Then, the extracted information would be transformed to a decision (usually motor goal) based on a certain S-R mapping, be it hard-wired or ad hoc (either loaded from memory, or created by real-time computation, or both). Finally, the decision would be implemented into actual movement commands.

Therefore, I separated functions into the following types based on the affected behaviors described in the literature:

- Visual: Basic visual processing in the occipital lobe.
- Motor planning -- command: Stimulation to this region triggers elemental movements.
- Motor planning – somatosensory: somatosensory input has been shown critical for motor performance (Meyer et al., 2014).

- Motor planning -- implementation: Damage to these regions leads to impairments of certain actions, but component motor behavior can still be performed when triggered in other ways.
- Response configuration: Damage to these regions leads to Apraxia, but the capability of performing motor movements remains intact. This category includes action-selection regions and action-planning regions (e.g. the former decide to grab a mug, and the latter plan for the grab).
- Task-related: Damage to this region leads to impairments of S-R tasks, but patients may still be able to perform the action if more cues were provided, which indicates that at least part of the S-R association is still intact but difficult to be tapped.
- Switching: Damage to this region impairs inhibition or initiation of action, but the capability of carrying out the action is largely intact.
- Other: functions other than the above.

The brief descriptions of affected behaviors, references, and types of potential functions are summarized in Table 4-3.

Table 4-3

Inferred roles of brain regions based on causal studies. Notice that no lesion or brain-stimulation studies were found for precuneus. Functions of occipital lobe, precentral gyrus, postcentral gyrus, and PO (where the secondary somatosensory cortex lies) are established and the literature survey for them was skipped.

Region	Affected behavior	Reference	Type

ACC	impaired suppression of reflexive saccades; conflicts monitoring	Paus, 2001; di Pellegrino et al., 2007; Hikosaka & Isoda, 2010	Switching
AnG	Action sequencing; visual neglect; imitation of meaningless gestures; limb-related action recognition and execution; gesture representations; Gerstmann syndrome; appropriate grasp of tools	Bienkiewicz et al, 2014; Mort et al., 2003; Goldenberg and Hagmann, 1996; Rusconi et al., 2010; Randerath et al., 2010	Response configuration
CDh and CDb	Multiple cognitive and motor tasks; inhibition; category learning	Bhatia and Marsden, 1994; Benke et al., 2003; Ell et al, 2010	Switching; task-related
CDt	Visual-motor association, category learning	Yamamoto et al, 2012; Ell et al, 2010	Task-related
opIFG (PMv)	Rehearsal (left), hand selection, inhibition, task-switching; action recognition	Baldo and Dronkers, 2006; Schluter et al., 1998; Aron et al., 2003; Swick et al., 2008; Aron et al., 2004; Tranel et al., 2003; Aron et al., 2014	Switching; task-related
IFG (FO and trIFG)	Rehearsal (left), inhibition; expressive language	Baldo and Dronkers, 2006; Swick et al., 2008; Whitakeret al., 2007	Switching, task-related
aOFC and mOFC	Outcome evaluation	Izquierdo, 2017; Bechara et al., 2000	Switching
lOFC	target-defining visual dimension change; Reward Learning and Decision Making; reversal learning	Pollmann et al., 2007; Izquierdo, 2017; Fettes et al., 2017	Switching
aIns	Amusia, aphasia, Dysphagia, Impaired risk adjustment, speech	Jones et al., 2010	Switching; other
ICC	EDSS, motor coordination	Charil et al., 2003	Motor planning: implementation
MFG	Task-set control; language	Aron et al., 2004, Sierpowska et al.,	Switching;

	switch; ideomotor limb apraxia	2018; Haaland et al., 2000	Response configuration
MTG	Functional knowledge of tools; action recognition	Bienkiewicz et al., 2014; Kalenine et al., 2010	Task-related
Vis	Visual	(skipped)	Visual
PMd	Selection of movements; conditional motor behavior	Schluter et al., 1998; Kurata 1994	Motor planning: implementation
precentral	Motor	(skipped)	Motor planning: command
postcentral	Somatosensory	(skipped)	Motor planning: somatosensory
PCu	N/A	N/A	N/A
PO	Sensorymotor	(skipped)	Motor planning: somatosensory
Put	Multiple cognitive and motor tasks; category learning	Ell et al., 2006; Bhatia and Marsden, 1994;	Task-related
RO	Opercular syndrome; speechless without aphasia	Mariani et al., 1980; Cappa et al, 1987	Other
SMA	motor inhibition; perform learned motor sequence	Sumner et al., 2007; Nachev et al., 2008	Switching; Motor planning: implementation
preSMA	Learning new motor sequence; task switching; inhibition	Nachev et al., 2008; Rushworth et al., 2002	Motor planning: implementation; switching
STG	receptive language; global or local visual processing	Banerjee et al., 2015; Lamb et al., 1990	Task-related
SPL	optic ataxia	Andersen et al., 2014	Motor planning: implementation
SMG	Incorrect demonstration of tool use; phonological processing; apraxia	Bienkiewicz et al., 2014; Baldo and Dronkers, 2006; Bienkiewicz et al., 2014	Response configuration
Cerebellum: VI (ext. CrusI)	Attention; motor; CCAS; Trail making B	Tedesco et al., 2011; Timmann et al., 2008; Stoodley et al., 2016	Motor planning: implementation; switching
Cerebellum:	Multidomain; WCST(Crus II)	Tedesco et al., 2011; Stoodley et al.,	switching

CrusII		2016	
Cerebellum: VIIb, VIIIa, VIIIb	Multidomain; WCST	Tedesco et al., 2011; Stoodley et al., 2016	switching

Candidates of task-set regions

The neural mechanisms of S-R actions are largely a puzzle, and solving the puzzle is not intended here. Rather, the aim is to identify regions that are most likely part of the task set. Following the previous section, I separate stages of performing an S-R task into stimulus processing (visual), S-R transformation (response configuration and task-related), and Response implementation (motor planning). Summarized from Table 4-3, candidate regions of the three stages are:

- Stimulus processing: Vis
- S-R transformation: AnG, SMG, MFG, MTG, STG, IFG, BG (including CD and Put)
- Response implementation: ICC, PMd, precentral, SMA, preSMA, SPL, Cerebellum.

Regions for stimulus processing and response implementation have been intensively studied and less controversial, and their specific functions will not be discussed here. What is worth noting is that, most cue-responding regions belong to this part, which suggest that the use of cue might be mostly for helping motor preparation. A bigger puzzle would be how these regions function during task switching, which will be discussed in Chapter 5.

Lesion to IFG (along with AnG damage) has been reported to cause inappropriate grip of tools (Randerath et al., 2010), and TMS to PMv (which is located in IFG) has been shown to affect grasping (Davare et al., 2006) and movement selection (Schluter et al., 1998). Given that multiple pathways from frontal, temporal, parietal, and occipital lobes are crossing at IFG (Catani, 2019), it is not surprising that this region has also been found in more complex behavior, such as expressive language. It has also been suggested to activate posterior regions in working memory tasks (Baldo and Dronkers, 2006), which might be an elemental feature for performing rule-based categorization. Notice that IFG is heterogeneous in terms of neuroanatomy, with different sub-regions being found to respond to different types of tasks. Lesions to IFG were typically extensive, making it difficult to attribute specific functions to its sub-regions. Brain-imaging techniques and intraoperative stimulations have been used to pinpoint sub-regions for specific functions, but detailed discussion is beyond the scope of this chapter. For the purpose of the current study, IFG as a whole is considered part of the task set.

Notice that while IFG has been shown to be critical for language, it does not necessarily imply that rule-based categorization requires internal language. Rather, considering information from multiple pathways converge on and are possibly manipulated in IFG, aphasia caused by IFG lesion should be viewed as a demonstration of the importance of multi-circuit coordination for fluent speech.

Data analysis has found category-specific activations in STG, MTG, and SMG. Interestingly, activations were also observed in MTG and SMG (extended to AnG) when receiving negative feedback in both conditions. It could be an indication of updating action decisions or associated outcomes. MTG and SMG were not found in a-maps of attention and difficulty, which suggest that their functions are less likely visuospatial or domain-general. STG is connected with occipital, parietal, temporal and frontal lobes. Similar to IFG, this complicates its involvement in multiple types of functions.

STG and MTG have been associated with action semantics (Johnson-Frey, 2004; Bienkiewicz et al., 2014). Damages to these regions may impair action recognition, and lead to agnosia and receptive aphasia, but patients may still be able to manipulate tools, which might indicate that the S-R association was still intact (Johnson-Frey, 2004). Particularly, it has been reported that an Agnosic patient with bilateral temporal lobe lesions had considerable difficulty in identifying the functions of tools or the contexts for their use, but was capable of manipulating these items skillfully (Sirigu et al., 1991). However, patients with STG and MTG lesions were impaired in WCST and relational reasoning (Baldo et al., 2010), which suggest that STG and MTG might be elemental for rule-based decisions. Activation found in MTG while receiving negative feedback also supports its role in declarative reasoning.

Unlike STG and MTG, lesions to SMG impair the capability of retrieving motor skills (Johnson-Frey, 2004; Bienkiewicz et al., 2014). At least for automatized skills, SMG seems to be where the S-R association stores or where the integration takes place. This is supported by observation with cell-recording in monkeys that IPS neurons selectively respond to categories but not specific motor movements (Freedman and Assad, 2016). For the correct S-R association to be fixated, SMG would have to receive the action-outcome updates at the learning stage when the skill has not been automatized. Indeed, activation on negative feedback was observed in SMG; this observation is also consistent with previous findings (O'Connor et al., 2010).

However, SMG may not connect with occipital lobe directly (Burks et al., 2016). The input information is probably passed to SMG via AnG and STG, and the two pathways seem to function differently. AnG damage can lead to correct use but wrong grip of tools, which suggests that part of the S-R association is preserved – in the case of tool use, the S-R transformation might have relied solely on the knowledge of tools provided by STG when AnG is absent. A similar dissociation between S-R association and the precise motor plan was also observed in the current study: most of the "wrong key" responses were wrong choices of index versus middle fingers, but the decisions for left versus right were correct (see section "Sources of interference" in Chapter 3 for details).

As aforementioned, the ability of tool use could still be intact when damage is limited to the temporal lobes. Therefore, the information provided by AnG seems to be more direct for the S-R association of learned skills. Unlike the purely visual role of the occipital lobes, AnG also plays an important role in processing of body representation. It has connections with sensory cortex and SPL (Burks et al., 2016), and lesions to it lead to multiple types of motor impairments (see Table 4-3 for examples). Therefore, S-R transformation may require intimate coordination between AnG and SMG.

MFG and IFG have been found to connect with SMG (Burk et al., 2016; Miller et al., 2015), and thus may be the source of a top-down influence on SMG. MFG has been associated with action recognition and task-set control; intraoperative stimulation to MFG can induce language switch (see Table 4-3). MFG (along with FO) was also observed to respond to cues, which were present before the specific category could be determined. As discussed earlier, brain activations on cues seem to be for motor preparation. These all indicate that MFG is more likely involved in top-down action control than implementing S-R transformation per se.

BG has been associated with category learning. Particularly, it has been suggested that the S-R association is formed in the striatum at the learning stage for II categorization. The focus of the task set here, however, is on learned S-R transformation, which might have been transferred to cortical regions. Nonetheless, BG would still be part of the task set, for any S-R

transformation must pass through the striatum. Indeed, Lesions to different parts of basal ganglia impair a diverse range of cognitive and motor processing (Bhatia and Marsden, 1994), and stimulation to CDt has been shown to affect categorical motor decisions in animals (Yamamoto et al, 2012).

Notably, none of the S-R transformation regions except for MFG and FO responded to cues, which indicates that their involvements are more likely for implementing specific S-R transformation than for motor preparation.

Conclusion

In this chapter, several candidate task-set regions were identified. In summary, the inferred scheme assumes that a task set contains three parts: stimulus processing, S-R transformation, and response implementation. Stimulus (cue or target) would firstly be processed by the occipital lobes. When cue is perceived, many response-implementation regions would be activated, perhaps with the top-down mediation by MFG. When target stimulus is perceived, the S-R transformation process would be activated for making the specific action decision.

The S-R transformation network includes IFG, MFG, MTG, STG, SMG, AnG, and BG. Except for MFG, these regions only activated to targets. IFG might play a role in activating

relevant circuits for manipulating conceptual information, which may be held in MTG and STG. The IFG-temporal pathway might be for rule-based categorization. Non-rule-based (e.g. procedural or automatized) categorization might depend on SMG and AnG, although for both rule-based and non-rule-based tasks, response decision would be sent to SMG, which might receive top-down influence from PMv (part of opIFG) and MFG for creating motor plans. If this scheme is correct, MTG/STG and SMG would have to receive outcomes of actions; and indeed, feedback-related activations were observed in MTG and SMG. Lastly, all of the cortical activations would be mediated by BG.

The view that PFC manipulates information in the posterior lobes, instead of holding the information in itself, is in line with observations in brain-injury patients (Baldo and Dronkers, 2006) and recent MVPA findings of working memory (Sreenivasan et al., 2014). Importantly, this inference is a result of convergence from two exploratory methods without presumptions: by summarizing neuropsychological observations, as well as whole-brain SVM searchlight analysis in this study (namely, the category-specific activations were found in parietal and temporal lobes, but not the frontal lobes). For identifying category-specific activations, MVPA (including SVM classification) is advantageous over GLM contrasts for two reasons: 1. if the difference between categories is not in the form of relative strength, but the activity pattern, there is no way for contrasts to identify it. 2. Due to individual differences, the

category-specific voxels might be small in number and widely distributed, and therefore difficult to identify during group analysis. On the contrary, MVPA would detect the difference if those voxels are covered by a bigger sphere, and there is higher chance to find an intersection of spheres from individuals.

In this chapter, several brain regions have been suggested as task set regions. How might they take part in task switching? One possibility is that they receive request of updates and take actions accordingly. The other possibility is that task sets of each unit task also recruit the same control systems as task switching, and thus contains overlapping regions. For example, even a single categorization task requires participants to switch between responses, and thus response-switch mechanism will be involved. As what will be revealed in next chapter, the former seems more likely.

As reasoned in Chapter 1, even task-set regions can show switch-related activations, which is exactly what was found in this chapter (e.g. MFG, SPL, IPL, and cerebellum). When evidence from causal studies suggests that a region may have a basic function, such as SPL for sensory-motor processing, it might be better to consider this region being part of the task sets but not part of the switch-control systems. Next chapter will provide in-depth discussions on this topic.

Chapter 5. Task Switching and Executive Control

One of the most important goals of task switching studies is to reveal the key mechanisms of executive control that carry out cognitive flexibility. For our brains to flexibly switch among tasks and thoughts, multiple task sets have to be ready for selection and manipulation (i.e. task-set activation, can be top-down, bottom-up, or both), while their mutual interference has to be managed. Besides, interference can be overcome positively by enhancing the relevant task set, or negatively by inhibiting irrelevant task sets. To simplify the discussion, excitatory (positive) interference control is considered part of the task-set activation, and only the top-down influence is discussed in this chapter. In brief, this chapter focuses on the top-down influence of task set activation and inhibition.

Based on the more inclusive definition of task set that covers the whole neural network for carrying out a simple task (e.g. categorization), it may contain regions that exert top-down influence to the configuration of perceptual processing, S-R transformation, and motor planning. Obviously, these "influencer" regions can also be classified as part of the executive control circuits. This is especially true under experimental contexts, where virtually all the measured behavioral data are generated while participants are executing what they have been instructed. Note that some researchers (e.g. Dosenbach et al., 2006) confine the scope of the task-set unit to the component that carries out executive processes, which is similar to the

"influencers" mentioned above. Then, the first question would be whether or not task switching requires additional executive control from regions other than the influencers of the underlying task sets. An example of the negative view is the model of Altmann and Gray (2008), which assumes that task switching requires no additional processes other than normal memory retrieval, whereas all of the other models in Table 1-1 postulate a mechanism that is aware of and responds to the switching need.

The inhibitory control problem asks how the task sets may be interfered and how the interference may be inhibited. It can be separated into cognitive inhibition (of irrelevant thoughts), perceptual inhibition (of irrelevant features), and response inhibition (of competing responses) (e.g. Richter & Yeung, 2014; Diamond, 2013). Inhibitory control may involve local inhibitory circuits (Tremblay et al., 2016; Markram et al., 2004) as well as long-range inhibitory circuits such as the hyperdirect pathway (Aron et al., 2016) and direct striatal-cortical projections (Saunders et al., 2015). However, evidence shows that LFP largely reflect activities of inhibitory circuits (Teleńczuk et al., 2016; Buzsáki et al., 2012; Trevelyan, 2009), which are important for normal functioning as well as computations (Isaacson & Scanziani, 2011; Buzsáki, 2010). What further complicates the issue is that even long-range excitatory projections can exert inhibitory effects byactivating local inhibitory circuits (e.g. Jackson et al., 2018). Therefore, there may not be a reliable analytical method that can untangle

local excitatory and inhibitory induced BOLD changes (see also Herreras, 2016; although it is claimed that DCM has taken the excitatory-inhibitory balance into consideration; see Friston et al., 2015). Therefore, the current study does not try to identify the cortical-cortical inhibitory control. Rather, it focuses on a well-recognized inhibitory control system -- the hyperdirect pathway, and tries to reveal features of inhibitory control by observing switch-related BOLD patterns along this pathway.

In search of the switch control circuit

The idea that a unit selects which task to perform, and thus is separate from the unit that performs the task (i.e. the task set), is in retrospection, challengeable. However, to verify or falsify this basic assumption by searching for the switch-specific regions in a multitasking brain is no easy job. As discussed in Chapter 3, the existence of mixing costs suggests that there is some persisting influence on both switch and stay trials in multitask contexts. Then it would not be surprising if the same is observed in the brain, i.e. switch-specific activations sustain even on stay trials. Indeed, Ruge et al. (2013) reviewed dozens of fMRI studies and only found one study with special design that reported switch-related preparatory BOLD activation in precuneus (labeled as “medial SPL” in the original article). Similarly, Table 4-1

showed that most of the activated regions were responsive to all types of trials, with the only exceptions of STG and MTG, both of which showed category-specific activations.

There are several possible explanations for the lack of localization selectivity for switch trials. First, with the requirement of quick alternating tasks, it is unrealistic for our brains to eliminate recently activated synaptic activity from a previously irrelevant task before carrying out a newtask. The residual activity from preceding trials has been observed in some fMRI studies (e.g. Shi et al., 2014; Wylie et al., 2006; Yeung et al., 2006), and multiple physiological mechanisms have been found to lead to changes of excitability of neurons that last after the original stimulus has been removed, and heightened attention may pose similar triggering factors (Zylberberg & Strowbridge, 2017). The lingering activations can be viewed as the physiological realization of task-set inertia. This hypothesis predicts that the activated regions are overlaps of underlying task-set regions.

Second, the switch-control circuit, assuming that it is not part of the task-set network, may have to stay active throughout the multitask context for detecting the switch needs. Findings of non-task-set regions that are activated in task switching would support this hypothesis. For example, Braver et al. (2003) compared BOLD patterns of multitask and single-task blocks, and found that ACC showed sustained activation in multitask blocks. Importantly, those activations were not switch-trial specific.

Third, even cognitive tasks that are not designed for examining task switching may trigger task-switching mechanisms; especially in fMRI experiments where alternating events may contain intrinsic task-switching features. The fact that ACC is also regularly reported in various single-task fMRI studies supports this hypothesis (e.g. Dosenbach et al., 2006; see also Table 5-1 below). Supporting evidence for the second hypothesis would also support this one, with a major difference: the third hypothesis predicts that these regions would also be found in pure-task experiments.

The forth possibility is that there is a common executive control system that controls each and every consciously monitored action. This hypothesis only holds when there are regions that are consistently reported in all of the cognitive studies, which is not likely the case.

In summary, this section starts from looking for non-task-set regions that were activated in the fMRI sessions. If the switch-control circuit exists, there are two possible time points for it to exert the executive influence: when the cue or the target is presented. For each possibility, the executive influence may act just on switch trials, or on both switch and stay trials. This section examines these possibilities.

Preparatory activities during the cue interval

In this study, multiple regions were found to be active to both the cues and the crosshairs, including precentral gyrus, postcentral gyrus, FO, SPL, SMG, PMd, SMA, and cerebellar

lobule VI (see Table 4-1). Since the crosshairs did not have any predictive value, these activations are more likely to reflect general alertness. In addition, MFG (BA 9) was found to respond to cues in the RB-II condition. These findings are consistent with Brass and von Cramon (2002), who conducted an fMRI study that compared three types of trials: cue plus target, target only, and cue only. They found that precentral gyrus, SMA, FO, MFG, SPL, AnG, PCu and MTG showed stronger activations to cues relative to baseline – only PCu and MTG were not found here. Note that in the study of Brass and von Cramon (2002), both the stimuli and responses were bivalent, which means no specific response set or perceptual biasing can be prepared in advance when receiving a cue. In other words, activations in these regions can only reflect general alertness or preparation for task rules. According to the a-map of attention created by Neurosynth, most of these regions, except for MTG, are regularly reported in attention studies (see Table 4-1). Unlike the current study, Brass and von Cramon (2002) required relevant task rules to be determined during the cue interval but not the target interval, which might explain their particular finding of MTG activations to cues.

Note that among these regions, only SMA was found to be activated by cues and crosshairs but not target stimuli, which might indicate that SMA is recruited for general rather than specific motor preparation. Besides, BA 9 was only found to be activated by the cues in the RB-II condition but not in the RB-RB condition. In other words, the early task preparation

processes in BA 9 were absent in the condition that only contained rule-based trials. Another candidate of executive control is FO, because it is not associated with any particular motor or perceptual functions, nor does it seem to be the storage of S-R mappings. All other regions are related to motor planning (see discussions in Chapter 4). Note that all of these regions were also found to be activated during motor imagination in a meta-analysis of 75 studies (Hétu et al., 2013), which supports their involvement in the preparation of response sets rather than of category sets.

As discussed in Chapter 3, the presence of preceding cues seems to facilitate task preparation for both switch or stay trials, and the results showed stronger evidence for response-set preparation during the cue interval. Consistent with this finding, fMRI contrasts of cue greater than crosshair found SMG and SPL (both are response-set regions) for both conditions. In addition, direct contrasting activations to cues of stay and switch trials did not find any significant results, which does not support a switch-specific beneficial effect. In fact, it is not uncommon for task-switching studies to report null results when contrasting switch and stay trials (Ruge et al., 2013). Therefore, the observations of switch-stay activation difference during cue interval in some studies may be design-specific. At least in the current study, cues appear to benefit response-set preparation for both switch and stay trials, and both

the cues and the crosshairs appear to induce early activations in response-set regions for general alertness.

During processing target stimulus

As briefly mentioned earlier, many of the brain areas reported in task-switching studies are also regularly reported in other tasks. For a specific example, IFJ, SPL, Ins, pre-SMA, IFC, and BA10 are often reported in task-switching studies as well as in studies of memory retrieval (Richter & Yeung, 2014). While the current study did not contain single-task blocks in the fMRI sessions, regions reported in single-task categorization studies that used gabor stimuli were compared with current findings and organized in Table 5-1.

Table 5-1

Comparing Table 4-1 with results from single-task categorization studies with gabor stimuli.

Region	Data analysis (on Target)	Categorization studies
ACC	General; Task-separable	II: Waldschmidt and Ashby, 2011; RB: Helie et al., 2010; Kahnt et al., 2011
AnG	General; Task-separable	N/A
CDh and CDb	General, biased to switch	II: Waldschmidt and Ashby, 2011; II and RB: Nomura et al., 2007
CDt	General	N/A
FO	General	II: Waldschmidt and Ashby, 2011
trIFG	General; Biased to RB1	
orIFG (BA 47)	General	II: Waldschmidt and Ashby, 2011
opIFG (PMv)	General; task-separable	RB: Helie et al., 2010; II: Waldschmidt and Ashby, 2011
OFC	General; task-separable	N/A
aIns (ext. orIFG)	General; biased to switch	RB: Helie et al., 2010; II: Waldschmidt and Ashby, 2011

ICC	General	RB: Helie et al., 2010; II: Waldschmidt and Ashby, 2011
MFG (BA9, BA10)	General; biased to 2D stimuli	RB: Helie et al., 2010; II: Waldschmidt and Ashby, 2011
MTG	Category specific	N/A
Vis	General, biased to RB1 or 2D (different divisions)	RB: Helie et al., 2010; II: Waldschmidt and Ashby, 2011
PMd	General, biased to switch	RB: Nomura et al., 2007
Precentral	General	RB: Helie et al., 2010; II: Waldschmidt and Ashby, 2011
Postcentral	General	II: Waldschmidt and Ashby, 2011
PCu	Biased to 2D stimuli and switch	II: Waldschmidt and Ashby, 2011; RB: Nomura et al., 2007
PO	General, biased to switch; motor related	N/A
Put	General	RB: Helie et al., 2010
RO	General; motor related	N/A
preSMA (ext. mSFG)	General; task-separable; biased to switch	II: Waldschmidt and Ashby, 2011; RB: Nomura et al., 2007
STG	Category specific (RB-II condition), biased to RB1 (RB-RB condition)	RB: Nomura et al., 2007
SPL (ext. SMG)	General; biased to switch; motor related	RB: Helie et al., 2010; Kahnt et al., 2011
SMG	General; Category specific	II: Waldschmidt and Ashby, 2011; RB: Nomura et al., 2007
Cerebellum: V	Biased to the RB-RB condition; motor related	RB: Helie et al., 2010; II: Waldschmidt and Ashby, 2011
Cerebellum: VI, CrusI	General; biased to 2D; motor related (VI)	RB: Helie et al., 2010
Cerebellum: CrusII	General; biased to 2D	N/A
Cerebellum: VIIb, VIIIa, VIIIb	General; motor related (VIIIa, VIIIb)	N/A

As the table shows, there is much overlap between Table 4-1 and the results from the selected single-task categorization studies. There are at least two possible explanations. First,

when our brains carry out tasks on a trial by trial basis, it may adopt similar techniques as during task switching; namely, enhance activation for the current task and/or inhibit irrelevant effects (from competing task sets or other distractions). This hypothesis predicts that regions known to be involved in task switching in lesion studies would also be active in single-task studies. Activations in ACC, CD, FO, IFC, Ins, MFG, and preSMA satisfied this prediction. Particularly, ACC was not task-related (see Table 4-1), which further supports this hypothesis.

The second explanation is that those regions are part of the task sets (e.g. for motor reaction or memory retrieval), and switch-related BOLD changes in these regions reflect the update of task sets or the fMRI adaptation effect. fMRI adaptation is the observation that BOLD activation decreases as the same group of underlying neurons are repetitively stimulated (Grill-Spector et al., 2006). Note that this effect is particularly applicable when a region is activated on all types of trials, because it allows "relatively stronger activation on switch trials" to be interchangeable with "relatively weaker activation on stay trials". fMRI adaptation may be the most straightforward explanation for motor-related regions in the current study, since some of the stay trials used the same fingers and may lead to fMRI adaptation, but the switch trials never did.

The second hypothesis predicts that regions with switch-related BOLD changes (including regions identified with MVPA) would also be active in single-task blocks. In the

current study, these include CD, Ins, PMd, PCu, preSMA, SPL, IPL, BA 9. Among them, only PMd, SPL and PCu are accordant with this prediction but not the previous one. Again, PMd and SPL are part of the response set, and fMRI adaptation may be sufficient to explain the lower activation on stay trials in these regions.

Among the regions that were not reported in the selected studies, only PO showed stronger activations on switch trials. RO, CDt, and OFC were activated on all types of trials; AnG was found to be task separable by MVPA; and MTG showed category-specific activations. As discussed in Chapter 4, MTG is more likely to be recruited for processing concepts of categories; PO and RO are recognized to be involved in somatosensory processing and motor planning, respectively; and AnG is associated with S-R transformation. These regions are more likely to be influenced by, rather than exerting the switch control. Note that fMRI studies typically report peak regions and results of research interests but not a full list of activations, thus it is also possible that these unreported regions were also activated but not reported in the selected studies.

Similar to previous task-switching studies, OFC did not appear in fMRI contrasts here. Rather, it was found to be activated on both switch and stay trials of all categories. This region was not reported in single-task categorization tasks, and I am not aware of any lesion studies that reported OFC to cause impairment to learned knowledge or skills. Besides, OFC lesioned

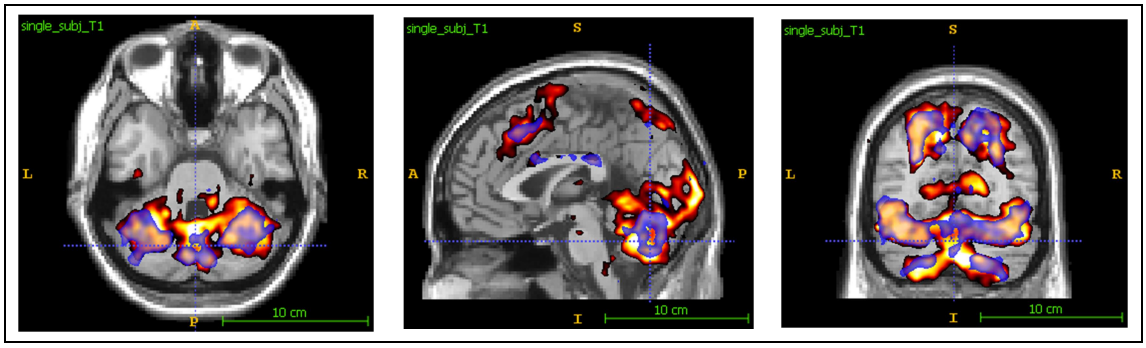
patients did not seem to be impaired in inhibitory control (Swick et al., 2008). Furthermore, lesion studies suggested that this region is related to behavioral flexibility, such as reversal learning (Izquierdo, 2017) and the reallocation of attentional resources (Pollmann et al., 2007) according to changing demands (see also Stalnaker et al., 2015). In short, this region may be related to monitoring context changes, but its specific function is relatively unclear.

Until recently, not many cognitive studies have focused on cerebellar regions, thus it is not surprising that there are verly little discussions about its functions in categorization. An exception is the work by Ell and Ivry (2008), who looked at RB and II in cerebellar patients and found no impairment on either task. Nonetheless, Crus I, Crus II, and lobules VII-VIII have been reported to cause cognitive impairments without cerebellar motor syndrome (Stoodley et al., 2016). Particularly, Crus II and VIIb were found to be less active on switch trials in the RB-RB condition. In the cerebellum, weaker activations may reflect that inputs to these regions are less synchronized (Buzsáki et al., 2012); and on the switch trials, this may be explained by that the input of the current trial differed from the previous trial. In general, contrast analysis found that activations in most of the cerebellar regions were more evident and extensive in the RB-RB condition than in the RB-II condition (Figure 5-1). The more extensive activation in cerebellum also indicates a stronger load for switching between two rule-based tasks than between RB and II tasks. Notably, CrusI and CrusII were activated stronger to 2D (II

and RB) categories. This finding is consistent with Turner et al. (2017), which reported that CrusI and CrusII were activated on II stay trials. This may be because 2D stimuli require simultaneous processing of two features (orientation and spatial frequency) so that more information is sent to the cerebellum. However, the null results in Ell and Ivry (2008) suggests that the cerebellum may work like a co-processor of the cerebrum (see also D'Angelo & Casali, 2013 for discussions).

Figure 5-1

Activated brain regions to all types of trials (blueish: the RB-II condition; golden: the RB-RB condition). The threshold is t value greater than 5.



Tail of the caudate (CDt) has been rarely reported mainly due to segmentation issues: it is small and close to the putamen. In the current study, activations were determined to be located in CDt, because they extended to the caudate body but not the putamen. This region has been associated with visual-motor association and category learning (Yamamoto et al, 2012; Ell et al., 2010; Nomura & Reber, 2008). The heavy connectivity between CDt and extrastriate visual cortex also strongly implicates its involvement in S-R transformations (Seger, 2013).

PCu and ICC are not be discussed here for the following reasons. First, these regions have been found to have higher false alarm rates than other regions in fMRI GLM analysis (Eklund et al., 2016). Second, virtually no studies have reported cognitive impairments caused by lesions in PCu, thus any inference about its function would be too speculative. Third, ICC only contains crossing axons but not neurons.

In summary, fMRI data revealed a potential large-scale network (including ACC, CD, FO, IFG, Ins, MFG) that exerts top-down control. This network appears to be also active in single-task categorization as well as a broad range of cognitive tasks (see the "meta-analysis" column in Table 4-1 for examples). In addition, OFC may be particularly involved in monitoring the switch needs. Switch-related BOLD changes in the rest of the regions may reflect updates of task sets or the fMRI adaptation effect rather than exerting executive control, because their functions in motor configuration (PMd, preSMA, SPL) and S-R transformation (CDt and AnG) are relatively clear. The following section investigates how this network behaves on switch trials.

Between-system switch vs. Within-system switch

The previous section leads to two preliminary conclusions: first, a large-scale control network of ACC, CD, FO, IFC, Ins, and MFG seems to be active in both single-task and

multitask contexts; second, OFC may be active for monitoring the switch needs in multitask contexts. This section further considers how the network might work differently for the two conditions by comparing the fMRI contrast results.

As listed in Table 5-2 and Table 5-4, switching between two RB tasks appears to recruit more conscious processing (ACC, MFG, FO, Ins, VIIb, CrusII), semantic processing (MTG and IFG), and motor planning (MFG, preSMA, SMG, AnG, Put, RO, PO, PMd, SPL, I-IV, V, VIIIb) than switching between RB and II tasks. Particularly, cerebellar regions I to IV were found to be only activated in the RB-RB condition but not in the RB-II condition, and these regions are known to be recruited in motor planning (Guell et al., 2018; Stoodley et al., 2016; Timmann et al., 2008). In other words, switching between two RB tasks seems to require more closely monitored motor planning.

Besides, BOLD responses in MFG, VIIb, and CrusII on switch trials were weaker than on stay trials in the RB-RB condition, but no such differences were found in the RB-II condition. The finding of weaker activations in VIIb and CrusII on RB2 switch trials is consistent with the assumption that switch costs toRB2 were higher than II. As mentioned earlier, relatively weaker BOLD responses in a cerebellar region on switch trials may occur because the input to this region is weaker or less synchronized. To examine which explanation is more plausible, a DCM analysis of BA 46 projects to CrusII was conducted, since anatomical studies in monkeys

reported that CrusII is strongly connected with area 46d (e.g. Kelly & Strick; 2003). The results showed that the influence from BA 46 to CrusII was enhanced rather than decreased on switch trials, which supports the assumption that the decreased activations in CrusII reflect the desynchronization (but not decrease) of input. The desynchronization may be due to the fact that the input on the current trial to CrusII was largely different from that of the previous trial.

On the other hand, relatively decreased BOLD in a region on stay trials may reflect the fMRI adaptation effect. These regions include SMG, SPL, BA6, precentral gyrus, SMG, VI, PCu and ICC. Note that all of these regions, except for PCu, are motor-related.

Table 5-2

Regions that showed stronger activations in the RB-RB condition than in the RB-II condition.

Events	Implication	Regions
S21	RB2 task inertia; RB2 to RB1 switch control	V, RO, ACC, BA6, precentral
S12	RB1 to RB2 switch control	V, BA6, preSMA
S11	RB2 task inertia	V, BA6, BA40 (SMG), Put
S22	RB1 task inertia; RB2 task set	VIIIb, I-IV, V, AnG, SPL, BA6
C22	RB2 task preparation (manage RB1)	Ins
C12	RB2 task preparation (manage RB1), switch control	SMG

Table 5-3

Regions that show up in contrast analysis in the RB-II condition but not in the RB-RB condition.

fMRI contrasts	Implication	Findings
A > B and C > D / B > A and D > C	Left/right hand	VIIIa
C > A and D > B	II task set	BA46, BA10, OrIFG, SMG
S21 > s11	RB1 switch; II inertia	Precentral
S12 > s22	II switch; RB1 inertia	VI, ICC

Table 5-4

Regions identified in contrast analysis in the RB-RB condition but not in the RB-II condition.

fMRI contrasts	Implication	Findings
A > B and C > D / B > A and D > C	Left/Right hand	PO, VIIIb
A > C and B > D	RB1 task set	BA10, MTG, TrIFG
C > A and D > B	RB2 task set	PCu, BA9, SPL
S21 > s11	RB1 switch; RB2 inertia	SMG, SPL
S12 > s22	RB2 switch; RB1 inertia	BA6, precentral, SMG
S11 > s21	RB1 task set	MFG
S22 > s12	RB2 task set	VIIb, CrusII, MFG

Activities modulated by switch

This section tries to identify switch-modulated activities with two foci: 1. the interaction of OFC and cortical regions; 2. the interaction of the cortical regions and the STN (i.e. activities along the hyperdirect pathway).

As mentioned in Chapter 1, many computational task-switching models do not have inhibitory components, with the assumption that interference is overcome by enhancing relevant activations. Some researchers argued that the selective interference control from PFC is mainly through enhancing relevant down-stream task sets, and against the role of hyperdirect pathway on cognitive processes (e.g. Munakata et al., 2011). However, evidence showed that the capability of top-down inhibition is deteriorated more severely than top-down enhancement with normal aging (Gazzaley & D'Esposito, 2007; Gazzaley et al., 2008), which

appears to be against the prediction that they should be affected equally if interference control is carried out simply in the form of top-down enhancement.

If the activities along the hyperdirect pathway are found to change according to the switch needs, it would be reasonable to consider the possibility of selective interference control by inhibitory mechanisms, as well as the involvement of the hyperdirect pathway in cognitive functions. However, STN is very small and heavily involved in motor control (Accolla et al., 2014), which may seriously contaminate measured responses that are related to cognitive functions, such as switch control. This may explain why most of the evidence of STN in inhibitory control is from studies in the response domain (e.g. see Aron et al., 2016 for a review), in which the exertion of executive control is expressed and measured as a form of response inhibition, but not studies of inhibitory control on thoughts or perceptual attention when responses are still conducted. Nonetheless, some researchers have tried to identify STN's involvement in cognitive function by analyzing its coactivation patterns with specific network, such as language processing (Manes et al., 2014). In the current study, no event-specific BOLD changes were detected in STN, and DCM analysis was used to reveal its involvement in task switching.

Hyperdirect pathway: cortical regions to STN

The first DCM model is shown in Figure 5-2. IFG, ACC, and preSMA are known to project to STN, and they have all been implicated in inhibitory control (see Table 4-3). OFC is assumed to exert its influence on each of the cortical regions. The results are shown in Table 5-5.

First, all the functional connections were significant. Most of the strengths were positive, except for in the RB-RB condition, activity of OFC appeared to have an adverse relationship with IFG activations, and its influence to ACC was very small. Second, the influence of ACC to STN did not seem to be affected by the switch need, but ACC to preSMA did. Assuming that ACC detects the conflict on switch trials and manages it by outward projections, as often suggested (e.g. Kerns et al., 2004; Bissonettea et al., 2013), the switch-specific interference-control by ACC may not be through STN. Instead, the ACC-preSMA connection may be a better candidate for supporting this assumption, whereas the ACC-STN connection may exert interference control for anti-automation (Hikosaka & Isoda, 2010; Paus, 2001). Third, the top-down influences of IFG and preSMA to STN were affected by the switch needs. This finding suggests that STN received different input patterns across switch and stay trials. However, since switch trials always require motor changes whereas stay trials do not, this observation may still reflect its involvement in motor control. Fourth, the switch modulation

effect on outward influences of IFG is not consistent (e.g. in the RB-II condition, IFG to preSMA was decreased but IFG to STN was increased on switch trials), which suggests that the decrease of influence is unlikely to be caused by the overall inhibition to IFG. Lastly, one might expect to find consistent patterns across conditions if the hyperdirect pathway only works for controlling the motor output. However, switch modulation effects on multiple connections showed the opposite patterns across the two conditions.

It is worth noting that it has been reported that the category-response mapping can be re-assigned more swiftly in RB tasks than in II tasks (Maddox et al., 2010). This might indicate that the brain more actively controls the category-response mapping with declarative systems for RB tasks. The influence of OFC to preSMA was much stronger in the RB-RB condition than in the RB-II condition, which may indicate higher level of conscious monitoring on motor planning when the session contains only rule-based tasks. Besides, the increased influence from IFG and OFC to preSMA on switch trials in the RB-RB condition also supports this hypothesis.

Could the performance of task switching be explained solely by the involvement of OFC detecting and handling the switch need? As shown in Table 5-5, the influence of OFC to ACC was not modulated by switch in the RB-II condition, and the influence was generally small in

the RB-RB condition. Even so, the influence of ACC to preSMA was modulated by switch, which implies that the modulation effect may not be from OFC.

Figure 5-2

The cortex-to-STN model. OFC, IFG, pre-SMA and ACC are assumed to be driven by target stimuli.

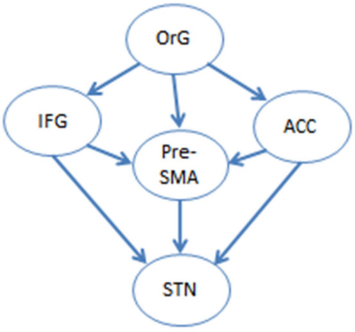


Table 5-5

The mean values of fixed connection strength and modulation effect of the first DCM model. Negative values are in gray. "n.s." means "not significant".

Functional Connection	Strength		Switching Modulation effect	
	RB-II	RB-RB	RB-II	RB-RB
OFC to IFG	0.2181	-0.3248	-0.0567	0.0885
OFC to ACC	0.1544	-0.0066	n.s.	-0.1206
OFC to preSMA	0.0325	0.1940	0.0358	0.0820
IFG to preSMA	0.2499	0.3733	-0.2724	0.0190
ACC to preSMA	0.3422	0.2180	0.2107	-0.1027
IFG to STN	0.0590	0.0436	0.0994	-0.0396
ACC to STN	0.1092	0.0778	n.s.	n.s.
Pre-SMA to STN	0.1188	0.1914	-0.1514	0.0283

Hyperdirect pathway: STN to cortical regions

The second DCM model is shown in Figure 5-3. This model tests whether the activity of STN influences the aforementioned task-set related cortical regions (BA 9, IFG, and BA 46).

preSMA is also included to show its influence on motor planning. The results are shown in Table 5-6.

The influence from STN to cortical regions, presumably through enhancing the inhibitory projections from GPi to thalamus and breaking the cortical-thalamic loop, was expected to reduce the cortical activations (i.e. be negative). However, the results showed that all of the functional connections were positive and significant. Since DCM only considers the relations of the time series of the selected regions, a possible explanation is that the influence of STN on other regions indirectly facilitated the selected cortical regions.

More importantly, the results showed that the influence of STN on multiple cortical regions was modulated by switch, and the patterns were, again, different across conditions. If these relations were not merely by coincidence, the results suggest that some inhibitory control through hyperdirect pathway may be adjusted by switch and passed to the cortical executive-control regions.

Figure 5-3

Figure 5-3. The STN-to-cortex model. All of the nodes are assumed to be driven by target stimuli.

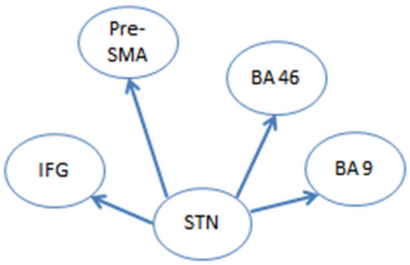


Table 5-6

The mean values of fixed connection strength and modulation effect of the second DCM model. Negative values are in red. "n.s." means "not significant".

Functional Connection	Strength		Switching Modulation effect	
	RB-II	RB-RB	RB-II	RB-RB
STN to preSMA	0.1438	0.1964	n.s.	0.0506
STN to IFG	0.0858	0.1437	n.s.	-0.0482
STN to BA 9	0.0744	0.1555	-0.1036	0.1672
STN to BA 46	0.1148	0.1435	0.0635	0.0467

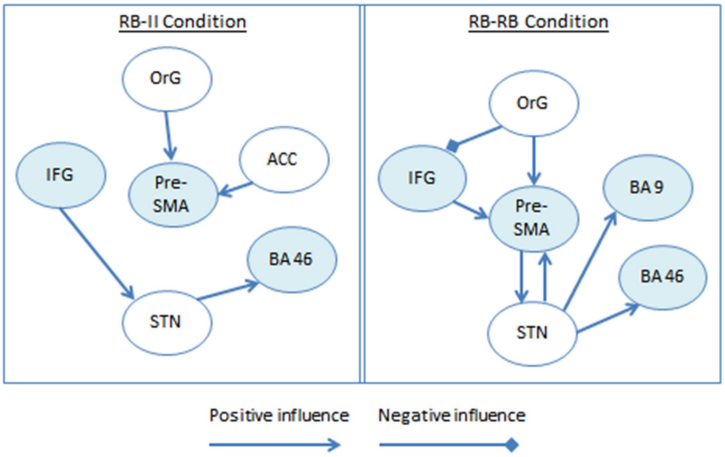
Putting them together

To illustrate the difference of switch modulation effects across conditions, functional connections enhanced on switch trials from the two DCM models are shown in Figure 5-4. Note that IFG, MFG (BA 9 and 46) and pre-SMA are task-related, which means that lesions to these regions would disrupt the underlying task sets. The task-related regions may initiate the updates of the task sets, whereas ACC is more likely to be a conflict detector and reacts for resolving the conflicts (Hikosaka et al., 2010). Pre-SMA is the final stop in PFC for motor planning, and the enhanced IFG influence to pre-SMA in the RB-RB condition may reflect pre-SMA receiving updates of reasoning results from IFG, whereas the enhanced ACC influence to pre-SMA in the RB-II condition may indicate that the motor switching was driven by detecting the conflict of response sets. The enhanced IFG influence to STN in the RB-II condition may act to inhibit the irrelevant task set, which is not evident in the RB-RB condition. MVPA analysis also found that activations in IFG were task-separable in the RB-II condition,

but not in the RB-RB condition. In other words, the interaction between IFG and STN appeared to reflect the transition of task sets in the RB-II condition. Besides, OFC appeared to participate in assisting motor switching in both conditions, which supports its role in persistently monitoring the switch needs.

Figure 5-4

Functional connections that were enhanced on switch trials. Shaded nodes are task-set regions.



Conclusion

The current study provides two types of switching for investigating how the brain exerts executive control when multiple tasks have to be carried out in a narrow time-window. The results suggest that task switching is not a uniform process, and the specific feature of individual task has to be considered. While no strong evidence was found for a dedicated task-set network for a specific task, how the network functions to carry out the task appears to

be specific. Namely, switching between two RB tasks appears to recruit more consciously monitored S-R transformation processing, whereas the situation with intermixed RB and II tasks seems to allow early preparation of more specific response sets, perhaps because the brain does not anticipate a need for ad hoc S-R mapping. This hypothesis leads to a verifiable prediction: bottom-switch costs in the RB-II condition would be higher than in the RB-RB condition.

Notably, two non-task-set regions, ACC and OFC, were found to be activated in task switching. Neither region was identified in fMRI contrasts, but both were found to be task-separable in MVPA analysis. Besides, ACC was also found to be activated in single-task categorization studies using similar stimuli. Previous lesion studies suggestthat both regions play a role in task switching (e.g. Bissonette et al., 2013; Ragozzino, 2007; Pollmann et al., 2007), and more importantly, lesions to these regions did not impair the capability of single motor decisions (typically simple categorization tasks). Considering ACC's role in anti-automaticity (Hikosaka & Isoda, 2010; Paus, 2001), it is not surprising that any task that requires response changes would recruit ACC.

Furthermore, evidence suggests that task switching is the result of interactions between OFC, ACC, and the task-set network. While the overall fluctuation of OFC did not appear to be switch-specific in the current study, its influences to other cortical regions appeared to be

modulated by switch needs, which suggeststhat this region changes its output according to the needs. Furthermore, ACC also appeared to adjust its output based on the switch needs, and this adjustment did not seem to be caused by changes of OFC. Notably, evidence suggests that functions of the two regions are dissociable. Specifically, OFC appears to be selective to a constantly changing context that requires ready changes of behavior, as happens during multitasking, and ACC is often reported to react when conflict occurs (Bissonette et al., 2013).

In addition, DCM analysis suggests that the hyperdirect pathway may be recruited in different ways for task switching across the two conditions. Specifically, the STN appeared to be recruited for the transition of task sets in the RB-II condition (the IFG-STN-MFG pathway), whereas STN was more affected by changes of rule-based motor decisions in the RB-RB condition (the IFG-preSMA-STN-MFG pathway). These findings provide a new direction to investigate the involvement of the hyperdirect pathway in executive control, which may be helpful for resolving the debate about whether the interference control in task switching recruits inhibitory mechanisms.

Chapter 6. General Discussion

Performance in task switching (TS) is an important measure of cognitive flexibility. A better understanding of TS mechanisms not only has potential clinical value to improve precision treatments, but also can help to improve the quality of life. However, many puzzles in this field remain unresolved after decades of research, which prevents the development of a coherent TS theory, and limits the application of insights from TS to other fields. One of the reasons is that most TS studies included only rule-based tasks with shared sets of stimuli and/or responses (i.e. "bivalent" sets), which may obscure the interpretation. For example, how much does task-set inertia (TSI) contribute to an error? With bivalent stimulus sets and response sets, one can claim that errors are due to random distractions or input-driven activation of irrelevant task sets rather than TSI, whereas with univalent stimulus sets, errors of wrong response-set selections on stay trials observed in the current task can hardly be explained by any of them. In the latter case, a more plausible explanation would be insufficient interference control on TSI. Besides, the usage of bivalent sets is also closer to daily-life scenario so that the inferences can be more applicable. In addition, the current study compared within-system switching (with two rule-based tasks) against between-system switching (with a rule-based task and a procedural task), which provides a new angle to investigate TS mechanisms. With GLM, MVPA and

DCM analyses of fMRI data, it revealed some of the key features of executive control in TS and added evidence for resolving the puzzles.

Broadly speaking, both single-task categorization and multitask categorization appeared to recruit similar networks in the brain. Brain imaging data in this work, along with evidence from other single-task categorization studies, suggest that rule-based and procedural categorization tasks also recruited similar networks. In fact, this seems to be true for a broad variety of S-R tasks (e.g. see Dosenbach et al., 2006 for a comparison of 10 different S-R tasks). If so, what might the functional localization reports in fMRI studies on S-R tasks really suggest? A possible answer is that it reflects a specific component of the network responding to certain task demands at a specific time point (typically identified by contrast analysis of specific events), rather than where the network locates. For example, activations in SPL in memory tasks may reflect the response sets being activated upon memory retrieval for reaction, just as is observed in task-set preparation during task switching. Another example is that ACC activations in a wide variety of tasks may simply reflect anti-automaticity when the constant changes of responses are necessary (Hikosaka & Isoda, 2010; Paus, 2001).

In other words, what really matters is the dynamic: at which time point, which component of the network responds to a specific task demand. Take the current study as an example. Brain imaging data provides evidence that PFC exerts executive control on down-stream regions,

such as to activate relevant S-R transformations by working with AnG and SMG, to prepare appropriate motor outputs by working with SPL, motor cortices and the cerebellum, and to conduct interference control through BG. Notably, ACC appears to be recruited to keep the flexibility of response changes, and OFC may be activated to monitor the changing demands in multitask contexts. Along with these processes, perceptual processing in the visual cortices and semantic processing in the temporal lobes were also observed. The next section provides details of these inferences by demonstrating how questions raised in the preceding chapters can be responded by filling in details of TS mechanisms into this broad scheme.

Response to challenges on TS theories

Does TS really involve multiple tasks?

The premise of task switching is there are at least two tasks to switch between, which is assumed to be carried out by changing the underlying neural task sets of individual tasks. In other words, evidence is needed for showing that the brain treats the two tasks differently. In the current study, both behavioral and neural imaging data support that there are multiple tasks. Behaviorally, there are evident patterns of intertask interference, such as significant switch costs, and errors of response-set selections (i.e. using wrong fingers for correct categorization outputs). Furthermore, MVPA analysis on fMRI data found that activations in higher cognitive

regions were task separable (such as OFC and ACC in both conditions, and IFG in the RB-II condition), which supports that these regions (or our cognition) are handling the two tasks differently.

Does task switching recruit unique mental processes?

In brief, the neural processes of TS appear to possess common, characteristic features, although the expressed behavioral and neuronal patterns are determined by specific dynamics of task demands.

First of all, evidence suggests that the neural process of TS is not just a combination of underlying task sets. Specifically, OFC and ACC appear to selectively respond to multitask and multi-response demands, respectively. Lesions restricted to these regions typically impair performance that requires evaluation and selection, but not the underlying S-R behaviors, which suggest that they are unlikely to be task-set regions (e.g. see the studies listed in Table 4-3). Although many non-TS cognitive tasks also report these two regions, a careful inspection may find that such tasks contain TS demands. Notably, OFC and ACC may not be identified by fMRI contrasts in TS studies, because their activities are not restricted to switch trials.

However, evidence suggests that the brain handles task switching based on specific task demands, which means the observed neural and behavioral patterns may not be consistent across studies. Take the current study as an example, consciously monitored motor-planning

activations were more evident when the two tasks were both rule-based. The neural activations in the RB-RB condition showed that on switch trials, preSMA exerted stronger influence on STN; and as the number of categories increase, the workload of motor-planning increases and the involvement of motor-planning regions in cerebellum becomes evident. These findings may reflect that the brain anticipates ad hoc S-R mappings for rule-based category decisions. In contrast, when switching between rule-based and procedural tasks, early motor preparations appeared to be initiated during the cue interval, presumably because the upcoming task was predictable; IFG appeared to increase its influence to STN on switch trials, presumably for facilitating the switch of response sets.

Similar inconsistency can also be found in clinical observations in PD patients. Specifically, PD patients are found to have a deteriorated capability of sensory filtering via BG (Lee et al., 2010), but the influence on behavior differs with task demands, such as impairments of switching to a new rule in WCST, and increased RT on stay trials during task switching. Both can be explained by insufficient inhibitory control on irrelevant task sets, but the dysfunction is more evident on switch trials in WCST, and more evident on stay trials in TS.

Timing for specific types of executive control

There are three profound, long-lasting debates that fall in this topic.

1. Are task sets only updated on switch trials, as proposed by the task-reconfiguration theory?

Evidence from the current study supports the opposing view. First, preceding cues benefit response preparation on both stay and switch trials. Second, similar errors occur on both stay and switch trials. If task-set configuration occurs only on switch trials, such error should not happen on stay trials. Lastly, the switch vs. stay contrasts on brain imaging data only revealed differences in motor-related regions, which can be better explained by fMRI adaptation effect.

Since task-set configuration occurs on both stay and switch trial, the switch costs most likely reveal how the interference of TSI on the relevant task set is managed. Importantly, there are empirical findings that pure TSI theories fail to explain (discussed in Chapter 3), which the can account for if the dynamic of interference control on TSI is also considered. For example, the absence of RISC with variable RSI may be explained by the hypothesis that the slow decay of irrelevant task sets has to be inhibited by executive control, thus when the timing of target onset is unpredictable, such inhibitory control has to be postponed until the target stimulus is perceived.

The view that switch costs reflect the interplay between task-set activation and inhibition is not new (e.g. Vandierendonck et al., 2010). The key difference between the above argument and the view of Vandierendonck et al. (2010) is that task sets are not assumed to be configured

only on switch trials. In this way, there is no need to make exceptional assumptions about how task sets are reconfigured on switch trials, and no need for the tailored logic of "if switch, then…" in some TS models. The observation that OFC, ACC and IFG showed task-separable, but not switch-specific activations also supports that task-set configuration is based on task demands rather than switch demands.

2. Is task set configured proactively before onset of the target stimuli? Or can it be solely reactive?

Here, proactive is defined as top-down activated task sets, whereas reactive is input-driven (see Braver, 2012 for a review). With the definition that task set is composed of perceptual set, S-R transformation, and response set, the current study only found evidence for the response set being activated proactively. In other words, only part of the task set was activated before the stimuli were presented. Notably, the observation that OFC, IFG and ACC did not respond to cues suggests that interference control might not be conducted proactively.

Of course, this dynamic may be design-specific – because the S-R transformations (i.e. category sets) in the current study can be solely determined by the target stimuli. As a contrary example, MTG (presumably for semantic processing) was found to be activated to cues in Brass and von Cramon (2002), where the task sets had to be determined by cues but not by

target stimuli. In other words, task sets can be activated proactively, but the recruitment of specific components depends on specific task demands.

3. Do switch costs measure executive control?

It has been suggested that switch cost is not a valid measure of the duration of an executive control process if the task reconfiguration theory does not hold (Schneider, & Logan, 2005). The argument is that the switch costs mainly reflect effects of passive priming or interference. However, since the interference is managed by executive control, the characteristics of switch costs can still contribute to the understanding of executive control.

An example comes from errors on repeat trials in the current study (i.e. wrong selection of finger and a tendency to switch sides when the response should be just repeated). They can serve as strong evidence for the existence of TSI (as discussed in the first paragraph), lessened interference control on TSI, and trial-by-trial task-set configuration.

Another example comes from the absence of RISC effects with variable RSI. As discussed above, this observation implies that when RSI is fixed (i.e. the onset of targets are predictable), the interference are proactively inhibited. Importantly, the absence of RISC may indicate that the decay of TSI is too slow to be observable within seconds when inhibitory control is absent. This hypothesis is consistent with the increased perseveration in PD patients, which may be also due to the absence of inhibitory control (discussed in the next paragraph).

While it has not been suggested, these two observations may provide a way to measure the decay of task sets without inhibitory control.

Yet another example comes from the observation that PD patients showed increased mixing costs and decreased switching costs in TS studies, but increased switch costs (perseveration errors) in WCST. Specifically, the latter excludes the possibility that the increase of mixing costs was due to strong anti-perseveration mechanisms. Besides, since the most prominent dysfunction in PD patients is in BG, which is comprised of inhibitory circuits, the most likely explanation for these observations is the dysfunction of inhibitory control. Indeed, it has been found that the filtering capability (i.e. inhibitory control on irrelevant signals) through BG in PD patients is deteriorated (Lee et al., 2010). Besides, evidence from animal models has provided evidence that PFC can exert selective inhibitory control through BG (Nakajima et al., 2019). Together, these findings strongly suggest that BG may be recruited in inhibitory control during task switching.

Do irrelevant task sets receive inhibitory control, rather than just be suppressed by lateral inhibition (as in winner-take-all models)?

Some researchers claimed that overcoming interference from irrelevant task sets can be achieved solely by enhancing the relevant task set (Munakata et al., 2011; see also models listed in Table 1-1). Indeed, there is evidence for enhancive interference control, such as

increased response-changing errors on repeating trials in the current study (because lessened executive control is more likely to happen than intentionally changing responses on repeating trials). However, there is also evidence that supports inhibitory control on irrelevant task sets during task switching, such as increased perseveration errors and increased mixing costs in PD patients (both can be explained by deteriorated inhibitory control through BG), and the N-2 effect, which can be best explained by persisting selective inhibition on task sets (at least response sets). Besides, DCM in the current study also implicates STN's involvement in TS, which is recognized for being part of the inhibitory systems.

Implications to fMRI studies

It is well-recognized that fMRI analysis has its limitations in making causal inferences. Therefore, all the inferences here were made with the supplement of lesion and neural stimulation studies. Along the discussion in Chapters 4 and 5, some of the important implications to general fMRI studies were also revealed.

Discrepancies between findings from fMRI and lesion studies

Such discrepancies can be separated into two types: regions identified in lesion studies are rarely reported in fMRI studies, and the other way around.

OFC is a good example for the first type in TS studies. Similar to previous fMRI studies of TS, no switch-specific activations were found in OFC by fMRI contrasts. This would not be surprising if OFC has to be activated for monitoring the constantly changing demands. In this case, MVPA and analysis of functional connectivity would be better tools for identifying its involvement. Indeed, MVPA revealed that activation patterns in OFC differed by tasks, and its influence to other cortical regions was modulated by switch needs.

ACC is a good example for the second type. While lesions to this region rarely lead to incapability of S-R behavior, this region is regularly reported in a wide range of tasks, and sometimes contradictory conclusions are drawn (see Bernal & Perdomo, 2008 for a short list of studies). Considering evidence of ACC's function in the most basic motor control -- resisting automatic motor actions (Hikosaka & Isoda, 2010; Paus, 2001), activations in such a diverse fMRI literature may simply reflect the fact that the brain is exerting its influence to counteract inappropriate responses, and the versatile signals associated with ACC may reflect demands from other regions in responding to task demands.

These confusions signify the importance of consulting causal studies. As a concrete example, SPL is often reported in TS studies and has been suggested to have more complicated functions than sensory-motor processing suggested by causal studies (e.g. Kim et al., 2012; Richter & Yeung, 2014). However, its role in sensory-motor function may be sufficient for

explaining the highly frequent reports in TS fMRI studies, because BOLD contrasts of switch vs. stay trials may just reveal the adaptation effect on stay trials. In fact, this concern has been raised in De Baene et al. (2012), which did not seem to draw enough attention as it should have (only being cited 45 times up to 2020/08/30, according to Google scholar).

Of course, these issues also occurred in some fMRI studies. For example, Konishi et al. (2000) compared old and new BOLD responses in a recognition task and identified SPL. In their study, there were twice as many new items as old items, which made the old events contained mostly switch trials (about 1/3) and the new events mostly stay trials (about 2/3), thus regions identified in old-new contrasts were very likely be affected by the adaptation effect. Besides, almost all the reported regions are motor related, which strengthens this concern.

TS demands in general fMRI studies

Given that many fMRI studies are highly complicated and require cognitive flexibility, it is worth noting that rarely any discussions on TS are included in most fMRI studies. This may be due to the lack of a coherent TS theory and marks the urgency of filling this need. It also means that evidence for TS theories can be drawn from fMRI studies outside this field. For example, in Simons et al. (2005), OFC showed activations to both task memory and list

memory (shown in Figure 3 in the article), but no discussions about OFC were provided. According to what was found in the current study, this may be an indication of task switching.

Since TS is so ubiquitous in cognitive behavior, a clearly defined language in TS theory would also help to explain general cognitive processes. Take Simons et al. (2005) as example: MFG (BA 10 and BA 45) was found to respond to both tasks, and its involvement was described as "retrieval orientation", which is very task specific. In fact, MFG has been associated with so many functions in all kinds of cognitive studies that its real role gets obscured (e.g. see Bernal & Perdomo, 2008 for a short list of studies). Referring to the scheme of TS proposed here, the activation of MFG may be simply described as providing top-down configuration of relevant task sets in those studies.

Toward a neural computational model of task switching

The field of task switching starts out to investigate cognitive flexibility, but the values of the findings may still be under-estimated. For example, virtually no fMRI studies outside the TS field have discussed how much TS may affect the neural processing in their particular designs. One possible reason for the neglect may be that a coherent TS theory, or more formally, a TS neural computation model is lacking.

The challenge of a coherent TS model comes from the great variety of TS behavioral and neural patterns, which are determined by the dynamics of common executive processes, such as monitoring of constant changing demands, proactive task preparation, and interference control, that respond to specific task demands at appropriate time points. Of course, these processes may appear in any cognitive task. What makes TS studies unique is that they are designed to probe how executive control handles multiple simple task sets with the aim of making the effects as evident and measurable as possible.

Meanwhile, the current study demonstrated the importance that fMRI studies of TS have to consult results from other fields. Specifically, since intact performance of TS requires the involvement of the whole network, and TS research is more about the dynamics – the timing of each specific function gets involved, it is important to have basic understanding about underlying components before developing a theory. For example, since SPL is recognized for its sensory-motor function, it may be more straightforward to explain the TS-related BOLD patterns in SPL with fMRI adaptation effect than assigning it a new cognitive role in the theory.

However, it becomes obvious from the above discussion that the goal of developing a uniform TS model would be too ambitious -- which would mean a model that accounts for any cognitive tasks. A more plausible approach may be to show how coherent TS principles can be

used to extend existing task-set models into TS models. Based on the evidence discussed so far, some of the principles may include:

1. The activations of task sets decay slowly, and do not decay to zero during the TS session. This is supported by neural-recording studies (Zylberberg & Strowbridge, 2017; Goaillard et al., 2010). Most neural computational models contain the assumption of decay as well, but the actual decay may be much slower than most models assume, considering that the decay curves may be from neural activities that have been affected by inhibitory control when being observed. The speculation of slow decay of task sets may be supported by the absence of RISC with variable RSI (which can be explained by that when inhibitory control is absent, the decay of TSI is unobservable), and that PD patients show strong perseveration errors. Accordingly, parameter adjustments can be made to fit these observations.
2. Action is taken only when the activation of corresponding task set goes above threshold, and this process requires time. This assumption is supported by all the neural recording data, and embedded in most neural computational models. Importantly, adding the assumption of slow decay to the modeling of task-set initiation can readily account for the increased mixing costs and perseveration errors in PD patients. Specifically, without

inhibition to the preceding, irrelevant task set, the initiation of the current task set would suffer from strong lateral inhibition from the rivalry task set.

3. Timing of activating a specific component in a task set depends on the specific demands of the task. For example, when a cue is presented, both semantic processing and response set were activated in Brass and von Cramon (2002), whereas only response set was activated in the current study. In fact, implementing the task-specific dynamics is exactly the purpose of any task set model.

4. Detecting a slower-than-normal activation of specific task-set component (i.e. the existence of interference) would trigger inhibitory control on corresponding components of TSI. This would account for the diverse phenomena observed in different TS designs without including tailored conditional ("if …, then …, else") assumptions.

With the accumulation of a huge body of data from TS and other cognitive studies that contain TS components, it is now the best time to re-examine the data and seek consensus of TS principles. An effort to integrate these principles into existing single-task neural computational models would be a good start for resolving the long-lasting puzzles and contribute to the understanding of executive control.

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