

Neural Correlates of Abstract Rule use within the Rostro-Caudal Axis of the Frontal Lobes

by

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Abstract

This paper presents 2 experiments aimed to address key limitations in the understanding of how abstract rules (i.e., matching, non-matching) are subserved by regions of the prefrontal cortex (PFC) and frontal lobes of the brain. A number of previous investigations have demonstrated convergent findings that the frontal lobes of the brain exhibit a functional hierarchy, in which increasingly abstract rules are associated with more rostral neuronal activations along a rostro-caudal axis (Badre and D'Esposito, 2007, 2009; Bunge and Zelazo, 2006; O'Reilly, 2010). However a recent investigation by Crittenden and Duncan (2014) has suggested that increased attentional resources is associated with more rostral neural instantiations, when abstractness of the action rule is held constant.

Experiment 1 assessed the validity of novel experimental manipulations, which were hypothesized to assess the independence between degrees of abstractness for action rules from that of the difficulty associated with the implementation of action rules. Experiment 2 implemented variants of these tasks during functional magnetic resonance imaging (fMRI) data acquisition. The results indicate that rule difficulty, via increased stimulus sets and memory load, bears important implications for the supposed functional arrangement of the rostro-caudal axis of the frontal lobes, specifically within the dorsolateral PFC. Findings from these experiments contribute to a better understanding of the functional arrangement of neural substrates within the frontal lobes.

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List of Abbreviations

PFC	prefrontal cortex
fMRI	functional magnetic resonance imaging
BA	Brodmann Area
DLPFC	dorsolateral prefrontal cortex
VLPFC	ventrolateral prefrontal cortex
OFC	orbitofrontal cortex
ACC	anterior cingulate cortex
MRI	magnetic resonance imaging
ATP	adenosine triphosphate
NaK ⁺	sodium potassium
O ²	oxygen
BOLD	blood oxygen level dependent
Voxel	volumetric pixel
TR	temporal resolution
PET	positron emission tomography
EEG	electroencephalography
MEG	magnetoencephalography
T	tesla
RLPFC	rostrolateral prefrontal cortex

CLPFC	caudolateral prefrontal cortex
pMC	premotor cortex
SEM	structural equation modeling
ROI	region of interest
pre-SMA	pre-supplementary motor area
PMd	dorsal premotor
pre-PMd	pre-dorsal premotor
MTS	<i>matching-to-sample</i>
NMTS	<i>non-matching-to-sample</i>
MDA	multiple demand activation
CC	corpus callosum
IFS	inferior frontal sulcus
SF	sylvian fissure
L	line
FD	fine discrimination
s	second
ms	millisecond
ITI	inter-trial interval
EPI	echo-planar imaging
TE	echo time
GLM	general linear modeling
mm	millimeter
RF	radio frequency

MNI Montreal Neurological Institute

FWHM full width at half maximum

Chapter 1: Introduction

According to Gazzaniga, Ivry, and Mangum (2013), *Cognitive Control* refers to an ability to use memory and perception in order to guide goal-oriented behavior. This cluster of higher cognitive functioning, sometimes called executive function, is said to include such complex abilities as creativity, predicting consequences, and planning for future events. A large consensus in the cognitive neuroscience literature is that neural mechanisms within the anterior portions of the frontal lobe, particularly the prefrontal cortex (PFC), are crucially involved in executing the actions of cognitive control successfully (Badre and D'Esposito, 2009). It should be noted that the PFC comprises nearly one-half of the human frontal lobe and includes five major anatomical subdivisions: motor cortex (BA 6), dorsolateral prefrontal cortex (DLPFC; BA 8, BA 9, BA 46), ventrolateral prefrontal cortex (VLPFC; BA 44, BA 45, BA 47), orbitofrontal cortex (OFC; BA 10, BA 11, BA 47), and anterior cingulate cortex (ACC; BA 24, BA 32, and BA 33). Given this relative cortical volume and number of subdivisions, it is not surprising that a modular model for functional divisions within the PFC has been proposed to better understand connectivity, or networks, within this region.

Studies exploring functional connectivity examine temporal correlations among measures of neural activity between brain regions (Friston, Frith, Liddle, & Frackowiak, 1993). Although localization is an important component in understanding cognition, estimating neural networks provides a more complete account of how the multiple brain regions contribute to such phenomena as memory, emotion, action, language, and attention. Such connectivity approaches aimed to provide a better understanding of PFC functioning hold significant potential for several

reasons. Notwithstanding Gazziniga et al's. (2013) definition of cognitive control, which implicates the PFC and likens it's construct to that of executive functioning, Miller, Freedman, and Wallis (2002) note the vitality of PFC functioning by pointing to attentional and goal-oriented dysfunction which are associated with damage to this region of the brain. There also exists a growing body of evidence implicating PFC functioning in developmental disorders such as autism (Soulières, Mottron, Giguère, Larochelle, 2011) dementia (Burgmans, van Boxtel, Smeets, Vuurman, Gronenschild, Verhey, Uylings, Jolles, 2009), cognitive impairment associated with aging (Addis, Giovanello, Vu, & Schacter, 2013), and Alzheimer's disease (Mimura & Yano, 2006). Continued research to enhance the understanding of functional networks within the PFC holds significant potential for improvements in diagnosis, treatment efficacy, and prevention assessments of human psychiatric pathologies given the implications of the PFC in these and other potentially related developmental and neurodegenerative disorders. Through models of healthy, typical PFC functioning, a better understanding of how cognitive deficits manifest in these populations is possible.

One approach to characterizing the functional organization within the PFC of healthy individuals (see figure 1) is a hypothesis of a hierarchical organization of complexity, in which increasingly abstract content is represented along a continuous axis originating in caudal frontal lobe regions and terminating within the rostral frontal lobe regions (Badre and D'Esposito, 2009; Bunge and Zelazo, 2006; O'Reilly, 2010). Where abstractness is defined as the degree to which a goal is a high-level, general task goal. The example of an abstract goal used is that of making a sandwich, which can be completed in a number of ways and is variable in which order the component actions are carried out. At the other end of the abstract goal continuum, concreteness is the degree to which an action is a low-level, highly specific motor response such as slicing

bread or applying a spread. Within this framework, action rules are said to be information which specifies an appropriate action given that certain conditions are met.

Figure 1

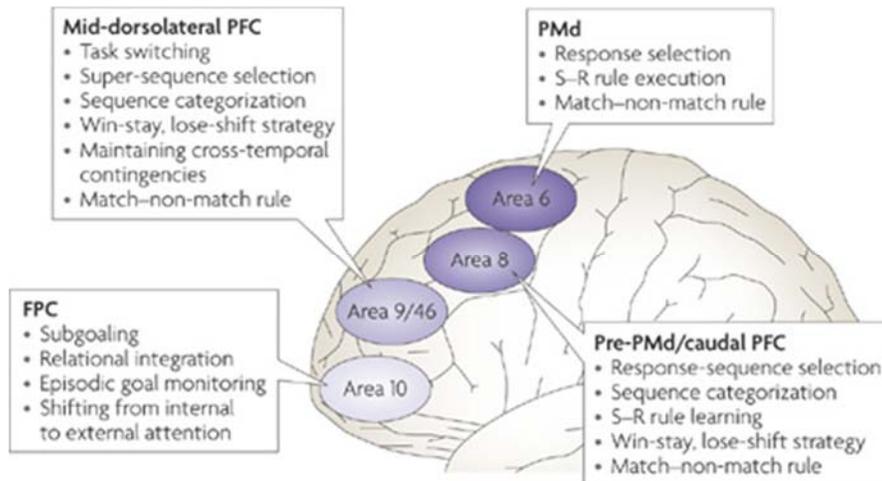


Figure 1. Badre and D’Esposito’s (2009) summary figure of functional findings from the literature reviewed. Brodmann areas correspond to clusters of cognitive control domains. From Badre and D’Esposito (2009).

Therefore abstractness of action rules, refers to the degree to which a rule depends on how specified that relationship is between conditions which are met and appropriate actions are executed. It is also important to note that Badre and D’Esposito (2007, 2009) define a scale for abstractness of action rules as a relative level of higher-order processing associated with planning and selection appropriate actions. Therefore, the use of higher-order rules to guide action should demonstrate the functional hierarchy depending on the specificity of perceptual inputs within the action rule. More abstract rules do not specify particular perceptual inputs for determining an appropriate action, but instead can be applied more generally and even in novel contexts. Simple, concrete action rules, on the other hand, would have highly constrained and

particular perceptual experiences which determine appropriate actions. Examples of abstract action rules, which are guided by highly generalized perceptual inputs, include matching/non-matching rules (i.e., do response x if stimuli are the same, do response y if stimuli are different) and greater-than/less-than rules (i.e., do response x if stimulus is the larger than a, do response y if stimulus less than a). Examples of concrete action rules, which are guided by constrained perceptual inputs, include Go/No-go rules (i.e., do response x if stimulus a is presented) and Go rules (i.e., do response x if, and only if, stimulus a, is presented, Do response y if, and only if, stimulus b is presented)

This dissertation shows how performance changes (i.e., accuracy, reaction time) across parametrically manipulated increasing task demands for simple, concrete action rules and compare performance functions to that of abstract action rule performance. Once these task's validity was established, both the abstract and concrete tasks were adapted for implementation during functional neuroimaging to examine neural instantiations of action rules varying in task demands. The following sequences of topics are presented. First, a rationale for the use of functional magnetic resonance imaging is briefly presented. Second, a review of empirical support from fMRI literature for the rostro-caudal hierarchy of the frontal lobe is discussed. Third, a select review of increasing task demands for cognitive control is presented. Fourth, a rationale for assessing contributions of task demands in abstract rule representations is provided. Next, the experiments and data analyses are presented. Finally, the outcomes and interpretations are discussed.

fMRI for use in studying abstract rules

Although magnetic resonance imaging (MRI) has long been a popular tool of neuroscience, functional magnetic resonance imaging (fMRI) is a rapidly growing neuroimaging modality within the vast field of cognitive-neuroscience research. In addition to being established as a valid method, MRI's non-invasive approach and general abundance in hospitals and research settings makes this imaging technique a viable and attractive method for researchers. fMRI is used to examine the underlying neural processes of cognition by making inferences about neural activations during controlled experimental tasks. This method is made possible by the paramagnetic property of deoxygenated blood present in the brain.

Neural activity requires the use of oxygenated blood to synthesize adenosine triphosphate (ATP). ATP is used as fuel by energy-dependent sodium-potassium (NaK^+) pumps which are critical in restoring the cellular homeostasis required for executing action potentials. As oxygen (O_2) molecules are removed from bonds to hemoglobin in the capillaries of the brain, MRI scanners record localized changes in O_2 concentration. These blood oxygen level dependent (BOLD) signals across time points during scanning allow researchers to estimate the reliability of neural activity in local regions of the brain. With a typical spatial resolution of about 2 or 3 mm^3 volumetric pixels (voxel) and 1000 to 5000 ms temporal resolution (TR), fMRI possesses a relatively high spatial resolution as compared to other functional neuroimaging methods such as positron emission tomography (PET), electroencephalography (EEG), and magnetoencephalography (MEG). BOLD signal fMRI provides an indirect measure of neural activity and lacks the particularly high temporal resolution of EEG and MEG, therefore it is not without limitations.

Another limitation is the ever-present changes in local blood flow and neural activity which are constants for the in-vivo neural networks of the brain. Functions such as memory, perception, and emotion remain active during fMRI data acquisitions researchers are implementing to study a particular function of the brain. One popular method to isolate regional activity associated with a particular task is known as the subtraction method. By acquiring imaging data within a context that most closely matches experimental conditions, except for the task manipulations themselves, fMRI researchers are able to subtract out, or contrast, activity associated with these control conditions in order to isolate BOLD signals associated with the particular brain function of interest. Although there may be an abundance of activity across regions of the brain at any given time, this subtraction method allows neuroimaging researchers to identify task dependent changes in local BOLD signals during scanning.

By overlaying BOLD signals onto anatomical MRI data for the same research participants, structures and regions corresponding to signals during particular conditions arranged during scanning point to both localization and networks underlying functions of the brain. BOLD fMRI has been both historically and recently used to examine localization and functional connectivity while engaging in a wide range of cognitive processes, such as cognitive control, memory, attention, perception, emotion, and language (for reviews, see Cabeza & Nyberg, 2000; Vul, Harris, Winkielman, & Pashler, 2009, Price, 2010). In addition to assessing the relationship between abstract rule-use and PFC functioning with a common modality to previous studies, the use of an ultra-high field, 7 tesla (T) Siemens MAGNETOM has yet to be implemented in this line of research. Through utilizing 7T fMRI, methods from prior abstract-rule literature could be easily adapted with an additional benefit of increasing the spatial signal resolution of anatomical and functional imaging inherent in high-field fMRI.

Review of fMRI findings supporting Rostro-Caudal Hierarchy of Abstract Rules

Functional magnetic resonance imaging (fMRI) data supporting the rostro-caudal hierarchy hypothesis was first experimentally demonstrated by Koechlin, Ody, and Kouneiher (2003). Although the role for the PFC in the higher cognitive functions was discussed extensively prior to these findings (for review see Fuster, 1995; Miller and Cohen, 2001), this seminal study provided the initial demonstration utilizing a functional task which directly manipulated the complexity of information processing completed by participants. In order to assess functional correlates of increasingly complex action requirements, two separate experimental manipulations assessed the effects of increasing the episode factor, or amount of contextual information required to make correct responses in a motor response task during fMRI scanning. Conditions testing the lowest episode factor of 0, deemed the stimulus condition, required participants to detect the presence of a visual stimulus and ignore a distractor stimulus via either a left or right hand-held response buttons. In the stimulus condition, a single response is only required in presence of the target stimulus and associations between stimuli and appropriate responses never overlapped, therefore the number of relevant cues is said to be 0 since stimulus-motor responses were not dependent on any additional cues, beyond the stimulus itself. In a second condition, deemed the context condition, participants again were required to ignore distractors, but had to make left-hand responses or right-hand button responses in the presence of a two distinct visual stimuli. The number of informational cues in the context condition is said to be 1 because participants must discern whether a left or right button press is appropriate given the presence of either of the two visual stimuli. In the final condition, visual stimuli could serve as either distractors or cues for a left or right hand-held button response depending on the presence of an instructional cue presented at the beginning of trial blocks. This

final condition was deemed the episodic condition due to overlapping associations for stimuli and motor responses. Left and right stimulus-response associations varied based on an initial instructional cue. Accordingly, this task required more than just memorization of responses and instead required participants to subsequently use information presented at the outset of a trial block. The number of relevant contextual cues to complete the episodic task is said to be 2 because participants are required to use information from an earlier episode to determine whether left or right button responses are appropriate.

The functional results revealed a continuous hierarchy in which episodic task demands showed the greatest PFC activation with intermediate activity observed during contextual task requirements, and the overall least amount of activation associated with stimulus task demands. The episodic condition showed activation in Rostral and Caudal lateral PFC (RLPFC, CLPFC) as well as the premotor cortex (pMC). During task conditions in which contextual control was necessary, only CLPFC and pMC were active. During task conditions which required responding based solely on presentation of stimulus, regardless of any contexts, only pMC activation was observed. These results lead Koechlin et al. (2003) to assert a functional cascade in which rostral-most regions appeared to enervate caudal regions in a unidirectional manner and contingent on the relative contextual information required to control responding.

Koechlin and colleagues (2003) bolstered these claims with a structural equation modeling (SEM) analysis on the regions of interest (ROIs) to examine the effective connectivity of this frontal lobe network (see Figure 2). In figure two, each node represents the ROIs, listed

Figure 2

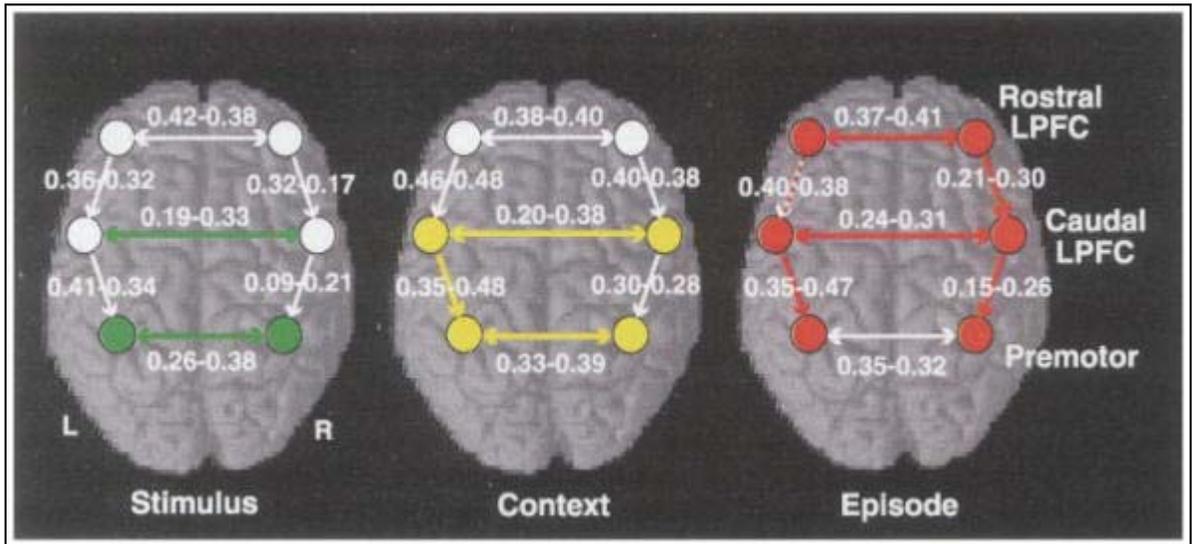


Figure 2. Effective connectivity diagram from Koechlin et al. (2003). Activations that significantly increased with task conditions and path coefficients are indicated in green, yellow, and red, respectively by condition. From Koechlin et al (2003).

on the right side of the figure. These regions include each of the aforementioned ROIs implicated in the analysis of functional data by task conditions of stimulus, context, and episode task conditions, listed at the bottom of the figure. Reliable regional signal activations are indicated in green, yellow, and red, respectively by condition. The results of the SEM analysis appear closest to each of the arrows connecting the ROIs in the figure. Reliable correlations between co-activated regions are indicated by colored arrows respective of the task conditions previously discussed. Figure 2 demonstrates that the effective connectivity observed in these experiments suggests a hierarchical mechanism, in which caudal regions of the PFC are not co-dependent on rostral regions during simple stimulus-motor control. However, during increasingly complex integrative control requirements, a robust co-activated network within the PFC emerges. These

results suggest neural network organized along the rostro-caudal axis of the human PFC, in which rostral PFC regions are recruited in a continuous manner for increasingly complex cognitive control and exert top-down control of caudal PFC and premotor regions (Koechlin et al., 2003).

Important to the validity of these findings was ruling out the potential role of increased effort, or task difficulty, modulating the neural correlates. Arguably, the increased mental effort across tasks could yield corresponding increases in activation along with the continuum of increased informational complexity. By showing that the greatest caudal and rostral lateral PFC activations were not modulated by degradations in behavioral task performance, but instead associated with greatest episodic retrieval, the authors suggested it was unlikely that their results reflected increased mental effort alone (Koechlin et al., 2003). Although these data suggest that the role of task difficulty, or mental effort, did not appear to mediate network connectivity or rostro-caudal response profiles, this interpretation is post-hoc and does not include direct manipulation of task difficulty for comparison.

Although Koechlin and colleague's (2003) findings provided the first instance of manipulated task features which demonstrated the cascade of functional activity along the rostro-caudal axis, subsequent studies examining additional cognitive control tasks have led to refined models. One limitation of Koechlin et al's. (2003) assertion of a rostro-caudal hierarchy is that their conclusions are limited to the use of memorized, stimulus-response rule sets and do not include additional tests for other domains of cognitive control (i.e., abstract rule use). One pair of studies by Miller and colleagues (2001, 2003) provided such an assessment of an additional domain by utilizing a task requiring the use of either simple concrete rules or abstract, relational

based rules. The results of Miller's studies yielded findings consistent with notions that a hierarchical model of functions extended to the domain of abstract rule use.

In the initial seminal study, Wallis, Anderson, and Miller (2001) demonstrated that neurons in the PFC could encode abstract concepts of *match* and *non-match* using a single neuron recording method. Rhesus monkeys were trained in a conditional discrimination task in which cues indicated whether performing a match or non-match judgment was appropriate after a short delay. During this training, neurons in the prefrontal cortex region including the dorsolateral PFC (DLPFC), the ventrolateral PFC (VLPFC), and the orbitofrontal PFC were recorded across 55 sessions. Sessions were run once per day and included approximately 1,000 trials and 4 new objects per session. Performance for novel objects was said to be accurate with novel images at 70% over 220 initial exposure trials. Results indicated that single neurons in the PFC showed strong rule-selectivity, with nearly 50% of neurons responding independently when match and non-match rules were in effect. Additionally, these rule-selective neurons appeared to activate independent of the specific cues used to signal the appropriate rule or by individual images (Wallis et al., 2001).

Wallis et al. (2001) provided a more advanced understanding of the role for the PFC in abstract rule-use, but arguably lacked a critical within-subject comparison to simple-stimulus response associations. Such a comparison might have been possible if the same single PFC neuron activity was recorded during a task which required the monkeys to simply memorize appropriate responses to an exact stimulus or stimuli. In doing so, meaningful functional distinctions between neurons in the PFC during abstract and concrete rule use would have been provided. Although this limitation makes the exclusive role in PFC functioning between abstract

and concrete rule use unclear, it does not preclude the implication of PFC activity associated with a higher cognitive function, such as the use of abstract matching and nonmatching rules.

In a follow-up study examining the complexity of abstract rules in humans, Bunge, Kahn, Wallis, Miller, and Wagner (2003) extended the previous comparison conditions in an analogous task by including a comparison to simple associations as well as employed the use of fMRI to conduct whole brain analyses. In this adapted version of the task (figure 3), two cue types consisting of pictorial cues and pronounceable non-words appeared at the beginning of each trial to indicate appropriate rules which varied along a continuum of complexity. Neural correlates for trials which required the use of simple, concrete rules (i.e., respond left or respond right), were compared with trials which required the use of more complex, abstract rules (i.e., indicating matching or non-matching images). An a priori criteria for regions or networks said to be associated with the maintenance of rules required that patterns of activity are non-specific to cue type show sustained activation through delays.

The results indicated that the left VLPFC (BA 44), frontopolar complex (FPC, BA 10), and pre-supplementary motor area (pre-SMA, BA 6/8) were regions which showed cue independent activity during delay periods. Also during delay periods, these regions showed sensitivity to rule type (compound > simple). The VLPFC showed the largest sensitivity to rule type maintenance. Curiously, the rostral-most ROI, the left FPC, showed sensitivity to non-match rules during maintenance, but showed no rule-selectivity between, match and simple go rules. Regions in the VLPFC also appeared to coactivate with temporal cortical regions to retrieve rules. During cueing, both left VLPFC and FPC were sensitive to rule complexity. These findings indicate a highly left lateralized network or regions implicated in the retrieval and maintenance of abstract rules. Left anterior VLPFC has been previously implicated in learning of

arbitrary rules whereas the more parietal region has been linked with verbal working memory. DLPFC showed some sensitivity to rule complexity during cueing, but not during the delay (Bunge et al., 2003)

One limitation discussed by Bunge and colleagues (2003) was the absence of visual attention required during simple rule conditions. During the go-left and go-right trials, participants need not attend to the sample/probe images, which may have led to more attentional effort required throughout abstract rule trials. Additionally, participants reported that during NMTS trials, they defaulted to a strategy of performing the opposite response, had the trial been cues as a matching trial. These reports suggest that a number of participants did not engage in matching or non-matching strategies depending on the cues, but instead judged whether samples and probes matched during either trial type and reversed the appropriate response depending on the cue. This greater elaboration on MTS rather than NMTS trials leaves a potential for increased FPC regional activity between these conditions due simply to adding an additional conditional cue for MTS, rather than an alternative cue signaling an equivalently demanding NMTS rule. (Bunge et al., 2003). By arranging the match and non-match trials as reversals of correct responses for identical trials, Bunge and colleagues (2003) were able compare these abstract rule types without variations in the exact stimuli which were viewed during the trials. However, this arrangement may not have actually engaged distinct abstract rule use in participants. A comparison of activations during correct trials in which sample and probes appeared as identical or non-identical in a task requiring only single response for either trial type would avoid such additional elaborations but lacks the ability for a simple contrast between match and non-match which includes viewing identical stimuli.

One final limitation, which is not discussed, is that participants need only learn four item-specific associations for the simple rule condition. During the abstract rule conditions, participants are learning responses for eight unique combinations of visual stimuli which again might require increased task demands of responding relatively less familiar items, outside of the manipulation of an increased abstract nature to the MTS/NMTS conditions. Bunge and Colleagues (2003) did not provide the same criterion for demonstration of abstract rule use in humans required for monkeys in their earlier study (i.e., correct responding to novel items; from Wallis et al., 2001).

Despite the noted limitations, Bunge and colleagues (2003) provided an important understanding of where abstract rules are maintained in the brain, independent of the cues which are associated with those rules. Importantly, these findings are discussed as consistent with the view that a hierarchical functional organization exists within the frontal lobes. Badre and D'Esposito (2009) summarized evidence in support of this functional organization model in a

Figure 3

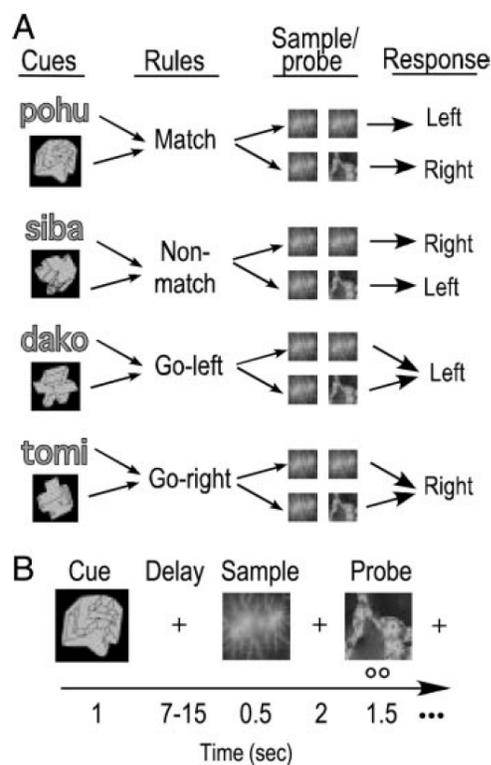


Figure 3. Depiction of trial progressions for each trial type from Bunge et al. (2003). Cues before each trial, either random polygons or non-sense syllables, indicated an appropriate response type for each of the four rules. These first two rules are said to more abstract and complex as they require a match or non-match rule between sample and probe items. The second set of rules are said to be more concrete and simple as they require memorization of a particular concrete response for each of the two sets of cues.

recent review which draws vastly from developmental, anatomical, and functional findings and spans across various action domains of cognitive control. Badre and D'Esposito's (2009) model has expanded the domain for the hierarchical gradient of cognitive control from the episodic control discussed in Koechlin et al. (2003), yet maintains a consistent modular organization along the rostro-caudal axis within the frontal lobe. The work of Bunge and colleagues (2003) formed an empirical foundation for the rostro-caudal gradient in abstract rule representations within the frontal lobe.

Interestingly, Studies which followed Koechlin et al. (2003) did not include functional or effective connectivity approaches to examine whether the hierarchical cascade model was observed across other domains and tests of cognitive control. Interestingly, Badre, Hoffman, Cooney, and D'Esposito (2009) noted that cognitive impairment in patients with PFC damage were consistent with a hierarchical cascade approach. Specifically, the authors noted that cognitive impairments were not independent across each level of abstract complexity and coincided with other equal or greater level-wise demand impairments for these patients.

Resource Demands and Cognitive Control

Bunge and Zelazo (2006) further discuss the representational relationship between abstractness and difficulty of task rules and in a review exploring the development of rule use in childhood (see Figure 4). According to this model, the simplest stimulus-response relation is a go-no go contingency (i.e., one stimulus cues a single appropriate response and an alternate stimulus cues any alternative response as appropriate). As the number of potential appropriate responses increase from one to two (univalent rules) and conditional cues indicating which rule is appropriate in the presence of the two stimuli (bivalent rules), complexity of the rules are said

Figure 4

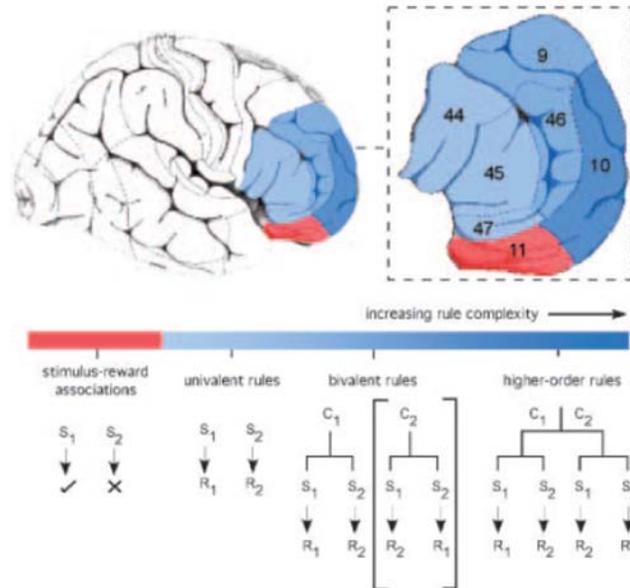


Figure 4. Depiction of the Rostro-Caudal hierarchy of increasing rule complexity representation in the lateral PFC from Bunge and Zelazo (2006). Examples of increasing complexity for

stimulus and response actions are seen at the bottom beginning with simple stimulus-reward associations and increasing in complexity to higher-order relations.

to increase. Adding an additional contextual layer to the bivariate rules leads to the greatest representational complexity and is said to be a higher-order rule because conditional cues vary in signaling an appropriate response. Although this model is consistent with the cognitive control hierarchy for neural substrates within the PFC, a hypothesis is discussed in which increased need for cognitive control is required for overcoming interference of competing task sets. In other words, as the number of overlapping stimulus-response associations increases as additional contextual knowledge is required. Accordingly, individuals must suppress conflicting rules for identical stimuli as the load of complexity for rules are increased.

Badre and D'Esposito (2007) addressed this account in an elegant and informative study using fMRI to record neural activations during task manipulations across four dimensions (i.e., responses, features, dimensions, and overlapping-cue dimensions). Although some important differences in activation were observed as a result of these manipulations, the findings were largely consistent with a systematic organization along the rostro-caudal axis for an abstract rule representational hierarchy within the frontal lobe (see figure 5). The researchers specifically dismiss the hypothesis of task difficulty in their discussion of the findings. By pointing to the manipulation of difficulty in their task, exclusive of degree of abstractness for rules, along two dimensions (degree of competition among appropriate responses, degree of competition among relevant features), the manipulation of increasing overlapping rules evidenced modulatory effects in caudal most regions of the frontal lobe including the dorsal premotor (PMd) and pre-dorsal premotor (pre-PMd), (Badre and D'Esposito, 2007). Badre and D'Esposito (2007) strongly suggest there is no role for conflict monitoring, or competition from overlapping cues in

Figure 5

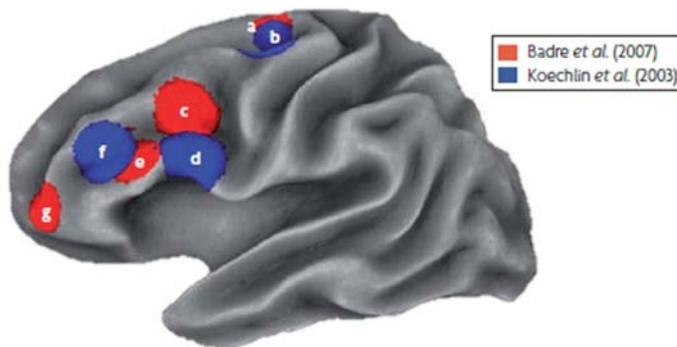


Figure 5. Figure depicting overlapping findings consistent with a rostro-caudal hierarchy of representations in the Frontal lobe across studies. Complexities of tasks are represented increasingly from areas labeled from A to G in these respective sites of activation. From Badre and D'esposito (2009)

the observed gradient for functional organization. Rather, that the regions implicated demonstrate modulatory effects based on the level of response conflicts at each level of complexity. It remains unclear, however, if increasing task demands besides those domains discussed by Bunge and Zelazo (2006) are impacting these observed activations. Although Badre and D'Esposito's (2007) study included an orthogonal assessment of task difficulty, this assessment was limited to tests of difficulty via response competition resolution and did not comprehensively examine other potential sources of task difficulty which may coincide with increasing the abstractness task demands.

One alternative hypothesis to the rostro-caudal hierarchy model, known as the Multiple Demand Activation (MDA) Model (Duncan & Owen, 2000) proposes that various increases in cognitive resources via task requirements leads to diffuse activation within the PFC. The MDA

model is in agreement with hierarchical rule abstraction model with regard to the localization of cognitive control function and action rule function within the PFC. Differing from hierarchical rule abstraction model, the MDA model asserts that connectivity spanning the entirety of anterior to posterior regions in the prefrontal cortex has been observed across various cognitive demands, and is sensitive to increased task requirements within these various domains. For example, cognitive demands, such as working memory ability and response competition resolution, can vary within each demand for task requirements, such as relative working memory load and strength of conflict, respectively.

Such within demand variability is said to reconcile the both consistent and inconsistent localizations of these demands across studies. To bolster these claims, Duncan and Owen (2000) provided a meta-analysis which examined foci reported in 20 studies spanning five cognitive demands overlaid on the same canonical rendering of a brain in standard Talairach space (see figure 6). The foci included only reflect subtractions of low task requirement from higher task requirement conditions across reported findings across such cognitive domains as response conflict, task novelty, working memory load, working memory delay, and perceptual difficulty.

Figure 6

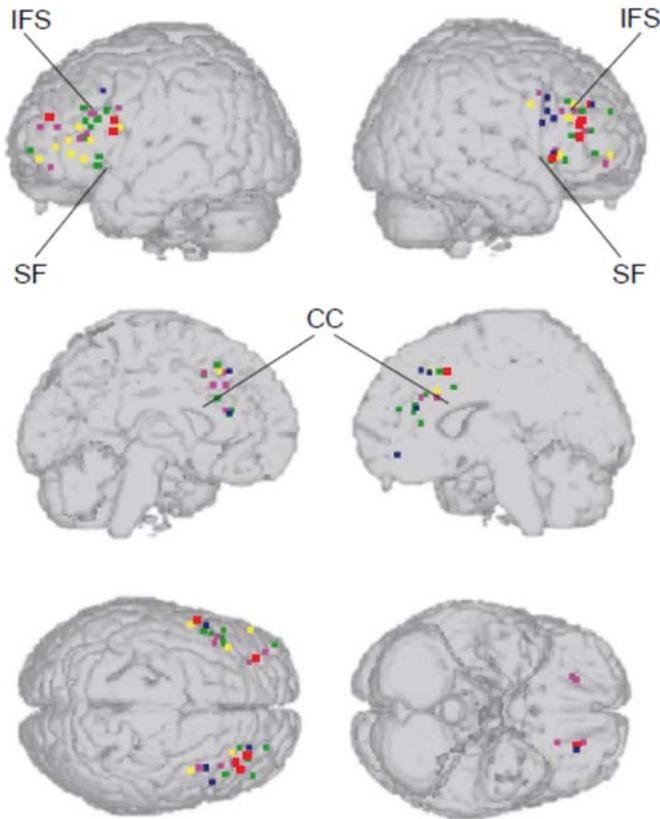


Figure 6. Figure 6 shows the results of Duncan and Owen’s (2000) meta-analysis which combined activations from studies of response conflict (green), task novelty (pink), number of elements in working memory (yellow), working memory delay (red) and perceptual difficulty (blue). Also depicted in the figure are several structures which have been implicated in fronto-parietal connectivity including the corpus callosum (CC), inferior frontal sulcus (IFS), and the Sylvian fissure (SF).

Duncan and Owen (2000) noted from the results seen in Figure 6 clustering in mid-dorsolateral, mid-ventrolateral and dorsal anterior cingulate PFC regions is very similar for the five different forms of cognitive demand. For both hemispheres, there was no apparent systematic variance across studies in localization of particular functions.

One limitation, as these results pertain to the hierarchical model of PFC networks, is that this study was conducted before the Rostro-caudal hypothesis had gained much of its current attention and therefore was not aimed at comparing levels of abstraction. Although Duncan and Owen (2000) implicate a diffuse PFC network which is active across demands, this analysis did not compare demands of varying abstraction. A more recent study conducted by Crittenden and Duncan (2014) compared the predictions of the MD model to that of Badre and D'Esposito's (2009) rostro-caudal hierarchy model.

Based on a prior finding that simple stimulus discriminations could be shown to activate anterior PFC regions if made difficult (Jiang & Kanwisher, 2003), Crittenden and Duncan (2014) designed a task in which difficulty and level of abstraction could be manipulated independently (see figure 7) during BOLD imaging acquisition. An initial condition of the task (4L) requires participants to choose a target line stimulus, appearing in varying locations, by pressing one of

Figure 7

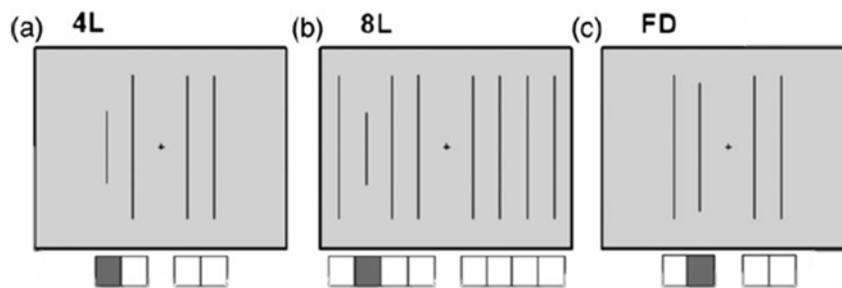


Figure 7. Figure 7 shows task a subset of task conditions from Crittenden and Duncan's (2014) comparison of task difficulty and rule abstraction. The condition on the left (a) reflects task conditions in which participants must choose a response which corresponds with a target item. The middle condition (b) reflects task conditions in which abstraction has been increased relative to the initial condition (a) in the target item response. The final right condition (c),

reflects task conditions in which task difficulty has been increased relative to the initial condition (a) in the target item response.

four response keys corresponding to presentations of arrays containing a target and three distractors. A second condition (8L) was introduced to assess an increase in rule abstraction via increasing the stimulus-response alternatives. In this second condition, the target was identical to the initial condition; however the number of distractors was increased to seven lines leading to a corresponding increase in potential correct responses. A third condition allowed for comparisons between increases in processing complexity due to abstraction versus a need for fine discrimination (FD). In this third condition, discrimination difficulty was manipulated via increasing the similarity between target and distractors in a task similar to the initial four-line condition.

Crittenden and Duncan's (2014) results are shown in figure 8. Reaction times in either task revealed no significant differences between the 8L and FD conditions. Both 8L and FD conditions showed increases in processing costs compared to the 4L condition. Furthermore, the imaging analysis revealed that increases in complexity both due to abstraction and due to discrimination difficulty were associated with anterior regions of PFC activity. This result lends strong evidence that rostral regions of the frontal lobes are recruited even during task conditions absent of requirements for abstraction representations when task difficulty is increased to comparable levels (Crittenden and Duncan, 2014). These results suggest that other examinations which have compared level of abstraction across task conditions, such as those cited in Badre and D'Esposito's (2009) review, may have produced results suggesting a rostrocaudal hierarchy simply because holding complexity due to task difficulty was not held constant between levels of abstraction.

Figure 8

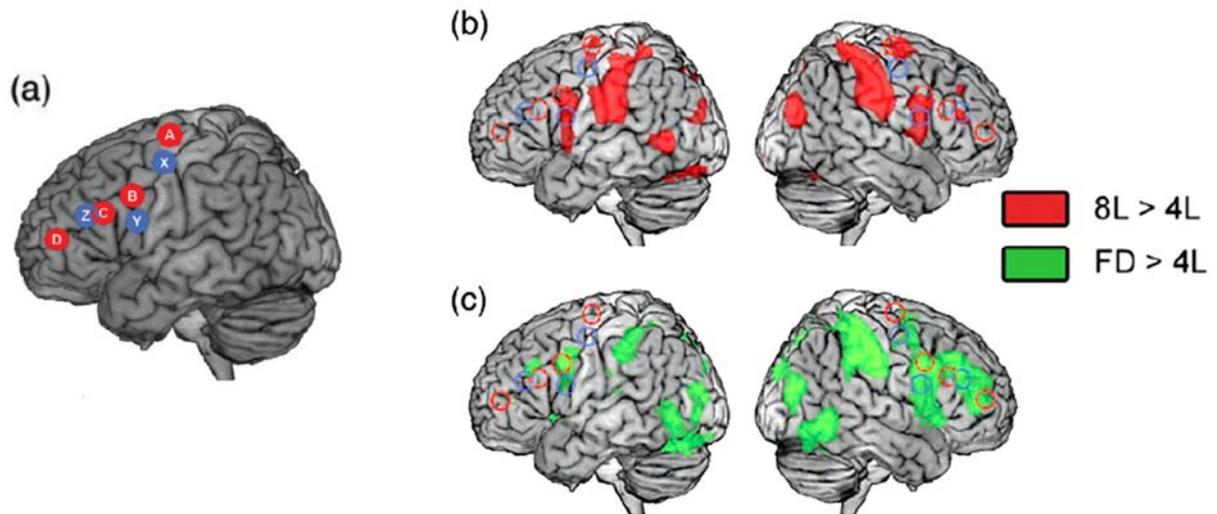


Figure 8. Figure 8 shows the findings from Crittenden and Duncan (2014). The rendering on the left (a) reiterates the reported foci from Badre and D’Esposito’s (2009) rostrocaudal hierarchy, with increasing task demands from separate experiments labeled in alphabetical order, respectively. These ROIs are overlaid on the results of Crittenden and Duncan’s (2014) investigation. The top right rendering (b) shows the results of the initial contrast which examines the effect of increasing the stimulus-response mapping complexity. The bottom right rendering (c) shows the results of a second contrast which examines the effect of increasing fine discrimination complexity.

Rationale

Although Badre and D’Esposito’s (2007) study strongly suggested that increase conflict monitoring was not modulating the rostrocaudal gradient effects observed, Crittenden and Duncan (2014) demonstrated that the effect of increasing the task difficulty in other domains

(i.e., fine discrimination) can lead to increases in anterior PFC activity. Given this recent development, a re-examination of Bunge et al.'s (2003) finding would suggest that the predominantly cited result regarding neural circuits subserving abstract rule use better fits the predictions of the MDA model, as compared to the Rostro-Caudal hierarchy hypothesis. Although Bunge and Zelzano (2006) provide a compelling reconciliation of these prior findings regarding the use of abstract rules, a direct comparison of concrete and abstract rules, in which task difficulty can be manipulated orthogonally, would serve to provide an interesting comparison of the predictions of the MDA and the rostrocaudal hierarchy models. Furthermore, such an approach would address several key limitations in Bunge et al.'s (2003) examination and provide further assessment of the differences in processing and neural underpinnings which subserve abstract rule use.

In a recent comparative study, Goodman, Magnotti, Wright, & Katz (2012) used a simultaneous two-item same/different task to directly compare abstract rule performance in humans using identical visual stimuli and comparable task methods to those implemented in non-human species (i.e., rhesus monkeys, capuchin monkeys, pigeons). Human participants were trained in a nearly identical task with the training set-size (2, 8, trial unique) was manipulated between groups. Like non-human versions of the task, two vertically aligned pictures and a small white box appeared on a touch-screen computer monitor in an L-shaped configuration. A forced-choice response to either the lower picture, for same trials, or the white box, for different trials, was required. Points appeared on the screen at all times and, paired with a tone, incremented increases occurred following correct responses. Participants were instructed that they would be using a touch screen and to complete the task, fully, until an end screen appeared. After a training phase, all groups received novel item trials intermixed with the training trials. The

results of these experiments show high proportions of participants reaching the performance criterion as well as full transfer suggest that, unlike all other non-human animals trained in an equivalent task, humans more readily use a, abstract, relational strategy and are highly resistant to memorizing relationships between individual configurations and correct responses.

An additional comparison condition was introduced, termed the pseudo-concept condition, in which all aspects of the task were identical to the actual conceptual conditions, except individual training image configurations from the 8-item training set-size were arbitrarily assigned a correct response. The purpose of implementing this pseudo-concept condition, in addition to the true-concept conditions, was to assess how readily, if at all, participants would form an item-specific strategy when correct responses were not exclusively based on the relationship of those images. Additionally, this condition would provide indication whether any training manipulations could impact the use of an abstract rule strategy when participants were introduced to novel items. The results of this manipulation revealed a significantly lower proportion of participants (.20) which reached the same performance criterion 75% accuracy as compared to the initial task (.72). Additional participants were included until the sample size of participants reaching the training performance criterion was equivalent to those in the 8-item true-concept groups. Of those participants, a failed transfer to novel items was observed, demonstrating that, under such conditions, humans would come under control of item-specific rules in a same/different task variant, even without being explicitly told to do so (Goodman et al., 2012). By examining how readily humans formulate and utilize a relational-based or item-specific-based strategy under varying task conditions, direct comparisons were made possible to Rhesus Monkeys and Pigeons based on an analogous task assessing effects of training set-sizes on transfer performance (e.g., Wright & Katz, 2006; Daniel, Wright, & Katz, In prep).

By adapting Goodman and colleague's (2012) task for use in the scanner, this novel approach should allow for several new comparisons to address limitations of Bunge et al (2003). First, this approach would eliminate the possible confound of increased memory load between match and non-match rules from Bunge et al. (2003). In this previous method, for example, participants admitted to using reversal of matching rules to respond to trials in which a non-match rule was appropriate. Because of this potential default strategy implemented by participants when the non-matching rule was prompted, it is possible that the same matching rule was maintained during delays with an added conditional variant of respond on the alternate hand-held buttons. This increased memory load between match and non-match conditions exists as a confound between comparisons of these rules types and may have led to the increased activity observed. Secondly, by implementing the non-alternating two-alternative forced-choice response from Goodman et al.(2012), as opposed to the reversed button responses used Bunge and colleagues,(2003), better comparisons between same and different judgments are possible including reaction times and neural correlates compared in simpler designs. This adaptation allowed for separate task runs for assessments of item-specific and relational rule use, rather than asking participant to switch strategies within runs. In doing so, the current study's experiments help to rule out any response monitoring effects from this task switching which may have affected the results in Bunge et al. (2003). Additionally, once the initial item-specific rule cue was presented in Bunge et al. (2003), participants need not attend to the images at decision. This difference in sustained attention and preparing for subsequent judgments, during delays may also contribute to differences in PFC activity observed between abstract and concrete rules. Another key limitation this novel methodology addressed was the potential for greater elaboration between variants of abstract rules (i.e., match, non-match) which may have led to the FPC

modulations observed in Bunge et al. (2003) during rule maintenance. Finally, this adaptation increased the demand on working memory load, independent of degree of abstraction. By increasing the number of stimulus-response rules participants must memorize, the effects of increased task difficulty via greater demand on memory load could be assessed and compared to increased demand due to abstractness. These simple associations followed a similar format of the pseudo-concept methods used by Goodman and colleagues (2012) which utilized identical stimulus presentations for item-specific memorizations as those used in abstract rule conditions, as well as variable mapping of items to prevent differences in sustained attention between trail types.

Chapter 2: Experiments

Experimental overview

The goals of the following experiments are both to assess whether increased memory load demonstrates increased measures of effort in a concrete rule-use task, and whether this increased effort would correspond to distinct profiles of neural modulations when compared to the neural correlates of the analogous abstract rule task. Memory load was manipulated via increasing stimulus set-sizes in the concrete task. In experiment 1, a mixed-model within- and between-subject design assessed the use of abstract and concrete rules for varying stimulus set sizes, respectively, on performance in the task. Following the demonstration of an interaction between set-size and rule-type in experiment 1, a new task was adapted which utilized a within-subjects manipulation for both factors of rule-type and stimulus set-size. Because within-subjects designs are optimal in studies which utilize fMRI data acquisition, experiment 2a tested whether this same functional interaction could be observed prior to testing in the MR scanning environment. Following the demonstration of a within-subjects interaction between set-size and rule-type in experiment 2a, experiment 2b implemented the newly adapted version of the task during fMRI data acquisition in order to assess the neural modulations associated with the manipulations of rule-type, stimulus set-size, and their interaction.

Experiment 1

The goal of Experiment 1 was to test whether increased numbers of stimuli affects difficulty in a concrete rule task but not an abstract rule task. Increasing the number of stimuli used in the concrete rule task necessarily increases the number of item-specific rules which must

be learned to complete the memorization task. Accordingly, task conditions which require the use of larger memory loads should be accompanied by increased demands. In order to confirm this relationship, it was hypothesized that accuracy of responding would decrease across the set-size manipulation in the concrete rule task. This same increase in stimulus set-size for the abstract version of the task should not lead to such an increase in the number of item-specific rules, because the *same* and *different* rules can be applied in a general and abstract manner. Accuracy in responding was hypothesized to remain constant across stimulus set-size because the number of flexibly applied, abstract rules (2) remain constant and do not depend on the item-specific associations that concrete rules require. Sessions containing 4, 8, or 16 pairs of images were created to assess the potential effects of increased effort across this stimulus set manipulation for a concrete rule task. Sessions containing 8, 16, or Unique pairs of images were created to assess the potential effects of increased effort across this stimulus set manipulation for an abstract rule task. Concrete rule and abstract rule task sessions containing both 8 and 16 image pairs were comprised of identical pairings, however correct responding in each task depended on these different rule types. The justification for an asymmetry in pairs of images for the 4 pair concrete condition and the Unique pair abstract rule condition are two-fold. First, because a Unique Pairs concrete rule session would require subjects to learn responses associated with 48 unique pairings and it is highly unlikely that participants would reach the performance criterion with only three training sessions. Second, task performance in these comparison conditions is not meant to assess responding when the image pairs are held constant between abstract rule and concrete rule conditions. Both the Unique Pairs, abstract rule performance and the 4 rule, concrete rule performance provided third measures for analysis of functional relationships on performance results for both tasks.

Method

Participants

Participants (N=24) were Auburn University undergraduates, with ages ranging from 19 to 27, enrolled in a psychology course. Participants were recruited via SONA systems website (auburn.sona-systems.com). All participants provided informed consent prior to beginning the experiment. The Auburn University Institutional Review Board approved all details of the protocol prior to beginning data collection.

Apparatus

Participants were tested in an unlit room, seated 30-cm away from a 17-in LCD monitor (1280 x 1024). All experimental events were controlled by a PC using a custom program created using E-prime 2 software (<http://www.pstnet.com/eprime.cfm>). All responses were recorded using a standard computer keyboard.

Stimuli

The stimuli were comprised of personal travel color images, cropped to 250 x250 pixels using Adobe Photoshop®, depicting various scenes (for examples see figure 9) determined by the experimenter to be relatively neutral in affective range. At the start of each trial, a small white fixation cross (100 x 100 pixels) was displayed at the center of black screen. Samples and probes appeared, centered on the monitor, sequentially and spaced by a 2000 ms delay on the same black background (adapted from Bunge et al., 2003). During choice (3000 ms), a prompt appeared centered on the black screen in size 40, white font, “1 or 2?” Feedback of “Correct!” or “Incorrect” appeared in the same font size and colored green or red, respectively, following each

response. In the event that no response was detected after 3000 ms, feedback of “No response detected” appeared in size 18 font and colored white.

General Procedure

Figure 9



Figure 9. Figure 9 depicts example images used as stimuli in both abstract and concrete rule tasks.

Participants were randomly assigned into one of three groups ($n=8$ per group). The progression of training and testing for each group can be seen in Table 1. Each group was further subdivided into one of two possible task progressions to control for potential order effects. Task progression 1 ($n=4$) consisted of participants who were given the Concrete Rule Task, Transfer Test A, the Abstract Rule Task, and Transfer Test B. Task progression 2 ($n=4$) consisted of participants who were given the Abstract Rule Task, and Transfer Test B Concrete Rule Task, and Transfer Test A. Transfer test A and Transfer Test B each contained a unique set of novel images and were used to test for use of relational strategy (i.e., novel item testing). Following

each Phase 1 transfer test, instructions and training for Phase 2 commenced after a 5 minute break.

Table 1

Progression	Group	Phase 1	Transfer Test	Phase 2	Transfer Test
1	Comparison group	4 Paired-item Concrete Rule Task	A	Unique Pairs Abstract Rule Task	B
1	4-item group	8 Paired-item Concrete Rule Task	A	8 Paired-item Abstract Rule Task	B
1	8-item group	16 Paired-item Concrete Rule Task	A	16 Paired-item Abstract Rule Task	B
2	Comparison group	Unique Pairs Abstract Rule Task	B	4 Paired-item Concrete Rule Task	A
2	4-item group	8 Paired-item Abstract Rule Task	B	8 Paired-item Concrete Rule Task	A
2	8-item group	16 Paired-item Abstract Rule Task	B	16 Paired-item Concrete Rule Task	A

Note. Rows depict the progression for each of the three experimental groups sub groups (n=4) by phases.

The comparison group received both a simple, 4 paired-item concrete rule task and Unique Pairs (i.e., novel images for each trial) abstract rule task. The remaining two groups also received both an abstract and concrete rule version of the task comprised of either an 8 or 16 paired-items. Each group received the same written instructions prior to beginning the task:

“In a moment you will begin several tasks that require you to make a response on the “1” or “2” keys depending on images appearing on the monitor. During the Same or Different Judgment task, you will be instructed to make your responses based on whether pictures appearing on the monitor are the *same* or *different*. During the Memorizing Pairs of Images task, you will be instructed to make your responses based on specific imaging pairs you have memorized. You will receive feedback for your responses in either task. You will be asked to repeat the training task if your level of accuracy is not high enough. Toward the end of the task, you will see several new images without feedback for your responses. Please

respond to these images using whichever strategy guided your responding during the preceding task. If you are ready to proceed, please let the experimenter know that you do not have any questions.”

After reviewing task instructions, participants completed 48 trial sessions which were generated in randomized order, without replacement, for each participant. Trials were counterbalanced such that each session contained an equal number of 1 and 2 responses and each pair of images appeared an equal number of times with the constraint that each block of 4 trials must contain 2 *same* and 2 *different* trial types. General trial progressions are seen in figure 10. Each trial began with the presentation of a fixation cue (1000 ms) followed by the presentation of sample item (500 ms). After a variable probe delay (2000 ms, 3000 ms, 4000 ms) in which the sample was removed, a probe item was presented (500 ms). The choice period (3000 ms) began with the termination of the probe presentation. Participants responded on either the “1” or “2” key within the 3000 ms choice period or the trial was scored as incorrect. Respective of whether a correct or incorrect choice was been recorded, written visual feedback was presented (500 ms) following the choice period. The trial then progressed to a brief (3000 ms) inter-trial interval (ITI) before the next trial began.

In the event that a participant did not reach the 80% criteria (greater than or equal to 40 responses correct out of 48), they received a prompt screen to notify the experimenter. At this point, the experimenter asked if there were any questions before restarting the task. The participant was then given another randomized session with a different trial order than the previous one. Participants were allowed to repeat training sessions for a maximum of three tries before being dismissed and excluded from the study, however no participants in the current study

exceeded this limit. Following training sessions in which the performance criterion was reached, all participants were then progressed to novel item testing continuously from the last trial of the training session.

Figure 10

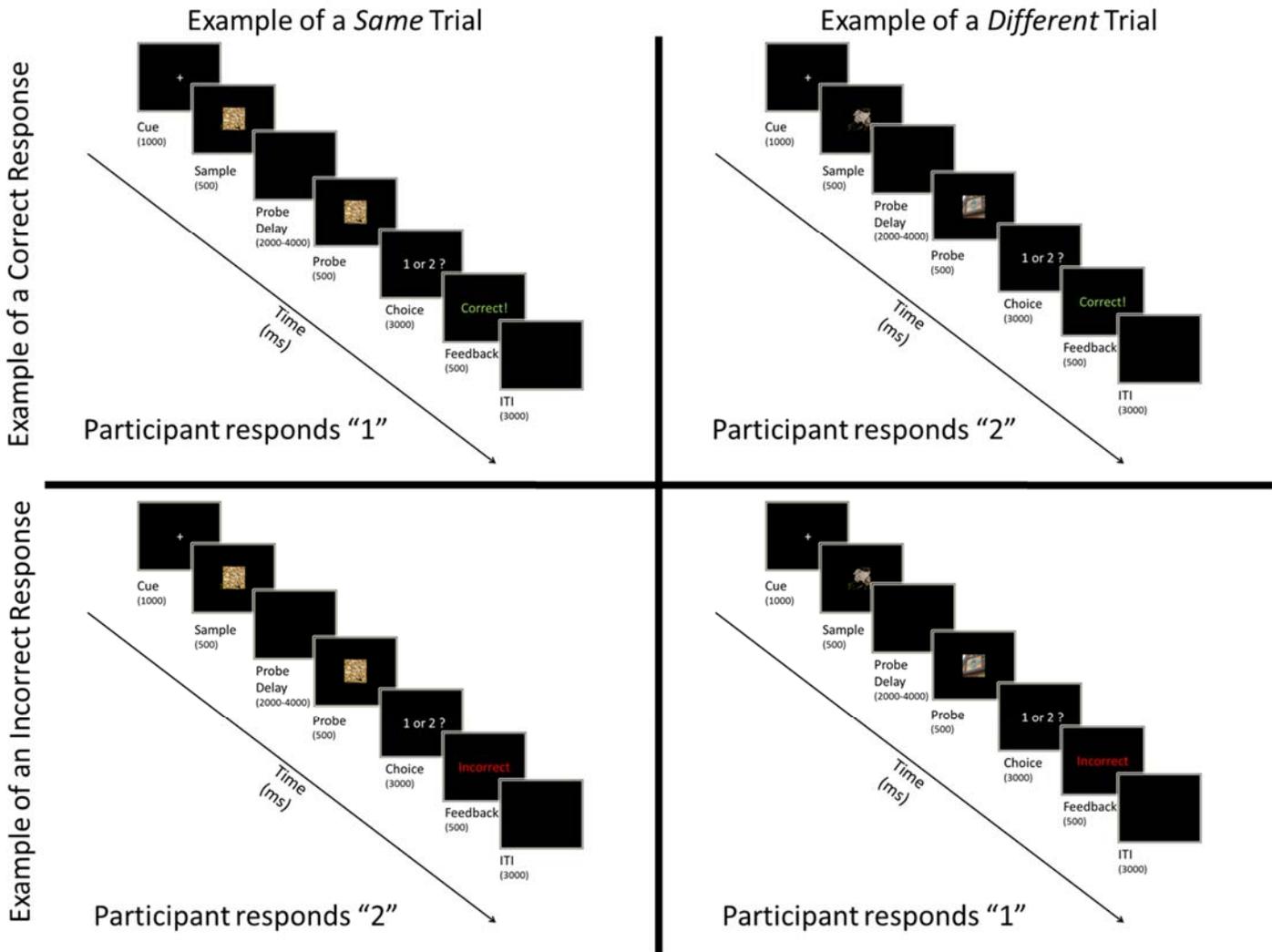


Figure 10. Figure 10 shows the trial progression used in both concrete- and abstract-rule task conditions of experiment 1. In all four panels, example trial responses reflect outcomes of only the abstract-rule task. The left panels show an example of a *same* trial and the right panels show

an example of a *different* trial. The top panels show an example of a correct response and outcome for either trial type and the bottom panels show an incorrect response and outcome for either trial type.

Novel-item Testing Phase. 12 total Transfer trials (6 same, 6 different) containing novel images appeared with 6 left correct and 6 right correct responses during both Transfer test A and Transfer test B. Transfer test A always followed the Concrete rule task and Transfer test B always followed the Abstract rule task. Regardless of which group that participants were assigned to, each participant received identical transfer test trials following training in each phase of experiment 1. The 12 novel item pairs were unique for Transfer test A and Transfer test B, however the same items were used across training groups (Comparison, 8 paired-items, 16 paired-items). The custom written program randomly selected these trials without replacement. The stimuli were novel images from those shown during training and appeared in the same dimensions and position as the training items. Responses were recorded as correct and incorrect based on 1 key presses for same trials and 2 key presses for different trials, however, no feedback was be given during these trials. All other aspects of these trials were identical to training trials.

Task Training Procedures

Phase 1: Concrete Rule Task. For the concrete rule task, all participants were given instructions prior to beginning the task in which they were explicitly shown item-specific rules that determine correct responding in the task (see figure 11 for instructions and configuration response assignment). For the 4 paired-item group, each of the four unique pairings appeared 12 times during training. For the 8 paired-item group, each of the eight unique pairings appeared six

times during training. For the 16 paired-item group, each of the 16 unique pairings appeared three times. Correct responses for all versions of the concrete rule task were arranged

Figure 11

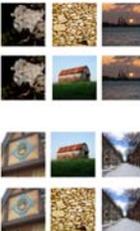
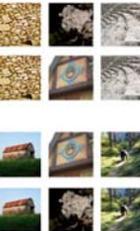
4 Paired-item set		8 Paired-item set		16 Paired-item set	
<p>Memorizing Pairs of Images Task: Below you will see 2 categories of pictures pairings. Each of the pairings represent pictures that you will view in a sequence (i.e., top picture first then bottom) followed by a prompt to make a response on button 1 or 2 during the task. You will press <u>button_1</u> after viewing a sequence of images appearing in the left column, labeled, "Press Button 1". You will press button 2 after viewing a sequence of images appearing in the right column labeled, "Press Button 2". Please try to respond as quickly and accurately as possible. If you understand these instructions, press any key to continue.</p>		<p>Memorizing Pairs of Images Task: Below you will see 2 categories of pictures pairings. Each of the pairings represent pictures that you will view in a sequence (i.e., top picture first then bottom) followed by a prompt to make a response on button 1 or 2 during the task. You will press <u>button_1</u> after viewing a sequence of images appearing in the left column, labeled, "Press Button 1". You will press button 2 after viewing a sequence of images appearing in the right column labeled, "Press Button 2". Please try to respond as quickly and accurately as possible. If you understand these instructions, press any key to continue.</p>		<p>Memorizing Pairs of Images Task: Below you will see 2 categories of pictures pairings. Each of the pairings represent pictures that you will view in a sequence (i.e., top picture first then bottom) followed by a prompt to make a response on button 1 or 2 during the task. You will press <u>button_1</u> after viewing a sequence of images appearing in the left column, labeled, "Press Button 1". You will press button 2 after viewing a sequence of images appearing in the right column labeled, "Press Button 2". Please try to respond as quickly and accurately as possible. If you understand these instructions, press any key to continue.</p>	
Press Button 1	Press Button 2	Press Button 1	Press Button 2	Press Button 1	Press Button 2
					

Figure 11. Figure 11 shows examples of instructions given prior to training for 4 paired-item, 8 paired-item, and 16 paired-item versions of the Concrete rule task.

such that the use of abstract, relational judgments could not produce correct responding in the task and attending to either samples or probes alone, could not produce accurate responding. For both 8 and 16 paired-item versions of the task, an additional stipulation was added which required that each image appeared as sample or probe in equal proportions for either correct response type. These criteria were designed to ensure participants maintained visual attention throughout the entire trial progression and were forced to memorize the pairs of images in order to reach high levels of accuracy in the task. For example, a participant could not memorize a single response associated with the barn image, as this image might signal a correct “1” or “2” key response. Furthermore, ignoring the image paired with barn (i.e., barn, or rocks) and trying

to memorize a response based on whether barn appeared first or second could not produce accurate responding in the task as this image appeared in both the sample and probe positions of both “1” and “2” key correct responses.

Phase 2: Abstract Rule Task. For the abstract-rule task, participants were told that they are about to complete a judgment of same or different images task (see figure 12 for instructions and configuration response assignment). Correct responses for the abstract-rule task depended solely on the identity relationship between images presented in succession. For the 8 paired-item

Figure 12

Unique Paired-item set		8 Paired-item set		16 Paired-item set	
<p>Judgment of Same or Different Images Task: Below you will see 2 categories of pictures pairings. Each of the pairings represent example pictures that you will view in a sequence (i.e., top picture first then bottom) followed by a prompt to make a response on button 1 or 2 during the task. You will press <code>button_1</code> after viewing a sequence of images appearing in the left column, labeled, "Press Button 1". You will press button 2 after viewing a sequence of images appearing in the right column labeled, "Press Button 2". Please try to respond as quickly and accurately as possible. If you understand these instructions, press any key to continue.</p>		<p>Judgment of Same or Different Images Task: Below you will see 2 categories of pictures pairings. Each of the pairings represent pictures that you will view in a sequence (i.e., top picture first then bottom) followed by a prompt to make a response on button 1 or 2 during the task. You will press <code>button_1</code> after viewing a sequence of images appearing in the left column, labeled, "Press Button 1". You will press button 2 after viewing a sequence of images appearing in the right column labeled, "Press Button 2". Please try to respond as quickly and accurately as possible. If you understand these instructions, press any key to continue.</p>		<p>Judgment of Same or Different Images Task: Below you will see 2 categories of pictures pairings. Each of the pairings represent pictures that you will view in a sequence (i.e., top picture first then bottom) followed by a prompt to make a response on button 1 or 2 during the task. You will press <code>button_1</code> after viewing a sequence of images appearing in the left column, labeled, "Press Button 1". You will press button 2 after viewing a sequence of images appearing in the right column labeled, "Press Button 2". Please try to respond as quickly and accurately as possible. If you understand these instructions, press any key to continue.</p>	
Press Button 1	Press Button 2	Press Button 1	Press Button 2	Press Button 1	Press Button 2

Figure 12. Figure 12 shows examples of instructions given prior to training for Unique paired-item, 8 paired-item, and 16 paired-item versions of the Abstract rule task.

item group, each of the 16 unique pairings appeared three times. For the Unique paired-item group, each of the unique pairings (48 pairs) appeared only once during training.

Data Analysis and Preparation

Training. In order to confirm that the increase in training set-size leads to selective increased task effort in Experiment 1, dependent measures of percent correct for all 48 trial responses during the training sessions in which the performance criterion was reached were calculated and compared for the concrete rule and abstract rule task conditions. Percent correct was calculated by determining the number of correct responses and dividing this amount by the total number of training trials (48 trials) and multiplying that proportion by 100 for each participant. Because the comparison group received the lowest number of pairs in the concrete rule task and the highest number of pairs in the abstract rule task, it would not be meaningful to directly compare the tasks for this group in an analysis in which the number of pairs is held constant for this comparison between other groups (i.e., 8 pair and 16 pair groups). Accordingly, two analyses were performed to assess the between-subjects effects of image set-size for abstract and concrete rule conditions individually.

The first set of analyses were aimed to assess the effects of the paired image set-size as a continuous variable to assess differential trends concrete rule task and the abstract rule task. For the concrete rule task, the comparison group completed a simple, 4 rule task designed to replicate Bunge et al's. (2003) original concrete rule condition. A one-way, between-subjects ANOVA was used to assess the main effect of Image pairs (4, 8, 16) on the percent correct for sessions in which participants reached criterion. It was hypothesized that increasing the stimulus set-size would lead to greater difficulty in the concrete rule task as confirmed by the analysis yielding a significant effect of image set-size on percent correct performance measures. For the abstract rule task, the comparison group completed a Unique Pairs task designed to assess performance under conditions in which no trial was repeated, and accurate performance could in no way be determined by memorization (i.e., concrete rules). A one-way, between-subjects ANOVA was

used to assess the main effect of Image pairs (8, 16, Unique) on the percent errors for sessions in which participants reached criterion. It was hypothesized that increasing the stimulus set-size would not lead to greater difficulty in the abstract rule task as confirmed by this analysis failing to yielding a significant effect of image pairs. If the hypothesis was incorrect, increased difficulty as a function of image pair set-size would be evidenced by a significant effect of image pairs on performance in the abstract rule task. By including the anchor values of the 4 item concrete rule task and the Unique pairs (48 item) abstract rule task to assess the effects of image pairs, first set of analyses provided analysis of trends in performance which was hypothesized to differ across these manipulations in the concrete task but not the abstract task.

Testing. In order to confirm the use of abstract, relational rules and item-specific, concrete rules in each respective task condition, a three-way mixed model Task (Abstract rule, Concrete rule) and Group (Comparison, 8, 16) and trial type (Baseline, Transfer) on the percent of correct trials assessed whether novel-item performance differed from baseline as a function of task or number of image pairs. Baseline accuracy was determined by calculating percent correct for the final 12 trial block of sessions in which participants reached criterion. Responses from these trials were compared to novel-item trials because accuracies derived for transfer performance were based on 12 trials and were administered in temporal proximity. Accuracy results of these transfer tests were hypothesized to correspond to the respective training condition (Abstract-rule, Concrete-Rule) as evidenced by failures to apply a relational rule (i.e., chance performance on novel item-trials) during testing following the Concrete Rule task, and full transfer of relational rules (i.e., novel-item performance equivalent to that of trained item trials) during testing following the Abstract Rule task. If this hypothesis was correct, the outcome of the three-way ANOVA would be a two-way interaction of Task and Trial type. There would be no

main effects or interactions of Group, as this manipulation would not lead to significant differences in accuracy between baseline and transfer trial types, regardless of the number of image pairs used in the concrete rule task. If the hypothesis that image pairs does not affect novel-item performance was incorrect and the number of image pairs does affect differences between transfer and baseline performance, interactions and main effects of group would be expected. Additionally, if the hypothesis that tasks preceding transfer tests do not affect whether relational rules are applied to novel items, there would be a non-significant interaction between task and trial type.

Results.

Training. Figure 13 shows mean percent correct for participants trained with 4, 8, and 16

Figure 13

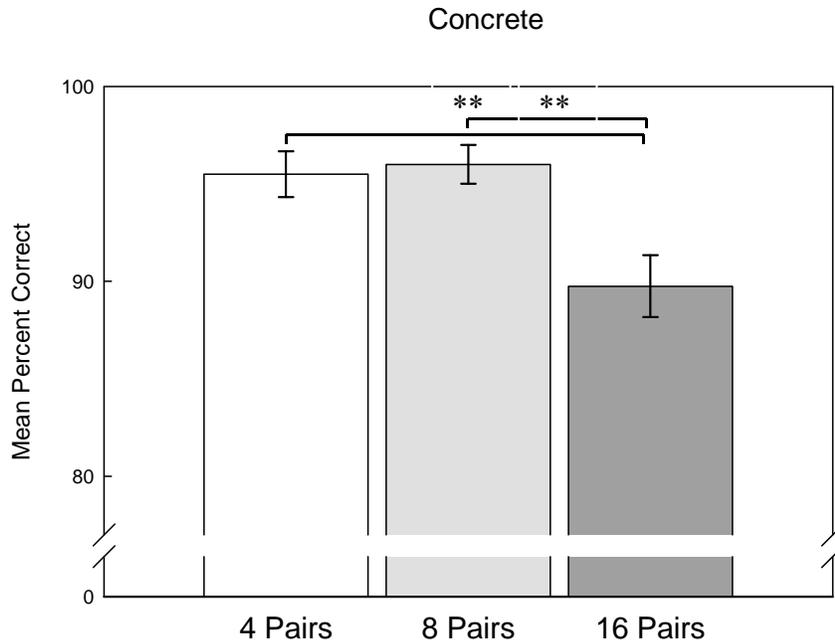


Figure 13. Figure 13 shows the mean percent correct across groups trained with either 4, 8, or 16 paired images in the concrete rule task. Performance was based on sessions in which

participant's reached the 80% performance criterion. Error bars represent 1 standard error of the mean (SEM). ** $p < .01$.

image pairs in the concrete rule task. Mean percent correct did not differ for 4 pairs and 8 pairs, but decreased for 16 pairs. This finding was confirmed a one-way between-subjects ANOVA of Image pairs (4, 8, 16) on percent correct, which yielded a significant effect of image pairs, $F(2, 23) = 7.36, p < .01, \eta^2 = .70$. Post-hoc tests found only significant differences when comparing percent correct for the 4 pairs and 16 pairs groups and when comparing the 8 pairs and 16 pairs groups, with mean differences > 5.70 , all $ps < .01, ds > 1.49$.

Figure 14 shows mean percent correct for participants trained with 8, 16, and Unique pairs

Figure 14

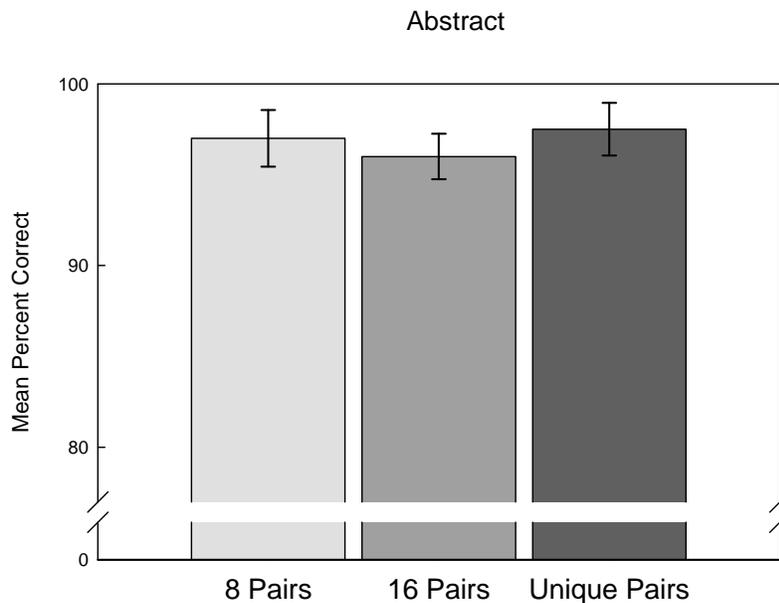


Figure 14. Figure 14 shows the mean percent correct across groups trained with either 4, 8, or 16 paired images in the abstract rule task. Performance was based on sessions in which participant's reached the 80% performance criterion. Error bars represent 1 standard error of the mean (SEM).

image pairs in the abstract rule task. Mean percent correct did not differ for 8 pairs 16 pairs and Unique pairs. This finding was confirmed a one-way between-subjects ANOVA of Image pairs (8, 16, Unique) on percent correct, which yielded a non-significant effect of image pairs, $F(2, 23) = 0.29, p = .75$.

Testing. Figure 15 shows the comparison of transfer and baseline trial performance across abstract and concrete tasks across groups. Across each of the abstract rule conditions,

Figure 15

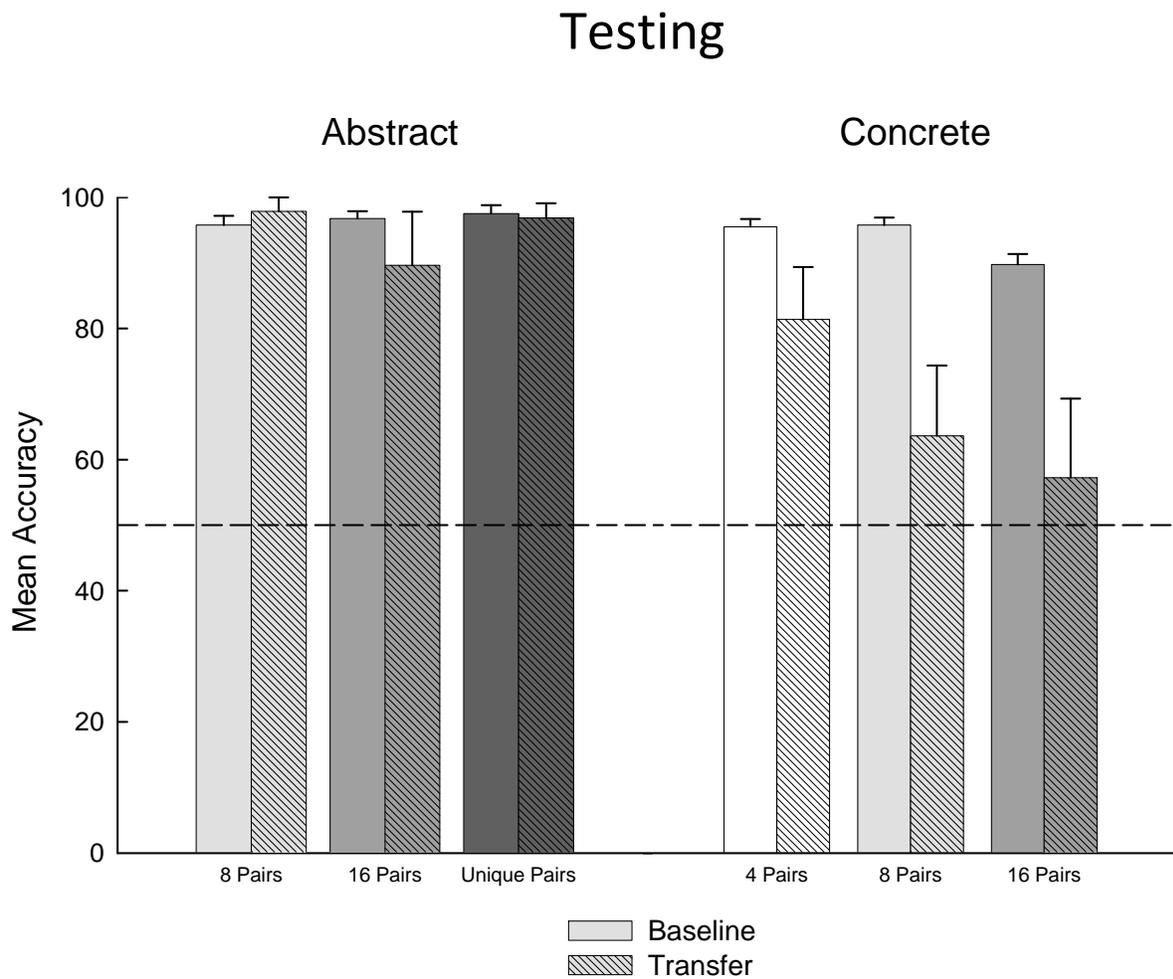


Figure 15. Figure 15 shows the mean percent correct, separated for transfer and baseline trial

performance, across groups for both the abstract rule and concrete rule tasks. Regardless of the training conditions, transfer trial performance was calculated based on “1” responses for a same trial and “2” responses for different trials. Baseline performance was based on the final 12 trials of training for sessions in which participant’s reached the 80% performance criterion. Error bars represent 1 standard error of the mean (SEM).

participants did not differ in performance for baseline and transfer. Mean percent correct for transfer trials did not differ when compared to baseline trials in the 8 pairs, 16 pairs, and Unique pairs conditions. Across each of the concrete rule conditions, mean percent correct for transfer trials was lower when compared to baseline trials in the 4 pairs, 8 pairs, and 16 pairs conditions. These findings were confirmed by a three-way mixed model Task (Abstract rule, Concrete rule) and Group (Comparison, 8, 16) and trial type (Baseline, Transfer) on percent correct, which yielded a significant interaction of task and trial type, $F(1, 21) = 20.66, p < .001, \eta_p^2 = .50$, and significant main effects of trial type, $F(1, 21) = 13.33, p < .01, \eta_p^2 = .39$, and task, $F(1, 21) = 32.73, p < .001, \eta_p^2 = .61$. All remaining interactions and main effects were not significant, all $F_s < 1.81$, all $p_s > .19$.

Experiment 1 Discussion.

Critically, these results demonstrated task difficulty can be manipulated via increasing the memory load, which was the primary reason for conducting Experiment 1. The outcomes of the training performance provided strong evidence that increased difficulty is needed to complete the concrete rule task as memory load was increased between groups. Importantly, these same effects were not observed for the abstract rule task performance, establishing that the effects observed across image pairs in the concrete rule task were not simply due to increased variability in images utilized in training. The results of the testing which commenced following sessions in

which participants reach the performance criterion validates the strategies utilized by participants matched the abstract and concrete training conditions rather than task names reflecting merely experimenter's intentions. With the additional assessment of novel item performance, it was confirmed that participants used item-specific, memorization strategies for the concrete rule task in contrast to use of a relational judgment strategy during the abstract task. Upon confirming the strategies used by participants, the effects of image pairs observed in the task training performance suggests that increasing the number of item-specific rules does lead to increased difficulty in the concrete task.

There are several important limitations of these findings which pertain particularly to the implementation of the tasks from Experiment 1 in the MR scanning environment. Foremost, Experiment 1 examined between-subjects effect of increasing memory load and number of image pairing. Experiment 1 only implemented a single within-subjects comparison, which examined differences in performance as a function of task rules using identical image pairs. For optimal fMRI task design, it is critical that all of these comparisons are made within-subjects. Additional task development and testing is needed to determine whether the differential effects of image pairs, observed in Experiment 1 would be observed if these manipulations were assessed as within-subjects factors. Regardless of this limitation, Experiment 1 validates both the use of relational rules in the abstract but not the concrete task conditions, and the selective effects of image pair manipulations which increase task difficulty in the concrete rule tasks but not the abstract rule task.

Experiment 2a.

Experiment 1 demonstrated evidence that, while holding potential sources of variance constant (e.g., stimuli, prolonged attentional requirements, binary responses) between abstract and concrete rule tasks, the manipulation of increases in working memory load led to increased difficulty for correct responding during the concrete task. Given this outcome observed in Experiment 1, the goal of Experiment 2a was to examine whether this outcome could be observed under similar conditions as Experiment 1, with factors of set-size and task rule as within-subjects conditions for a sample size comparable to that of a typical BOLD fMRI study (n=12).

Several adaptations from Experiment 1 were made before piloting the task, on the basis of necessity for a repeated-measures task design. Novel-item testing was not included in Experiment 2 given that this testing served the utility of establishing strategy use in Experiment 1 and was not necessary for assessing performance in the tasks. Also, instead of common image pairings for both the abstract and concrete rule tasks which expand across image pair set-sizes, unique pairings were used for each task rule and set-size condition. This adaptation ensured that participants would not experience carry-over effects across manipulations which might influence strategy use (i.e., relational rules, memorization). Additionally, all pairings in the concrete rule task were constructed as non-identical image pairs. This adaptation removed the possibility that participants could use a combined relational and memorization strategy approach to responding in the concrete task. The number of item pairs for each set-size condition was changed to 8, 16,

and 32 paired-items in both the abstract and concrete rule tasks. This adaption was carried out to ensure optimal and robust comparisons between all set-sizes, given the lack of significant differences in Experiment 1 between 4- and 8-item concrete task accuracy. Accordingly, this adjustment reflects the experimenter's intention to capture significant differences in behavioral performance at each level of memory load increase. Furthermore, by testing experimental participants with identical set-size manipulations for concrete and abstract tasks, a balanced experimental design ensured ideal statistical comparisons between these manipulations across tasks. A final adaption for BOLD fMRI data acquisition was to include a task familiarization phase prior to training and testing to reduce the likelihood that acquiring information regarding instructions, task progressions, and correct response mapping would influence responding during initial runs of BOLD data acquisitions.

Piloting results (not reported) of these above mentioned adaptations yielded inconsistent findings to that of Experiment 1. Namely, of the $n = 66$ participants who initially completed Experiment 2a, the negative relationship between image pair set-size and accuracy in the concrete rule task conditions was not observed across all levels of memory load. Accordingly, one data driven adaption from Experiment 1 was carried out in order to ensure valid measures of increased memory loads were obtained in Experiment 2a. Although task conditions would ideally remain entirely randomized and counterbalanced across participants, task and set-size progressions were created which increased the set-size from small to large sets for all participants. This adaption ensured participants did not experience carry-over effects of large memory loads during testing for intermediate and small memory loads. Several additional adaptations to the task from Experiment 1 were made based on Crittenden and Duncan's (2014) approach to increasing task difficulty orthogonally to the level of task abstractness. Instead of

trial progressions which provided feedback immediately following each response, feedback was provided at the end of 16 second task blocks, in which trials were presented in rapid succession. This adaption ensured that participants respond to a maximal number of rule-use instantiations in a limited temporal duration by combining the feedback from all trial responses during each task block into a single report. Along a similar emphasis for increasing rule-use instantiations within each task block, item pair presentations were changed from a sequential presentation, to a rapid simultaneous presentation in a manner similar to line judgments from the previously discussed task demands (Crittenden & Duncan, 2014).

Method

Participants

12 Auburn University undergraduates enrolled in a psychology course were recruited via SONA systems website (auburn.sona-systems.com), with ages ranging from 19 to 22. As in Experiment 1, participants provided informed consent prior to beginning the experiment. The Auburn University Institutional Review Board approved all details of the protocol prior to beginning data collection.

Apparatus

The laboratory, software, and apparatus used in Experiment 2a were identical to those used in Experiment 1.

Stimuli

The personal travel color image stimuli, fixation cross, and choice response prompt were identical to those used in Experiment 1. Unlike Experiment 1, image pairs in Experiment 2a appeared simultaneously for 200 ms, vertically centered and equidistant (100 pixels) to the left and right of the central fixation cross. A 4-s count down was presented as single digits, and prior to each trial block’s onset. Feedback prompts which reported the number of correct responses (“Point Score”), incorrect responses (“Error Score”), appeared above a message which reminded participants to, “Please respond as quickly and accurately as possible” appeared following each block of trials. All written feedback, countdowns, and prompts appeared centered on the black screen in the same font size and color as choice prompts.

General Procedure

Before task familiarization training began, participants were randomly assigned into sequences of task blocks using a partial Latin square. This method was designed and implemented to ensure that for each set-size, the order in which participant’s complete abstract and concrete task blocks were counterbalanced. Each group received the same

Table 2

Participant	Set-Size 8		Set-Size 16		Set-size 32	
	Phase 1	Phase 2	Phase 3	Phase 4	Phase 5	Phase 6
1	Concrete	Abstract	Abstract	Concrete	Concrete	Abstract
2	Abstract	Concrete	Abstract	Concrete	Concrete	Abstract
3	Concrete	Abstract	Concrete	Abstract	Abstract	Concrete
4	Abstract	Concrete	Abstract	Concrete	Abstract	Concrete
5	Concrete	Abstract	Abstract	Concrete	Abstract	Concrete
6	Abstract	Concrete	Concrete	Abstract	Abstract	Concrete
7	Concrete	Abstract	Concrete	Abstract	Concrete	Abstract
8	Abstract	Concrete	Concrete	Abstract	Concrete	Abstract
9	Abstract	Concrete	Abstract	Concrete	Concrete	Abstract
10	Abstract	Concrete	Concrete	Abstract	Abstract	Concrete
11	Concrete	Abstract	Concrete	Abstract	Abstract	Concrete
12	Concrete	Abstract	Abstract	Concrete	Concrete	Abstract

Note. Rows depict the progression for each participant by phases.

written instructions on the PC monitor prior to beginning familiarization training sessions and task sequences:

“In a moment, you will be asked to complete several tasks. Before beginning testing in each task, you will be given instructions and training to help you learn each task's requirements. Some tasks will require to judge if pictures are the same or different and others will require you to memorize the pairs of pictures and an assigned response. Take as long as you need to familiarize yourself with the instructions prior to beginning the training session. After you proceed from the instructions, a timer will count down 5 seconds until you begin the session. Please be sure that you are prepared to begin the training session when the timer terminates. At different points throughout the experiment, you will view a small cross in the center of the screen. Please focus your eyes on the cross whenever it is present. During the tasks, avoid averting your gaze from the cross to the pictures as best as possible. During training, you will earn points for correct responses. If you respond incorrectly, you will accumulate errors. If you exceed 2 errors or earn fewer than 5 points in any session, you will see a message box informing you that you will be required to repeat the session. When you reach the end of the training session, you will see a feedback screen which informs you of the number of errors and points you accumulated during training. Following the completion of each training session, you will

proceed immediately to the testing session. Testing sessions will contain identical picture pairs and correct responses to that of the proceeding training session. During testing sessions, you should use whatever strategy you developed to complete the training session. Testing sessions will be repeated, similar to training, except you will not see the message box in between sessions viewed during training. Before each testing session, a timer will count down 4 seconds until you begin. Please be sure that you are prepared to begin the training session when the timer terminates. During testing, you must attempt to earn the highest number of score points before proceeding to the training for the next task. If you are repeating a task, there will be brief delays between these repetitions where you will receive feedback for your responses. As in training, your goal is to get the highest score and the fewest errors possible in the 16 seconds given to complete the sessions. You will know that you have moved on to the next task when you see a new set of instructions and picture pairings. Before you begin training and testing, you will be asked to complete several familiarization sessions designed to give you a chance to complete two training sessions similar to those appearing in the actual experiment. You will not be asked to complete any test sessions following a typical training session during these familiarization sessions.”

After reviewing the general task instruction participants began the 4-item concrete training familiarization session. Task instructions always appeared vertically full screen and can be seen for the concrete familiarization session in Figure 16. Trials for each task block were generated in randomized order, without replacement, for each participant. Within each task block, each cycle of 4 trials were counterbalanced such that two correct “1” and two correct “2” responses always occurred in random order for both abstract and concrete task conditions.

Figure 16

4 Paired-item set

Memorizing Pairs of pictures Task:
 Below you will see 2 categories of pictures pairings. Each of the pairings represent examples of picture pairs that you will view. You will press button 1 if you view a pair of pictures appearing in the left column, labeled, “Press Button 1”. You will press button 2 if you view a pair of pictures appearing in the right column labeled, “Press Button 2”. Please try to respond as quickly and accurately as possible. Take as long as you need to view the pairs. If you are ready to proceed, please press any button to continue.

Press Button 1	Press Button 2
<div style="display: flex; flex-direction: column; align-items: center; gap: 20px;">   </div>	<div style="display: flex; flex-direction: column; align-items: center; gap: 20px;">   </div>

Figure 16. Figure 16 depicts the task instructions and item-pairs for the 4-item concrete familiarization session.

General trial block progressions for Experiment 2a are seen in figure 16. Each block of trials began with the presentation of a countdown (1000 ms/digit) followed by the presentation of an item pair (200 ms). After the pairs were removed, the choice period began which contained the test “1 or 2?” centered on a black screen. The choice period terminated once a response was made and began the variable inter-trial interval (ITI). Following the variable ITI (500 ms, 1000 ms, 1500 ms), the next trial commenced with the presentation of a fixation cross (200 ms) on a black screen immediately followed by the next item pair. This cycle of trials repeated for 16

Figure 17

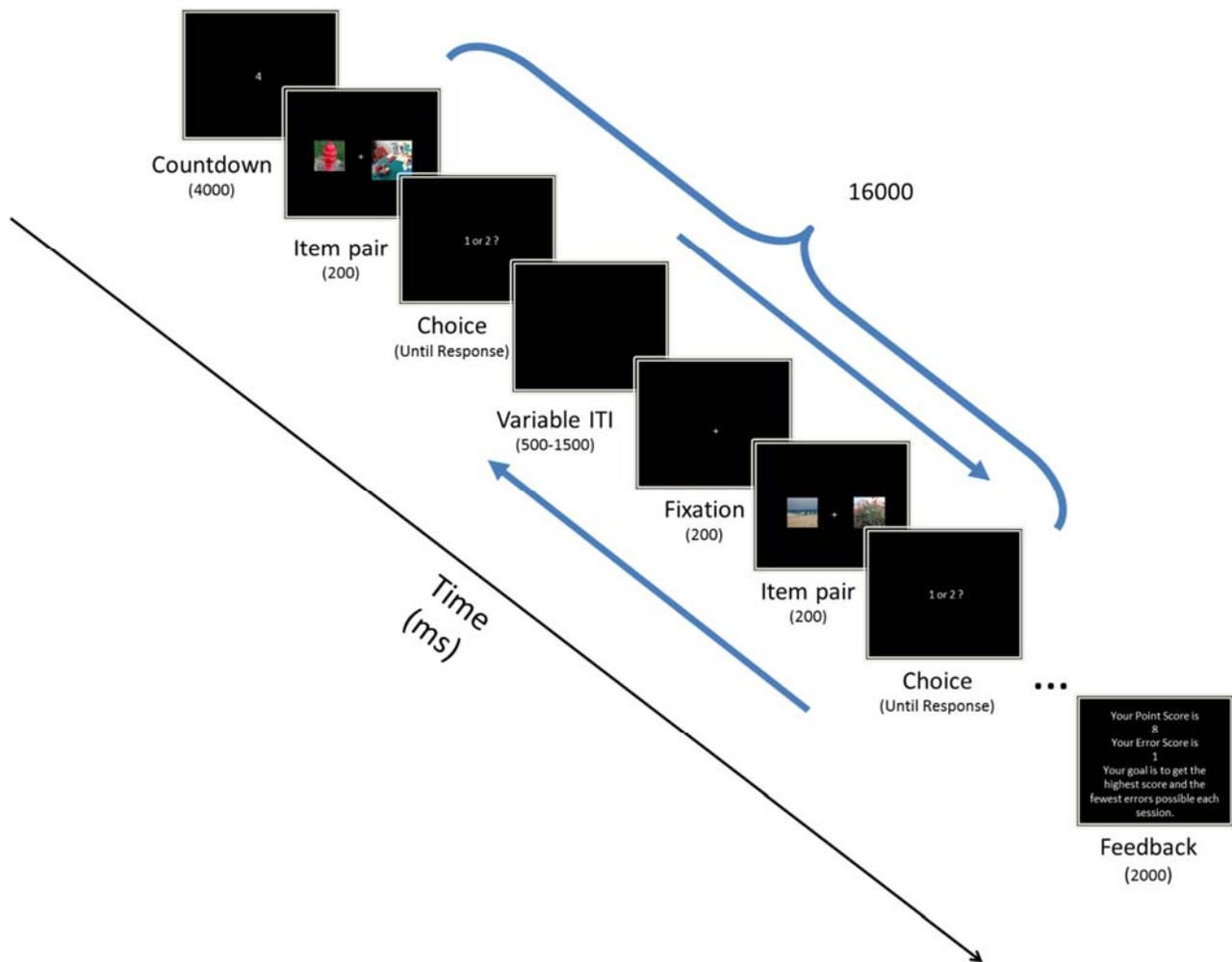


Figure 17. Figure 17 shows a typical trial block progression used in both concrete- and abstract-rule task conditions of Experiment 2a.

seconds and after the final response was made, the feedback screen immediately appeared. The feedback screen presented the total number of correct and incorrect responses and terminated after a 2 second duration.

In the event that a participant did not accumulate 5 or greater correct responses and 2 or fewer incorrect responses, a prompt screen appeared which conveyed that he or she would be required to repeat the training familiarization session based on the performance criteria. The participant was then given another randomized session with a different trial order than the previous one. Participants were allowed to repeat training sessions until the criteria was reached. Following training sessions in which the performance criterion was reached, all participants were then progressed to an instruction screen informing them that they had completed the concrete familiarization session and would now proceed to the next session. The 4-item abstract training familiarization session commenced immediately following the 4-item concrete training familiarization session. This session was identical to the previous familiarization session, with the exception that correct responses were determined by the relational properties of the item pairs. The instructions for the 4-item abstract training familiarization session can be seen in figure 18. Once participants completed both familiarization sessions, the following prompt appeared on the monitor:

“You have now completed the familiarization sessions designed to give you a chance to complete two training sessions similar to those appearing in the actual experiment.

Once you begin the actual experiment, you will be asked to complete testing sessions following each training session. Remember, each testing session will contain identical picture pairs and correct responses to that of the training session and instructions which you most recently viewed.

Figure 18

4 Paired-item set

Judgment of Same or Different pictures Task:
Below you will see 2 categories of pictures pairings. Each of the pairings represent examples of picture pairs that you will view. You will press button 1 if you view a matching or "same" pair of pictures. You will press button 2 if you view a non-matching or different pair of pictures. Take as long as you need to view the pairs. Please try to respond as quickly and accurately as possible. If you are ready to proceed, please press any button to continue.

Press Button 1	Press Button 2
 	 

Figure 18. Figure 18 depicts the task instructions for the 4-item abstract familiarization session.

Please note that the number of picture pairings will vary from task to task in the actual experiment.”

Participants then began to complete task runs outlined in Table 2.

Each task run began with an instruction screen followed by a training session similar to the training conditions for the familiarization sessions. The individual training instructions for each of the task runs can be seen in figure 19. Unlike the familiarization sessions, after each participant reached the performance criteria he or she viewed a feedback screen which notified them that the task training session was complete and they would now begin the testing sessions.

Figure 19

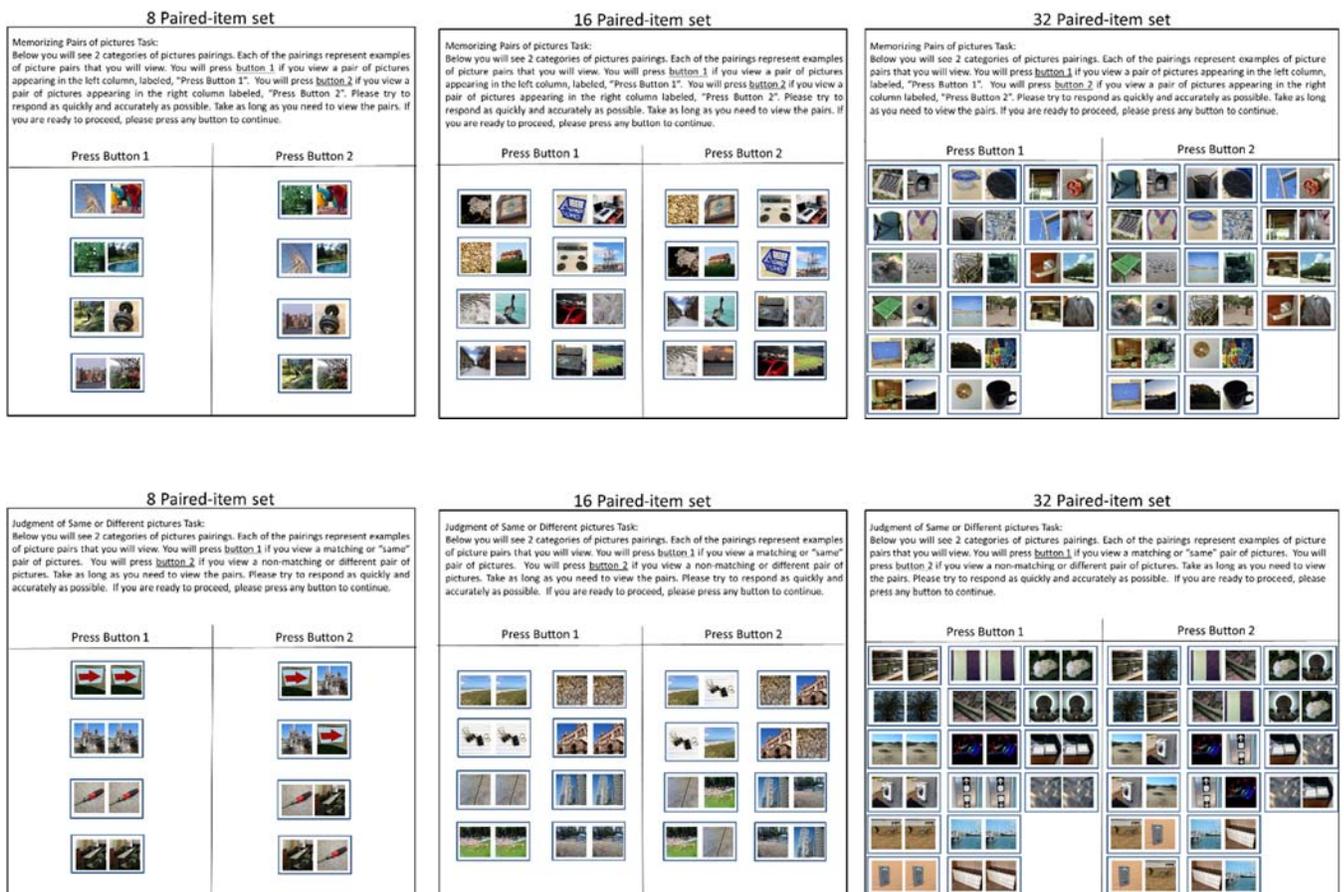


Figure 19. Figure 19 depicts the task instructions for each concrete and abstract training and testing session task runs. The top panel depicts each of the pairs for the concrete rule task conditions. The bottom panel depicts each of the pairs for the abstract rule task conditions. The left, middle and right panels depict each of the 8, 16, and 32 paired-items used in either of the task conditions, respectively.

Sequences of five task runs began immediately following training. Each task run began with the presentation of a fixation for 8 seconds until the 4 second countdown of the first trial-block began. The first block of trials then cycled for 16 seconds, in the same manner which trials progressed during training, and terminated with the presentation of the block feedback screen. Following this feedback, 16 seconds of fixation commenced until the next trial-block count down began. This cycle repeated until all 5 trial blocks had occurred (approximately 200 seconds). After the blocks were completed, a prompt appeared which instructed participants to prepare for the next task condition's training session. Immediately following this prompt, the task instruction for the next task training appeared centered on the monitor. This progression of training blocks followed by task blocks repeated until each participant completed the six total task conditions. Upon completion of all task conditions a prompt screen informed participants that the experiment was complete and thanked them for participating.

Data Analysis and Preparation

In order to confirm that the increase in item pair set-size led to selective increased concrete rule task difficulty as within-subjects factors in Experiment 2a, task performance was compared across each of the concrete and abstract rule task conditions. Dependent measures for percent of correct responses during each participant's individual task blocks were calculated by determining the number of correct responses made during each task block and dividing this

amount by the total number of trials completed during the block. This proportion was then multiplied by 100 for a continuous range of scores between 0, which would result in no accuracy in responding, and 100, which would result from no errors in responding. Although familiarization and training performance was recorded, these responses were not included in the analysis due to the emphasis on performance which would take place during the actual BOLD fMRI task scans planned for Experiment 2b.

A three-way repeated-measures ANOVA comparing factors of Task (Abstract rule, Concrete rule) and Set-size (8, 16, 32) and Trial blocks (1, 2, 3, 4, 5) on the dependent measures of percent correct assessed whether accuracy was selectively diminished across increasing set-sizes for the concrete rule task, but not the abstract rule task. Importantly, the factor of trial blocks was used to determine if performance was stable across blocks subsequent to training sessions in which the performance criteria was reached. Stable performance across task blocks is a critical outcome, given the need to collapse both behavioral response data and BOLD fMRI data across trial blocks during behavioral and neuroimaging results analysis planned for Experiment 2b. If the adaptations for Experiment 2a were found to demonstrate consistent functional relationships observed in Experiment 1, the outcome of the three-way ANOVA would be a two-way interaction of Task and Set-size. Post-hoc comparisons of this interaction would confirm that percent correct decreased across set-size, only for the concrete task blocks. There should be no main effects or interactions of Trial blocks, if task block accuracy remained stable across abstract and concrete set-size conditions. Cohen's d estimates of effect size would be used to examine any significant differences between task conditions and compare any changes in magnitude between these effects.

Results

Percent correct for each of the trials blocks did not differ within each set-size condition or differ between task rules or set-size conditions. Figure 20 shows the comparison of percent correct, collapsed across trial blocks, for each set-size condition of the abstract and concrete tasks. Overall, participants performed with a higher percent correct in abstract rule as compared to concrete task conditions. The set-size manipulation did not affect percent correct for the abstract rule task conditions. Alternatively, performance in the concrete rule task differed

Figure 20

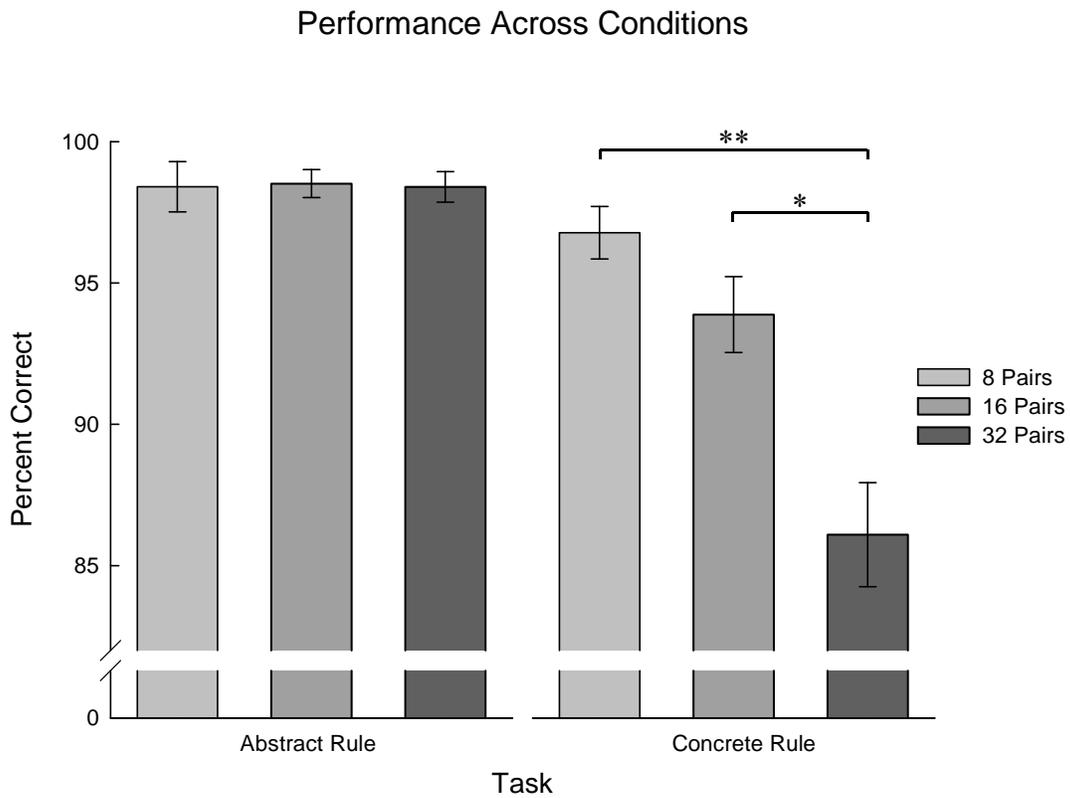


Figure 20. Figure 20 shows the mean percent correct, collapsed across trial blocks and separated by abstract rule and concrete rule tasks for each of the set-size conditions. Error bars represent 1 standard error of the mean (SEM). * $p < .05$; ** $p < .01$.

across some, but not all set-sizes. For the concrete rule task blocks, both the 8 and 16 paired-item conditions were greater in percent correct when compared to the 32 paired-item condition, but did not appear to differ significantly between these conditions. These findings were confirmed by a three-way repeated-measures ANOVA comparing factors of Task (Abstract rule, Concrete rule) and Set-size (8, 16, 32) and Trial blocks (1, 2, 3, 4, 5) on percent correct, which yielded only a significant interaction of Task and Set-size, $F(2, 22) = 13.03, p < .001, \eta_p^2 = .54$, and significant main effects of Task, $F(1, 11) = 35.57, p < .001, \eta_p^2 = .76$, and Set-size, $F(2, 22) = 8.72, p < .01, \eta_p^2 = .44$. All remaining interactions and main effects were not significant, all $F_s < 1.95$, all $p_s > .12$. Post-hoc tests examining the interaction between Task and Set-size on percent correct found only significant differences between 8 and 32 paired-item conditions, with a mean difference of 10.67, $p < .01, d = .86$ (large effect), and between 16 and 32 paired, with a mean difference of 7.78, $p < .05, d = .72$ (medium effect). All other comparisons were not significant with mean differences < 2.89 , all $p_s > .06$.

Discussion.

These results demonstrated that the increase in item-pair set-size led to selective increased concrete rule task difficulty for the novel within-subjects design and additional adaptations in Experiment 2a. Task performance was compared across each of the concrete and abstract rule task conditions using three-way repeated-measures ANOVA. The two-way interaction of Task and Set-size demonstrated that accuracy was selectively diminished across increasing set-sizes for the concrete rule task, but not the abstract rule task. These differences

were confirmed with the post-hoc comparisons of set-size for concrete rule task conditions. The increase in effect sizes for these differences between the 16 and 32 item-pairs and the 8 and 32 item-pairs demonstrated that difficulty was increased to a lesser degree between 16 and 32 paired-items than was observed between 8 and 32 items, which showed the greatest effect. Importantly, the failed main effects and interactions of trial block on accuracy demonstrated that performance remained stable subsequent to training sessions across abstract and concrete set-size conditions. This finding ensures that the task parameters lead to consistent task performance and would allow for averaging of BOLD fMRI signal acquisitions across trial blocks during neuroimaging analysis. The main effect of task demonstrated that, overall, the concrete task conditions were more difficult than the abstract task conditions. This finding is interesting given that previous experiments comparing abstract and concrete task demands, which require relatively fewer concrete rules to be utilized, yielded greater measures of difficulty for the abstract conditions. Given the reversal of this effect observed in Experiment 2a, it would appear that the number of concrete rules which are required to perform the task at least affect behavioral measures, when increased beyond a minimal memory load for rule instantiations (8 paired-items). Given the significant interaction of Task and Set-Size and results of the post-hoc analysis, the main effect of set-size was primarily driven by that variance in percent correct observed for concrete task conditions, which produced significant overall effects of set-size when collapsed with the abstract task conditions.

There are several important limitations of these findings which pertain particularly to the implementation of fMRI data analysis and conclusions about the manipulation of memory load in the concrete task conditions planned in Experiment 2b. Foremost, comparisons of concrete task performance for 8 and 16 paired-items were not significant (mean difference of 2.89, $p =$

.057). This finding would suggest that memory load increases between these task conditions did not lead to significant changes in difficulty, similar to comparisons made between small (4 paired-items) and intermediate (8 paired-items) set-sizes from Experiment 1. The absence of significant performance differences when comparing these conditions arguably precludes any BOLD fMRI signal contrasts aimed at comparing difficulty between a low and intermediate memory load conditions in the concrete task. However, given that both of the small (8 paired-item) and intermediate (16 paired-item) conditions demonstrated significant increases in accuracy from the large memory load condition (32 paired-items), contrasts for both small and intermediate memory loads should be possible if compared to the large memory load condition. Furthermore, each comparison demonstrated differences of effect size in a positive relation to memory load differences. Based on such differences of effects size, a functional relationship between memory load and difficulty was observed across small, intermediate, and large memory loads in the concrete rule task. Consequently, by implementing the novel task design from Experiment 2a during BOLD fMRI data acquisition in Experiment 2b, comparisons across set-size manipulations for both abstract and concrete rule tasks would elucidate the neural correlates of the functional relationships between factors of task and difficulty.

Experiment 2b.

Experiment 2a demonstrated evidence that the manipulation of increases in working memory load led to increased difficulty for correct responding during the concrete task with factors of set-size and task rule as within-subjects conditions for a sample size comparable to that of a typical BOLD fMRI study (n=12). Furthermore, the effects of set-size on task performance did not extend to abstract rule conditions demonstrating that difficulty did not increase based on the number of instantiations of the abstract rules of *same* and *different*. The goal of Experiment 2b is to examine whether the orthogonal manipulations of task abstractness and difficulty leads to findings consistent to models of functional organization for the frontal lobes (i.e., Rostro-caudal Hierarchy: Bunge et al., 2003, Badre & D'Esposito, 2009; Multiple Demand Activity: Crittenden & Duncan, 2014). The approach of Experiment 2b was to examine task dependent BOLD signal via fMRI, acquired while participants are completing both concrete and abstract rule tasks adapted to the MR scanning environment from Experiment 2a. These task conditions provided similar contrasts to those implemented in Crittenden and Duncan's (2014) orthogonal comparisons of increased task difficulty and abstractness. Experiment 2b specifically assessed whether increased difficulty in a concrete rule task, resulting from increases in memory load demand, would correspond to relatively rostral activity as is predicted by the MDA model. Alternatively, should neural correlates of concrete task conditions remain constrained to relatively caudal regions of the frontal lobe, regardless of memory load, findings from

Experiment 2b would provide results consistent with predictions made by the Rostro-caudal Hierarchy model.

Method

Participants

13 participants (12 right-handed; 7 male, 6 female) were Auburn University undergraduates, with ages ranging from 19 to 26, enrolled in a psychology course. Participants were recruited via announcements made during the psychology course's meetings. All participants provided informed consent prior to beginning the experiment and were awarded \$25 monetary compensation and course credit to thank them for their time. The Auburn University Institutional Review Board approved all details of the protocol prior to beginning data collection.

Apparatus

Scanning sessions took place at the Auburn University Magnetic Resonance Imaging Research Center (AUMRIRC), located at 560 Devall Dr. in Auburn, AL, using a Siemens 7 Tesla (T) MAGNETOM (Siemens Healthcare, Erlangen, Germany) scanner. BOLD signal imaging acquisition was obtained using a 32-channel head coil while participants actively responded to the task in head-first supine position. Prior to scanning, a standard PC, keyboard, and monitor located in the scanner control room was used to administer initial instructions and familiarization training sessions in a manner similar to the procedure noted in Experiment 2a. A standard, MR compatible, 4 button response box taped to participants midsection allowed participants to make responses while in the scanner. Participants viewed both written task instructions and task events via a mirror affixed to the head coil, which reflected their vision to a standard projection screen suspended from the top of the scanner's bore towards the rear

opening. The screen was illuminated by an MR compatible projector in the scanner room (Silent Vision Projector, Avotec Incorporated). All experimental events and participant responses were controlled and recorded by a PC using the same custom program from Experiment 2a.

Stimuli were identical to those used in Experiment 2a.

General Procedure

Participants first completed the informed consent and safety prescreening procedures in a reception area located near the entrance of the AUMRIRC. All aspects of the procedure were identical to those used in Experiment 2a, except those which were necessary for implementations of BOLD fMRI data acquisitions. Task condition progressions from table 2 were again used to assign participants to counterbalanced task condition sequences. Following this assignment, participant's informed consent was obtained and the Scanner Pre-training phase commenced.

Scanner Pre-training. Prior to scanning, instructions identical to those used in Experiment 2a were viewed by participants. Participants then progressed to identical familiarization phases to those used in Experiment 2a with one exception. Participants were informed that scanning would not be conducted during training sessions of actual task blocks once inside the scanner. Instead, following the completion of each training session, a scanner operator would communicate that scanning was about to commence, that task blocks would test them on the same pairs which they had learned in the immediate training session, and to press any key if they were ready to proceed. Once participants completed the familiarization training sessions, lasting approximately 15- 20 minutes, the MRI Scanning Phase commenced.

MRI and fMRI data acquisition parameters

Prior to the functional study, coplanar T1-weighted sequence, (TR/TE 8600/3000 ms, 20° flip angle) and a high-resolution MPRAGE sequence, (TR/TE 2.20/2.89 s, 7° flip angle, 0.72 mm isotropic) were obtained. These anatomical images were used on an individual participant basis for anatomical reference and normalization. A block design was used to estimate functional BOLD signal correlates during task related operations using a gradient echo, echoplanar imaging (EPI) sequence, acquiring 37 axial oblique interleaved slices (TR/TE 3000/28 ms, 70° flip angle, voxel size = 0.85 × 0.85 × 1.5 mm, FOV = 234).

The sequences of scanning protocols were identical for all participants and lasted approximately 1 hour from insertion into the scanner bore. Each participant was first submitted to brief anatomical localizer sequence in order to ensure that the partial brain field-of-view for BOLD fMRI image acquisition was positioned in an ideal manner. Following this localizer scan, a standard B₁ Map was collected in order to reduce inaccuracies for flip angles which might arise due to variable tissue density across participants. Following the B₁ Map, the scanner's radio frequency (RF) emissions were calibrated based on individual participant measures. A GRE-field map was collected following this calibration in order to correct reconstruction of image data based on any inhomogeneity in the magnetic field which existed within the scanner coils. After the GRE-field map was obtained, high-resolution anatomical images were obtained via custom T1-weighted, MPRAGE sequences. After this final anatomical imaging acquisition, participants were then informed that the task training followed by 5 trial blocks for each of the 6 task conditions would now commence. Responses on the MR compatible button box made during training and task scans were used to verify that subjects were engaged in the appropriate abstract and concrete rule strategies during scanning for respective task blocks. Additionally, these responses were used to confirm effects of task conditions on percent correct in an identical

manner to the methods used in Experiment 2a. Participants completed training and task blocks for each of the conditions in an identical manner to Experiment 2a, with the exception noted during the pre-scanning phase, in which fMRI scanning would take place only during the 5 task block repetitions for each task conditions, but not training sessions. Once all 6 abstract and concrete task conditions had been completed, participants were retracted from the MR scanner and thanked for their time before being escorted back to AUMRIRC's reception area.

Behavioral Data Analysis and Preparation

Data analysis and preparation for responses made during fMRI task scans was identical to these methods used in Experiment 2a. Results of this analysis served to provide validation for experimental manipulations of task difficulty, similar to those demonstrated in Experiment 2a.

fMRI Data Analysis and Preparation

DICOM files were first converted into NIfTI file formats using MRIcon (Rorden, 2012). All imaging data was prepared and analyzed using the FMRIB Software Library (FSL; Jenkinson, Beckmann, Behrens, Woolrich, & Smith, 2012). fMRI data preparation was then subjected to preprocessing steps in order to maximize quality and signal-to-noise proportions of BOLD signal measurements obtained during task runs. Preprocessing of EPI data began with brain extractions performed on both T₁ weighted anatomical and functional T₂ weighted EPI images using FSL's brain extraction tool (BET; Smith, 2002) using standard threshold intensities. Each brain extraction was examined for obvious artifacts and skull fragments before fMRI data preparation proceeded. Once quality assurance of the brain extractions had been performed, FSL's fMRI Expert Analysis Tool (FEAT; Jenkinson 2001, 2002) was used to perform realignment, slice-time correction, and normalization via registration of functional images to Montreal Neurological Institute (152 MNI, 2 mm anatomical) standard space. GRE-

field map distortion unwarping was omitted from preprocessing on the basis that the resultant T₂ echoplanar images appeared more distorted than images prior to unwarping upon inspection. Head motion correction was then performed using FMRIB's linear registration tool (FLIRT; Jenkinson, Bannister, Brady, & Smith, 2002). Spatial and temporal smoothing was performed using a 3 mm full width at half maximum (FWHM) Gaussian kernel and a high-pass temporal filter with a maximum threshold of 100s in order to maximize the signal-to-noise ratio by reducing the respective noise in data. The resulting functional data was inspected for goodness of fit for registrations prior to being advanced to data analysis.

fMRI data analysis began with a first-level analysis aimed to estimate task dependent activations during each of the task blocks for runs of each condition and subject. Regressor functions for each run were created by generating timing functions which began at the first trial's onset and terminated with the onset of feedback prompts for each of the 5 task blocks which occurring during task runs. All non-task related activations (i.e., fixation periods, feedback prompts, countdowns) as well as 6 standard motion parameters were added as regressors of no interest to General Linear Modeling (GLM) of BOLD responses. All task dependent activity was contrasted with the standard temporal derivatives, calculated by FEAT. All data were prewhitened using the FMRIB Improved Linear Model (FILM; Woolrich 2001) tool in order to increase the efficiency of statistical results for the first-level analysis. The 6 resultant beta weight images estimated for each participant's represented activation, collapsed across each of the task blocks, for each of the 3 set-size manipulations for both abstract and concrete rule conditions. A fixed-effects analysis was then used to assess activations characteristic of within and between specific task conditions for each individual participant. Initial separate contrasts were first performed across all abstract and all concrete rule set-size conditions. A second set of contrasts

identified regions recruited differentially across all set sizes for abstract conditions compared with all set-sizes for concrete conditions for each participant (i.e., Abstract > Concrete; Concrete > Abstract). The final set of contrasts assessed regions recruited to perform 16 and 32 paired-item by comparing each to the 8 paired-item for concrete rule conditions (Concrete 16 > Concrete 8; Concrete 32 > Concrete 8) and the abstract rule conditions (Abstract 16 > Abstract 8; Abstract 32 > Abstract 8).

Using the FMRIB local analysis of mixed effects (FLAME; Worsley 2001) tool, the results of the fixed effects analysis were examined at the group level. All activation maps resulting from group averaging and were thresholded to clusters with a minimum Z intensity = 2.3 and a false discovery rate (FDR) corrected p -value of $\alpha = .05$. The results of group analysis for the all abstract and all concrete contrasts served to confirm that robust visual (e.g., Primary visual cortex [V1]) activations were observed consistent with task versus non-task conditions. Additionally these contrasts served to demonstrate whether activations were accompanied by the regions previously implicated in abstract rule use (i.e., BAs 9, 46, 8, 6) and concrete rule use (BAs 8, 6) across the respective task conditions. Based on the predictions made by the rostro-caudal hierarchy model, the group level results of the Abstract > Concrete contrast should yield peak voxel activations distributed within bilateral rostral regions, namely the mid-dorsolateral PFC (BA 9/46), because of the increased abstractness of rule used in these conditions as compared to the concrete conditions, regardless of set-size. This anticipated outcome would be consistent with prior findings by Bunge et al (2003) and therefore would provide a replication of valid findings with a novel paradigm as well as rule out potential limitations which may have led to these prior results.

Based on the predictions made by the MDA model, the resultant activation maps from the group analysis for the Concrete 16 > Concrete 8, Concrete 32 > Concrete 8, or both contrasts should yield peak voxel activations distributed within bilateral rostral regions, namely the mid-dorsolateral PFC (BA 9/46), because of the increased difficulty of rule use across these conditions, independent of any increase in the abstract nature of the utilized rule. According to both the Rostro-caudal hierarchy model and the MDA model, these same set-size comparisons assessed in abstract task conditions at the group level should result in no difference of activation. This result was also important in order to rule out any increased activation resulting from the mere increase in paired-images or instantiations of rule use, which may have driven the results for the concrete set-size comparisons. Cluster visualizations were produced and examined using Mango software (<http://rii.uthscsa.edu/mango/mango.html>).

Results

Behavioral Results. Percent correct for each of the trials blocks did not differ within each set-size condition or differ between task rules or set-size conditions. Because accuracy was found not to differ across task blocks, each run was characterized by percent correct collapsed across this factor. Figure 21 shows the comparison of percent correct for each set-size condition of the abstract and concrete tasks. Overall, participants performed with a higher percent correct in abstract rule as compared to concrete task conditions. The set-size manipulation did not affect percent correct for the abstract rule task conditions. Alternatively, performance in the concrete rule task differed across some, but not all set-sizes. For the concrete rule task blocks, only the 8 paired-item condition was greater in percent correct when compared to the 32 paired-item condition. These findings were confirmed by a three-way repeated-measures ANOVA comparing factors of Task (Abstract rule, Concrete rule) and Set-size (8, 16, 32) and Trial blocks

Figure 21

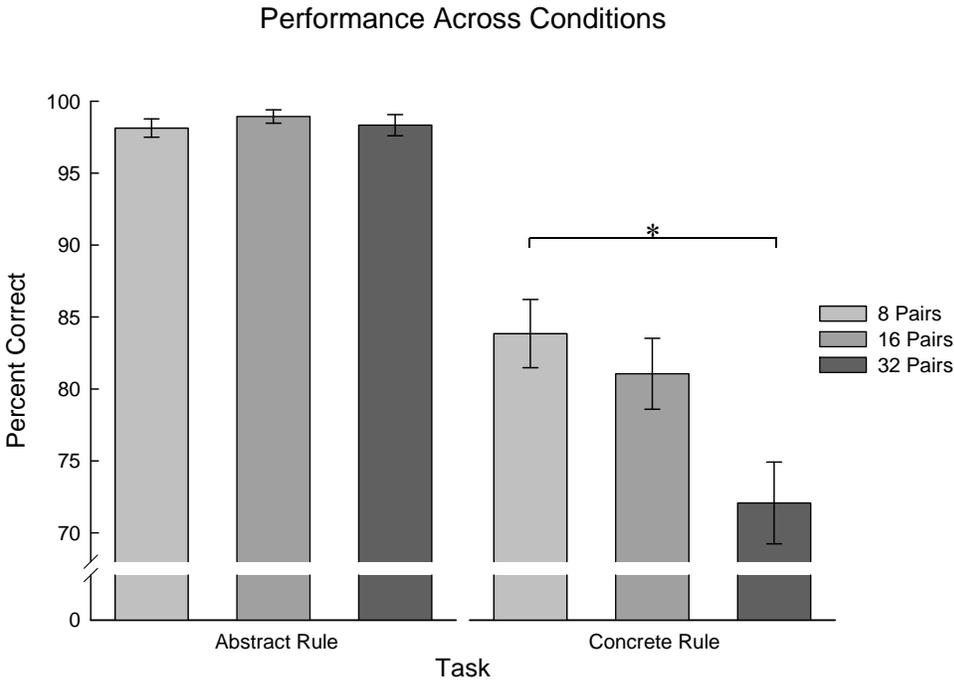


Figure 21. Figure 21 shows the mean percent correct, collapsed across trial blocks and separated by abstract rule and concrete rule tasks for each of the set-size conditions. Error bars represent 1 standard error of the mean (SEM). * $p < .05$.

(1, 2, 3, 4, 5) on percent correct, which yielded only a significant interaction of Task and Set-size, $F(2, 24) = 13.03, p < .05, \eta_p^2 = .23$, and a significant main effect of Task, $F(1, 12) = 55.75, p < .001, \eta_p^2 = .82$. All remaining interactions and main effects were not significant, all $F_s < 3.52$, all $p_s > .05$. Post-hoc tests examining the interaction between Task and Set-size on percent correct found only significant differences between 8 and 32 paired-item conditions, with a mean difference of 11.11, $p < .05, d = .55$ (medium effect). Although the post-hoc comparison for 16 and 32 paired items, with a mean difference 8.55, $p = .09, d = .43$, fell short of significance, a

small to medium effect size was observed. All other comparisons were not significant with mean differences < 2.55 , all $p_s > .16$.

fMRI results. To identify brain regions which were active during the abstract rule task, group cluster analysis assessed activity which was common to each of these set-size conditions.

Figure 22 shows the results of the group-level cluster analysis for brain regions which

Figure 22

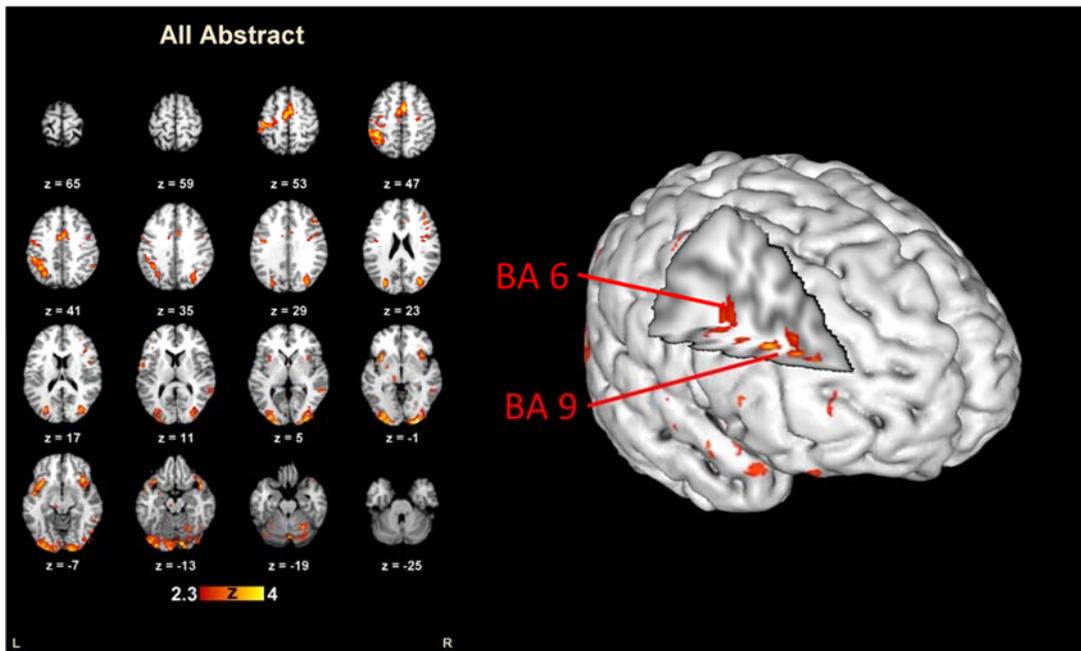


Figure 22. Figure 22 demonstrates the results of the group level analysis which identified regions of activation characteristic of abstract task activity overlaid onto a standard space MNI template. Warmer colors reflect higher z-statistics. The left panel shows slices along the z-axis, beginning with superior portions of the brain at the top left and ending with inferior portions of the brain in the bottom right. The right panel shows a 3-d rendering of the sample with overlay activation of MFG (BA 9) indicated with the red arrow.

demonstrated increased activation during abstract task conditions. Peak clusters included foci located within bilateral Insular regions (BA 13: -36, 12, -4; 36, 22, -8), V1 (BA 18: 28, -94, 0), medial cingulate gyrus (BA 24: -2, 0, 42) and the medial frontal gyrus (BA 9: 36, -4, 24). Additionally, voxels within significant clusters were located within mid-dorsolateral PFC (BA 9), PMd (BA 6). Table 3 identifies significant clusters of peak active voxels identified during the abstract task.

Table 3

Condition	Region of Activation	Cluster rank	Voxels	<i>p</i> value	<i>z</i> -statistic	X (mm)	Y (mm)	Z (mm)
<u>All Abstract</u>								
	Middle Occipital Gyrus	1	5884	0	5.64	28	-94	0
	Cingulate Gyrus	2	910	1.14E-15	4.53	-2	0	42
	Insula	3	492	8.55E-10	4.39	-36	12	-4
	Inferior Frontal Gyrus	4	470	1.91E-09	4.86	36	22	-8
	Middle Temporal Gyrus	5	231	3.31E-05	3.8	52	-44	2
	Insula	6	197	0.000168	3.2	36	-4	24
	Middle Frontal Gyrus	7	160	0.0011	3.92	42	26	22
<u>All Concrete</u>								
	Middle Occipital Gyrus	1	7809	0	5.03	34	-90	6
	Middle Frontal Gyrus	2	1250	4.04E-17	4.95	4	16	46
	Inferior Frontal Gyrus	3	952	5.40E-14	4.91	-38	4	24
	Insula	4	801	2.75E-12	3.92	38	24	16
	Inferior Frontal Gyrus	5	544	4.18E-09	4.86	-30	18	-12
	Inferior Frontal Gyrus	6	447	5.96E-08	5.48	34	22	-8
	Cuneus	7	284	2.65E-05	3.74	-10	-70	18
	Precentral Gyrus	8	217	0.000375	3.89	-32	-22	56
	Middle Frontal Gyrus	9	150	0.0071	3.85	24	-8	54

Table 3 reports the results of the group level clustering analysis for all Abstract and all Concrete conditions. Columns indicate condition, cluster rank order, the total number of voxels for each cluster, the probability corresponding to z-statistics for peak voxels in each cluster, and the coordinates in standard MNI space for peak voxels within each cluster.

To identify brain regions which were active during the concrete rule task, a group cluster analysis assessed activity which was common to each of these set-size conditions. Figure 23 shows the results of the group-level cluster analysis for brain regions which demonstrated increased activation during concrete task conditions. Peak clusters included foci located within bilateral Insular regions (BA 13: -30, 18, -12; 34, 22, -8), V1 (BA 18: 34, -90, 6), medial frontal

Figure 23

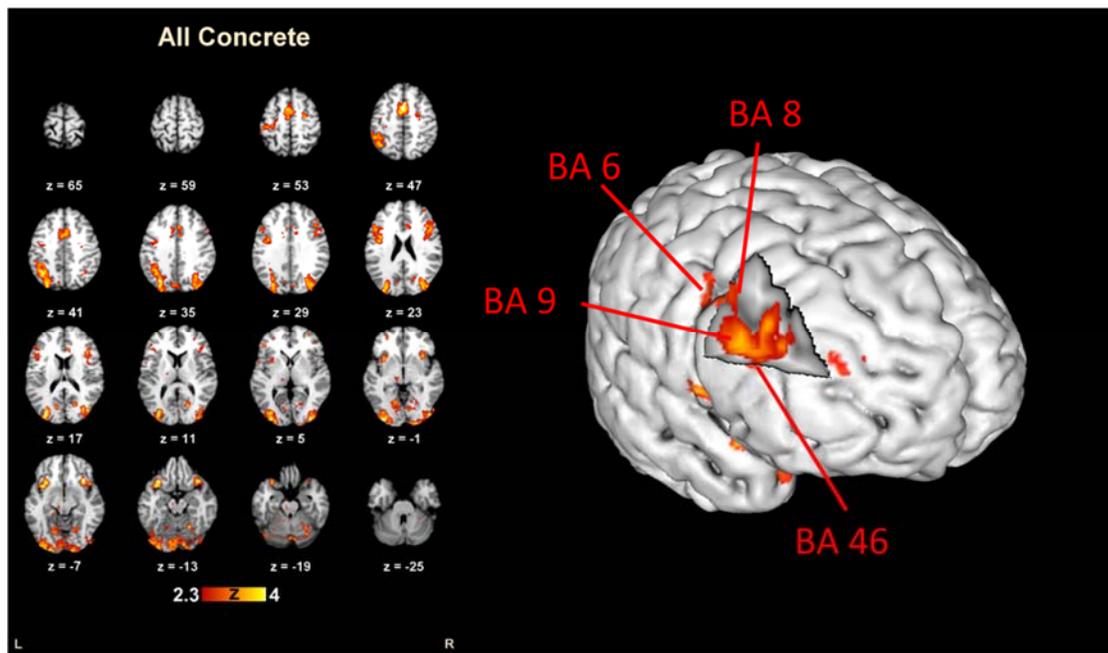


Figure 23. Figure 23 demonstrates the results of the group level analysis which identified regions of activation characteristic of concrete task activity overlaid onto a standard space MNI template. Warmer colors reflect higher z-statistics. The left panel shows slices along the z-axis, beginning with superior portions of the brain at the top left and ending with inferior portions of the brain in the bottom right. The right panel shows a 3-d rendering of the sample with overlay activation of MFG (BA 6) and mid-dorsolateral PFC (BA 9/46) indicated with the red arrows.

gyrus (BA 32: 4, 16, 46), and left lateral precentral gyrus (BA 6: -38, 4, 24; BA 4: -32, -22, 56). Additionally, voxels within significant clusters were located within mid-dorsolateral PFC (BA 9, 9/46, 6). Table 3 identifies significant clusters of peak active voxels identified during the concrete task conditions.

Based on the main effect of task from the behavioral results, two separate contrasts were performed at the group level to assess differences in clusters of activation characteristic of abstract and concrete task conditions, regardless of set-size. Figure 24 shows the results of the group-level cluster analysis for brain regions which demonstrated increased activation during the abstract rule conditions, as compared to the concrete rule conditions. Peak clusters included foci located within bilateral superior frontal gyrus (BA 8: -40, -2, -8; -22, 34, 32; BA 6: 12, 36, 52) and bilateral insular regions (BA 13: -40, -2, -8; 46, -6, 2). Additionally, voxels within significant clusters were located within OFC (BA 10), mdPFC (BA 9), and PMd (BA 6) regions. Table 4 identifies significant clusters of active voxels identified during this abstract and concrete

Figure 24

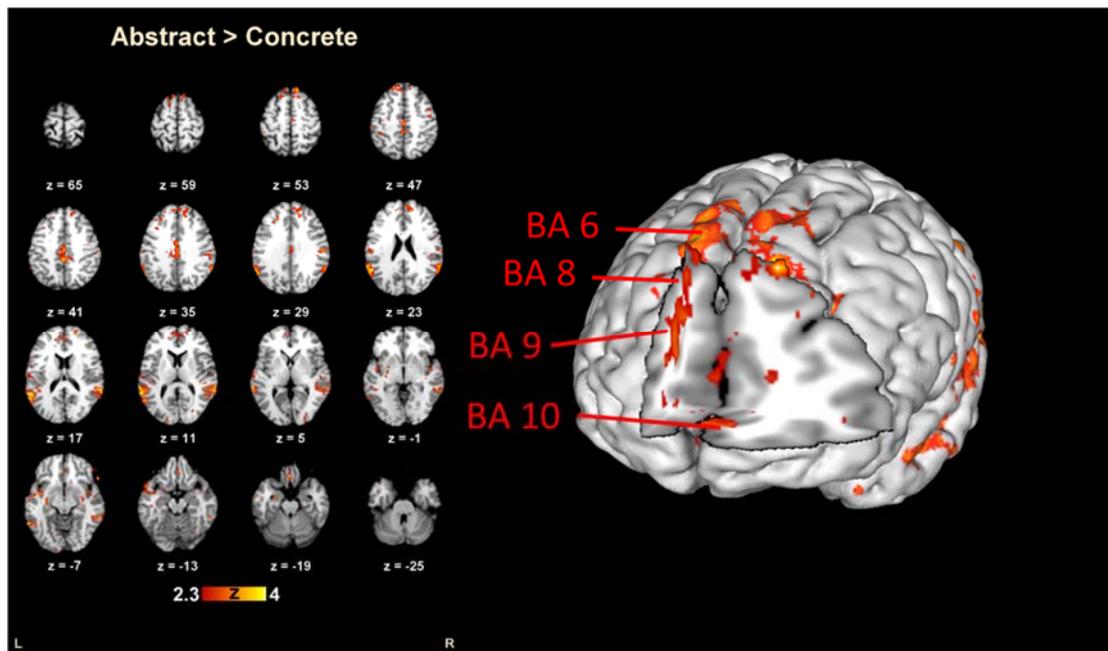


Figure 24. Figure 24 demonstrates the results of the group level cluster analysis which identified regions of activation characteristic of abstract task activity overlaid onto a standard space MNI template. Warmer colors reflect higher z-statistics. The left panel shows slices along the z-axis, beginning with superior portions of the brain at the top left and ending with inferior portions of

the brain in the bottom right. The right panel shows a 3-d rendering of the sample with overlay activation of MFG (BA 6), mid-dorsolateral PFC (BA 9/46) and OFC (BA 10) indicated with the red arrows.

Table 4

Condition	Region of Activation	Cluster rank	Voxels	<i>p</i> value	<i>z</i> -statistic	X (mm)	Y (mm)	Z (mm)
<u>Abstract > Concrete</u>								
	Supramarginal Gyrus	1	1295	5.39E-23	4.43	-56	-54	32
	Superior Temporal Gyrus	2	1098	2.10E-20	4.18	60	-40	14
	Superior Frontal Gyrus	3	838	9.88E-17	4.66	12	36	52
	Paracentral Lobule	4	681	2.50E-14	4.07	0	-18	44
	Temporal Lobe	5	282	4.17E-07	3.59	-40	-2	-8
	Superior Frontal Gyrus	6	271	0.000000656	4.01	-16	42	48
	Postcentral Gyrus	7	265	0.000000894	3.74	58	-18	28
	Medial Frontal Gyrus	8	171	0.000141	3.85	-2	28	-18
	Superior Frontal Gyrus	9	116	0.00417	3.97	-22	34	32
	Parahippocampal Gyrus	10	111	5.80E-03	3.36	-26	-8	-20
	Inferior Temporal Gyrus	11	106	8.11E-03	4.25	-60	-54	-4
	Superior Temporal Gyrus	12	98	1.40E-02	3.22	46	-6	2
<u>Concrete > Abstract</u>								
	Precuneus	1	2237	6.28E-34	5.22	-2	-68	38
	Precuneus	2	1229	3.84E-22	5.09	-30	-78	42
	Middle Temporal Gyrus	3	715	7.29E-15	4.42	46	-72	22
	Precentral Gyrus	4	655	6.50E-14	4.91	-36	4	26
	Middle Frontal Gyrus	5	344	2.10E-08	3.97	46	18	20
	Superior Frontal Gyrus	6	213	1.36E-05	3.6	-6	8	50
	Inferior Frontal Gyrus	7	164	2.13E-04	3.85	-32	14	-14
	Superior Frontal Gyrus	8	90	2.46E-02	3.58	-26	52	-4

Table 4. Table 4 reports the results of the group level clustering analysis for all Abstract > Concrete and Concrete > Abstract conditions. Columns indicate condition, cluster rank order, the total number of voxels for each cluster, the probability corresponding to z-statistics for peak voxels in each cluster, and the coordinates in standard MNI space for peak voxels within each cluster.

task group-level comparison (Abstract > Concrete). Peak clusters included foci of significant clusters were located within mid-dorsolateral PFC (BA 9/46), pre-PMd/CLPFC (BA 8), and PMd (BA 6). Table 4 identifies significant clusters of active voxels identified during this abstract and concrete task comparison (Abstract > Concrete). Figure 25 shows the results of the group-level cluster analysis for brain regions which demonstrated increased activation during the concrete rule conditions, as compared to the abstract rule conditions. Peak clusters included foci located

within right lateral inferior frontal gyrus (BA 9: 46, 18, 20), left lateral precentral gyrus (BA 6: -36, 46, 26), medial frontal gyrus (BA 6: -6, 8, 50) and superior frontal gyrus (BA 10: -26, 52, -4).

Figure 25

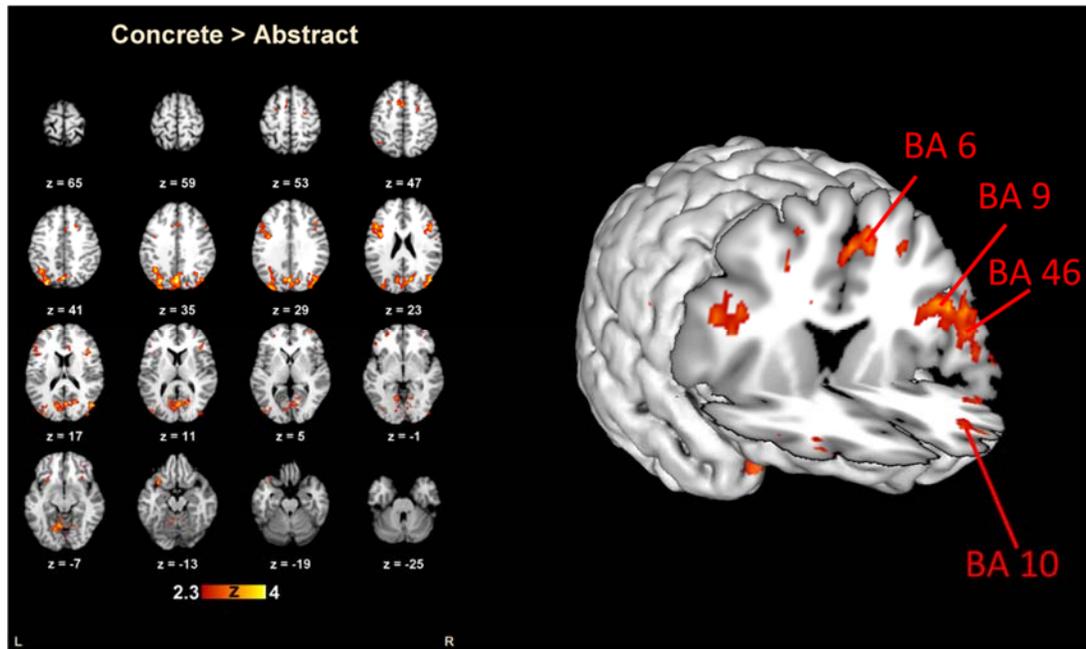


Figure 25. Figure 25 demonstrates the results of the group level analysis which identified regions of activation characteristic of concrete task activity overlaid onto a standard space MNI template. Warmer colors reflect higher z-statistics. The left panel shows slices along the z-axis, beginning with superior portions of the brain at the top left and ending with inferior portions of the brain in the bottom right. The right panel shows a 3-d rendering of the sample with overlay activation of MFG (BA 6), mid-dorsolateral PFC (BA 9/46) and OFC (BA 10) indicated with the red arrows.

Table 4 identifies significant clusters of active voxels identified during this abstract and concrete task group-level comparison (Concrete> Abstract).

Based on the interaction of task and set-size from the behavioral results, four separate contrasts were performed to assess differences in group-level activation characteristic of abstract

and concrete task conditions, when comparing large and intermediate set-sizes to small set-sizes. Figure 26 shows the results of the group-level cluster analysis for brain regions which demonstrated increased activation during the 16 paired-item abstract rule conditions, as compared to the 8 paired-item abstract rule conditions. Only one peak cluster was identified with a foci located within the culmen (32, -50, -20). Table 5 identifies significant clusters of active voxels identified during this Abstract task set-size comparison (16 paired-item > 8 paired-item).

Figure 26

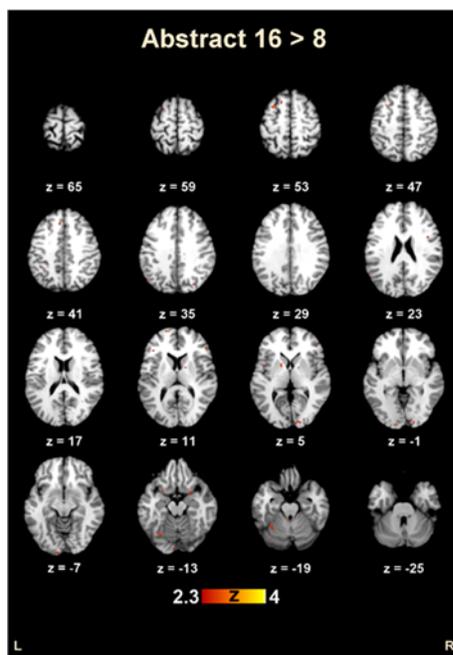


Figure 26. Figure 26 demonstrates the results of the group level cluster analysis which identified regions of activation resulting from 16 and 8 paired-item comparisons of the abstract rule task, overlaid onto a standard space MNI template. Warmer colors reflect higher z-statistics. Slices appear along the z-axis, beginning with superior portions of the brain at the top left and ending with inferior portions of the brain in the bottom right.

Table 5

Condition	Region of Activation	Cluster rank	Voxels	<i>p</i> value	<i>z</i> -statistic	X (mm)	Y (mm)	Z (mm)
<u>Abstract</u>								
16 > 8	Culmen	1	64	0.0427	3.31	-32	-50	-20
32 > 8	Lingual Gyrus	1	117	0.00068	3.62	18	-80	0
	Culmen	2	115	7.95E-04	3.53	-18	-50	-12
	Middle Occipital Gyrus	3	96	3.61E-03	3.65	-36	-86	12
	Superior Frontal Gyrus	4	66	4.84E-02	3.4	-22	18	48
<u>Concrete</u>								
16 > 8	Occipital Gyrus	1	80	0.0072	3.96	-32	-84	14
32 > 8	Precuneus	1	111	0.00072	3.43	32	-72	30
	Middle Frontal Gyrus	2	98	2.12E-03	3.15	40	30	22

Table 5. Table 5 reports the results of the group level clustering analysis for 16 > 8 paired-items and 32 > 8 paired-items comparisons for both Abstract and Concrete rule conditions. Columns indicate condition, cluster rank order, the total number of voxels for each cluster, the probability corresponding to z-statistics for peak voxels in each cluster, and the coordinates in standard MNI space for peak voxels within each cluster.

Figure 27 shows the results of the group-level cluster analysis for brain regions which

Figure 27

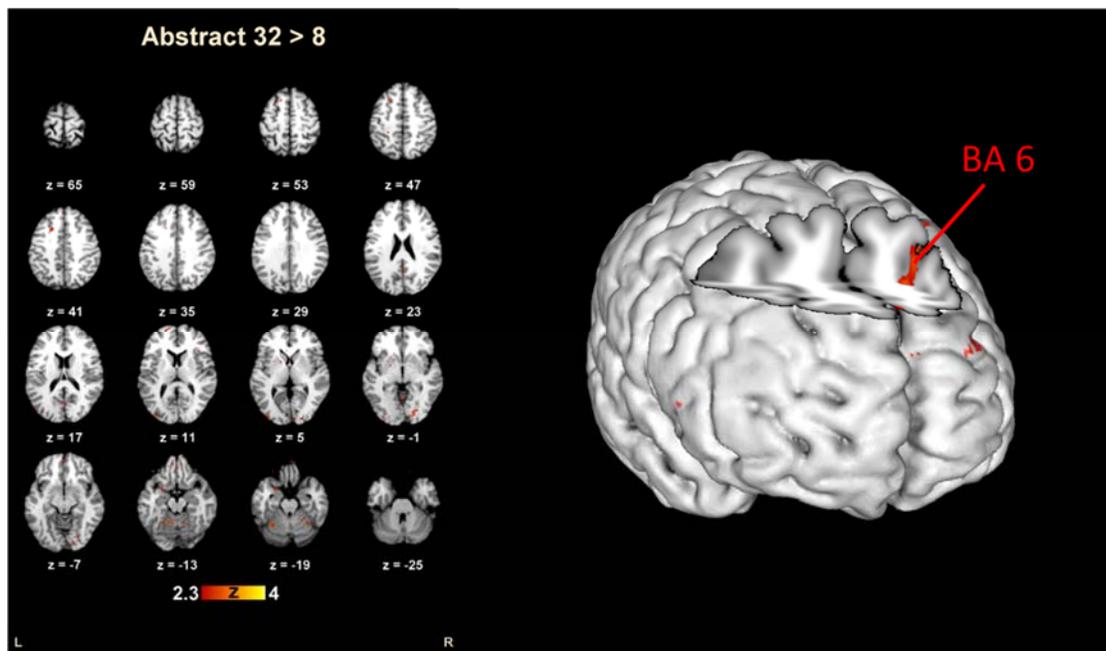


Figure 27. Figure 27 demonstrates the results of the group level analysis which identified regions of activation resulting from 32 and 8 paired-item comparisons of the abstract rule task, overlaid

onto a standard space MNI template. Warmer colors reflect higher z-statistics. The left panel shows slices along the z-axis, beginning with superior portions of the brain at the top left and ending with inferior portions of the brain in the bottom right. The right panel shows a 3-d rendering of the sample with overlay activation of MFG (BA 6) indicated with a red arrow.

demonstrated increased activation during the 32 paired-item abstract rule conditions, as compared to the 8 paired-item concrete rule conditions. Only peak clusters were identified with foci located within the lingual gyrus (BA 18: 18, -80, 0), culmen (-18, -50, -12), middle occipital gyrus (BA 18: -32, -86, 12), and superior frontal gyrus (BA 6: -22, 18, 48). Table 5 identifies significant clusters of active voxels identified during this Abstract task set-size comparison (32 paired-item > 8 paired-item).

Figure 28 shows the results of the group-level cluster analysis for brain regions which

Figure 28

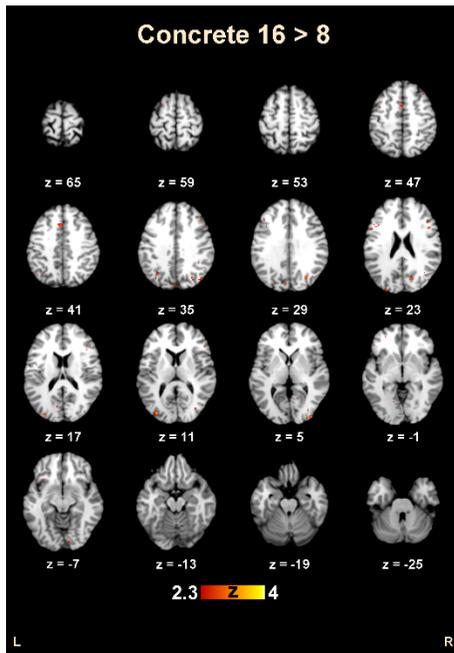


Figure 28. Figure 28 demonstrates the results of the group level cluster analysis which identified regions of activation resulting from 16 and 8 paired-item comparisons of the concrete rule task, overlaid onto a standard space MNI template. Warmer colors reflect higher z-statistics. Slices appear along the z-axis, beginning with superior portions of the brain at the top left and ending with inferior portions of the brain in the bottom right.

demonstrated increased activation during the 16 paired-item abstract rule conditions, as compared to the 8 paired-item concrete rule conditions. Only one peak cluster was identified with a foci located within the middle occipital gyrus (BA 18: -32, -86, 12). Table 5 identifies significant clusters of active voxels identified during this Concrete task set-size comparison (16 paired-item > 8 paired-item).

Figure 29 shows the results of the group-level cluster analysis for brain regions which

Figure 29

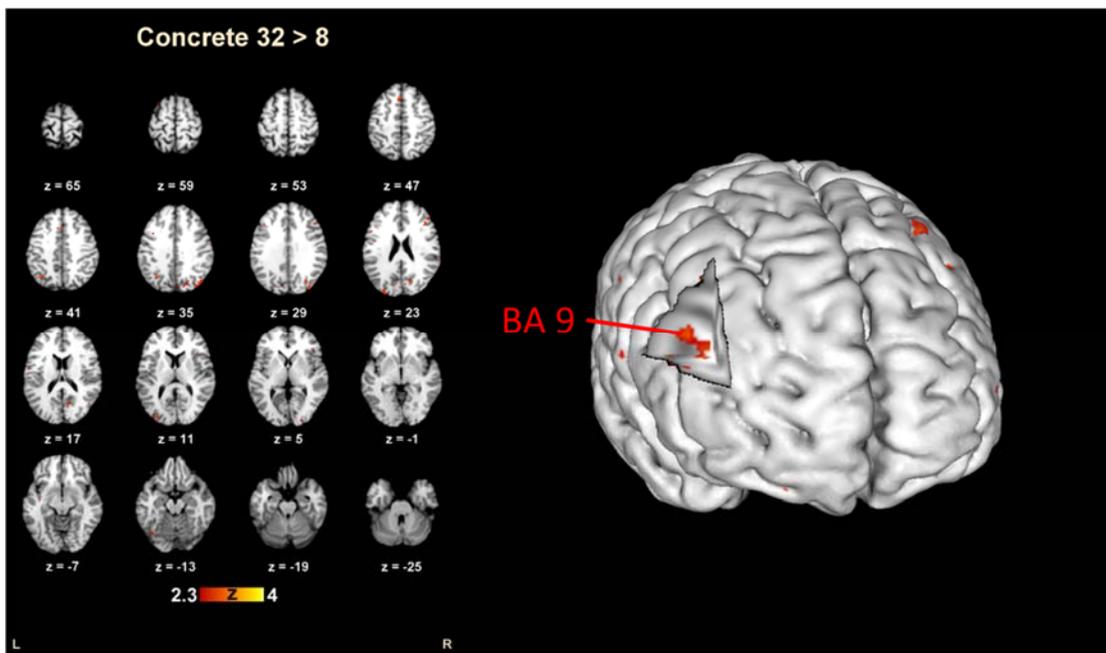


Figure 29. Figure 29 demonstrates the results of the group level cluster analysis which identified regions of activation resulting from 32 and 8 paired-item comparisons of the concrete rule task, overlaid onto a standard space MNI template. Warmer colors reflect higher z-statistics. The left panel shows slices along the z-axis, beginning with superior portions of the brain at the top left and ending with inferior portions of the brain in the bottom right. The right panel shows a 3-d rendering of the sample with overlay activation in the mid-dorsolateral PFC (BA 9) indicated with a red arrow.

demonstrated increased activation during the 32 paired-item abstract rule conditions, as compared to the 8 paired-item concrete rule conditions. Only peak clusters were identified with foci located within the precuneus (BA 31: 32, -72, 30), and right lateral middle frontal gyrus (BA 9: 40, 30, 22). Table 5 identifies significant clusters of active voxels identified during this Concrete task set-size comparison (32 paired-item > 8 paired-item).

Discussion

Consistent with Experiments 1 and 2a, the behavioral results of Experiment 2b yielded a significant interaction of task and set-size and a main effect of task. This finding indicated that the task manipulations remained valid even in the presence of the MR scanning environment. Unlike Experiment 2a, there was no difference between 16 paired-item and 32 paired-item performance in the concrete task conditions. Despite the only near significant difference ($p = .09$), the effect size for this comparison yielded a small to medium estimate ($d = .43$). By comparison, the difference between 8 paired-items and 32 paired-items in the concrete task yielded both a significant difference ($p < .05$) and a larger effect size ($d = .55$). Although the ideal

step-wise increase in difficulty across conditions was not observed, these degrees of difference provided a sufficient evidence that the concrete task conditions corresponded to relative increases in difficulty in a positive relation to set-size. Like Experiments 1 and 2a, there was no effect of set-size across abstract task conditions, demonstrating that difficulty was not increased with the number of rule instantiations (i.e., exemplars of which rules are applied) for these abstract *same* and *different* judgments. Given these behavioral findings, the results of the fMRI group cluster analysis could then be matched to differences in the functional correlates of these task conditions as a means of assessing the neural mechanisms underlying differences in performance.

The fMRI group cluster analysis results yielded several meaningful functional distinctions both within each rule task and across their respective set-size manipulations. The first group-level cluster analysis, which assessed common activation during all abstract rule conditions as compared to all non-task events, yielded clusters with peak activations in the primary visual cortex, bilateral insular regions, the medial cingulate gyrus, the medial frontal gyrus. Activation was also observed within the mdPFC and PMd. These results confirmed that robust visual (V1) activations were observed consistent with task versus non-task conditions. Furthermore, V1 activations were accompanied by the regions previously implicated in abstract rule use (i.e., BAs 9, 6) across the task conditions. The absence of activation in the remainder of the PFC network implicated by Bunge and colleagues' (2003) findings (BA 8, 46) is not surprising, given that this analysis served only to identify peak differences in activation across all task related activity, as compared to non-task related activity.

The second group-level cluster analysis, which assessed common activation during all concrete rule conditions as compared to all non-task events, yielded clusters with peak

activations in the primary visual cortex, bilateral insular regions, the left lateral precentral gyrus, the medial frontal gyrus. Activation was also observed within the mdPFC and PMd. These results confirmed that robust visual (V1) activations were observed consistent with task versus non-task conditions. Furthermore, V1 activations were accompanied by the regions previously implicated in concrete rule use (i.e., BAs 6, 8) as well as additional PFC regions (BA 9, 46) across the task conditions. These findings are consistent with the MDA model of PFC function and task demands, in that frontal lobe activity appears to be dispersed across posterior and anterior regions, despite the relatively concrete task demands. This conclusion is, however, not without limitations. Previous demonstrations compared concrete task demands to abstract task demands via statistical comparisons (i.e., Bunge et al, 2003; Badre and D'Esposito, 2007; Crittenden and Duncan, 2014). Although these preliminary results lend support to the MDA model of PFC functional organization, it was optimal to make statistical comparisons of these task conditions in order to provide a quantitative comparison for activations characteristic of either task. Additionally, the results of these subsequent contrasts served to subtract visual or other task dependent activations which may have obscured significant clusters within the PFC network.

The third group-level cluster analysis assessed the neural basis for performance differences during abstract and concrete rule conditions by subtracting all concrete task activations from all abstract task activations. The group level results of the Abstract > Concrete contrast yielded peak voxel activations distributed within bilateral rostral PFC regions, namely the superior frontal gyrus medial frontal gyrus regions. This result is consistent with predictions made by the rostro-caudal hierarchy model (Bunge et al, 2003; Badre & D'esposito, 2007, 2009) and therefore provide a replication of valid findings with a novel task paradigm. Furthermore the

current findings are not consistent with notions that findings from Bunge and colleagues (2003) and Badre and D'Esposito (2007) involving differential task difficulty between abstract and concrete task demands, may have led to the functional dissociations better explained by the MDA model. Interestingly, these activations yielded nearly exclusive medial clusters. These results are further discussed in light of the fourth group-level cluster analysis results.

The fourth group-level cluster analysis assessed the neural basis for performance differences during abstract and concrete rule conditions by subtracting all abstract task activations from all concrete task activations. The group level results of the Concrete > Abstract contrast yielded peak voxel activations distributed within bilateral rostral PFC regions, namely the lateral frontal gyrus, lateral precentral gyrus, later inferior frontal gyrus, and the superior frontal gyrus regions. This result is consistent with predictions made by MDA model (Crittenden and Duncan, 2014) and therefore provide a replication of valid findings with a novel task paradigm, which orthogonally manipulated abstractness and difficulty of rules, using novel cognitive domains to that of line judgments. In contrast, this finding is inconsistent with the rostro-caudal hierarchy model, in that a relatively concrete series of task demands (i.e., memorization) were demonstrated to correspond with increased activation in rostral regions. Figure 30 demonstrates that Concrete > Abstract task activations yielded nearly exclusive lateral clusters for all regions except the medial frontal gyrus. Taken together with the results of the Abstract > Concrete contrast, these findings suggest that the PFC network may involve a lateral to medial functional distinction for concrete task demands, as compared to abstract task demands. This finding is, however, limited in assessing the role of task difficulty via increased memory load for task conditions, particularly those which differed in behavioral measures of difficulty.

Figure 30

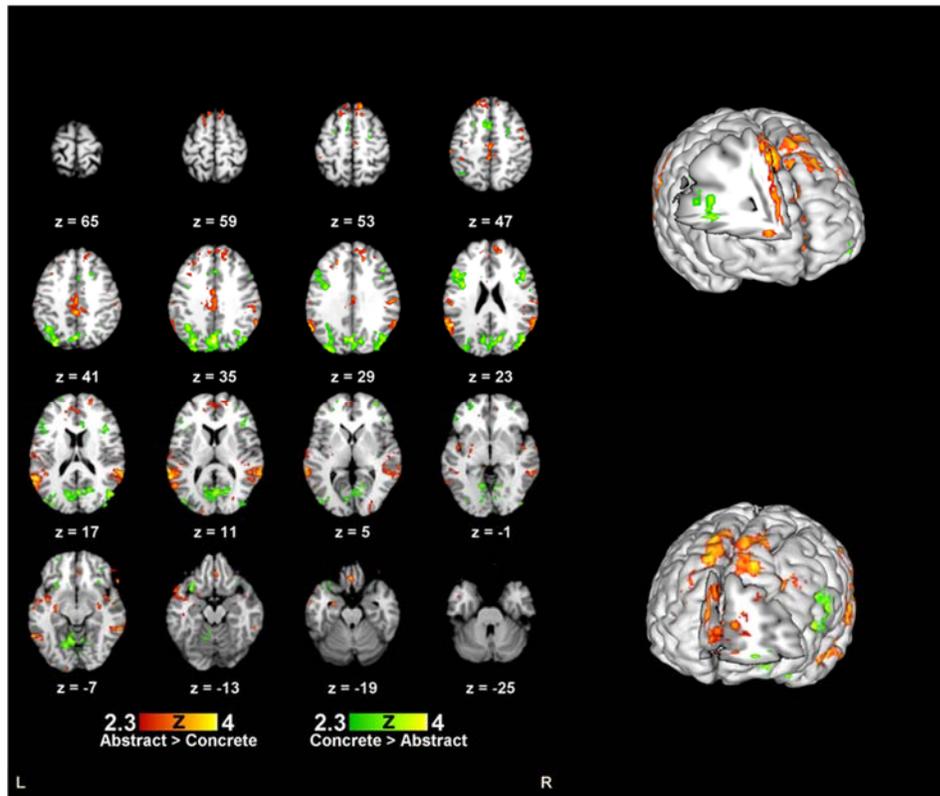


Figure 30. Figure 30 demonstrates a comparison of Abstract > Concrete and Concrete > Abstract results for the group level cluster analysis overlaid onto a standard space MNI template. The red to yellow colors indicate the results for the Abstract > Concrete comparison and the green to yellow colors indicate the results for the Concrete > Abstract comparison. In each scale, brighter colors reflect higher z-statistics. The left panel shows slices along the z-axis, beginning with superior portions of the brain at the top left and ending with inferior portions of the brain in the bottom right. The right panel shows a 3-d rendering of the sample with overlaid activation.

The fifth and sixth group-level cluster analyses assessed whether any brain regions demonstrated sensitivity to set-size across the abstract rule conditions by separately subtracting 8 paired-item task activations from 16 and 32 paired-item activations. The group level results of

the 16 paired-item > 8 paired-item contrast failed to yield peak voxel activations distributed within bilateral rostral PFC regions. This finding was expected based on the inference that such a contrast would be predicted by both the rostral-caudal hierarchy and MDA models and that no significant behavioral distinctions were observed during these task conditions. Unlike the 16 paired-item > 8 paired-item contrasts, the 32 paired-item > 8 paired-item group level cluster analysis yielded significantly increased activation in the superior frontal gyrus. This finding was somewhat surprising given that there were no observed performance distinctions between these task conditions. Considering the lack of behavioral dissociations for difficulty across these conditions, one potential explanation is that the superior frontal gyrus was sensitive to the number of exemplars which the abstract rule must be applied. This conclusion is, however, tenuous, given that the current study is the first to manipulate set-sizes when assessing neural correlates of abstract rule use.

The seventh and eight group-level cluster analyses assessed whether any brain regions demonstrated sensitivity to set-size across the concrete rule conditions by separately subtracting 8 paired-item task activations from 16 and 32 paired-item activations. The group level results of the 16 paired-item > 8 paired-item contrast failed to yield peak voxel activations distributed within bilateral rostral PFC regions. This finding was expected based on the inference that such a contrast would be predicted by the MDA model. This finding is somewhat surprising given the intermediate effect size for behavioral distinctions observed during these task conditions. Unlike the 16 paired-item > 8 paired-item contrasts, the 32 paired-item > 8 paired-item group level cluster analysis yielded significantly increased activation in the right lateral middle frontal gyrus. This critical finding supported the notions put forth by the MDA model, which asserts that increased task difficulty mediates activity in rostral PFC regions, previously believed to

exclusively maintain relatively abstract rule use. This result is bolstered by the significant behavioral differences in difficulty across these conditions. Taken together with the results from 16 paired-item > 8 paired-item contrasts, the 32 paired-item > 8 paired-item group level cluster analysis provides evidence, using novel cognitive demand domains for rule abstractness and difficulty, in support of the MDA model originally proposed by Duncan and colleagues (2000).

General Discussion

Across two experiments, the effects of varying abstractness and difficulty of rule use was assessed orthogonally. The broad goal of these experiments was to assess whether increased memory load demonstrates increased measures of effort in a concrete rule-use task, and whether this increased effort would correspond to distinct profiles of neural modulations when compared to the neural correlates of the analogous abstract rule task. An abstract, *same/different* rule task and a comparable concrete, memorization rule task were developed in order to compare two alternative models of the frontal lobe's functional organization by utilizing a converging operations approach. The primary conclusion is that rostral PFC regional activation was demonstrated to underlie relatively concrete rule use and did so in a positive relation to task difficulty.

In Experiment 1, a mixed, between- and within-subject task design assessed whether increased numbers of stimuli affects difficulty in a concrete rule task but not an abstract rule task. Based on an assumption that image-pair set-size would increase memory loads and difficulty in the concrete rule task but not result in increased difficulty and memory loads for the abstract rule task, groups were trained and tested for both abstract and concrete rule using different set-sizes. The results demonstrated that difficulty, assessed by the percent of correct

responses, increased across larger set-sizes for the concrete task, but not the abstract task. In order to confirm that strategies used in the task matched the experimenter's intentions, novel-item testing was implemented after each participant reached a performance criterion in either task. The results of novel-item tests revealed full transfer of abstract rule use for novel exemplars across all set-sizes of the abstract task conditions. In contrast, performance was inconsistent with abstract rule use for novel exemplars for all set-sizes of the concrete task conditions.

In Experiment 2a the initial abstract and concrete rule tasks were adapted as a pure within-subjects task design in order to assess these conditions in a manner optimal for fMRI data analysis. The primary goal of this experiment was examine whether the same functional relationships of set-size and task rule conditions observed in Experiment 1 could be demonstrated in a within subjects design with a sample size comparable to that of a typical BOLD fMRI study. The results of the newly adapted tasks yielded consistent functional relationships for set-size and task rules. Comparisons of percent correct across concrete task conditions yielded mean differences and effect sizes which varied in a positive relation to differences in memory load produced by set-size. The successful piloting in Experiment 2a enabled the implementation of the adapted task conditions during fMRI data acquisition in Experiment 2b.

The results of Experiment 2b provide valuable insight into the neural correlates of abstract and concrete rule use as well as the functional relationships of memory load to these tasks. The rostro-caudal hierarchy model (see Figure 1 for depiction) predicts that neural correlates of concrete rule use (i.e., S-R rule execution) reside in caudal regions including motor cortex (BA 6) and those of abstract rule use (i.e., Matching and Non-matching) reside across rostral to caudal regions of the PFC, including motor cortex (BA 6), dorsolateral prefrontal

cortex (BA 8, BA 9, BA 46). The specific distinctions were based, in part, on previous studies examining concrete and abstract rule task dependent activity in the prefrontal cortex (Bunge et al., 2003; Badre and D'Esposito, 2007). The prior studies each contained the limitation of holding task difficulty constant across increased rule abstractness. Experiment 2b provides preliminary findings that the factor of task difficulty is important in assessing the potential for a hierarchical, functional organization of the PFC. These findings were largely consistent with the multiple demand activation model originally proposed by Duncan and Owen (2000). Activations spanning the rostro-caudal axis of the frontal lobes were found during both abstract and concrete rule use, when collapsed across set-size. Interestingly, relatively lateral regions for concrete rule use and medial regions for abstract rule use were observed within this functional network. The critical finding of Experiment 2b was the sensitivity of rostral regions of the rostro-caudal axis (i.e., right lateral middle frontal gyrus) to task difficulty, via memory load demands when comparing 32 > 8 for the concrete task. This result provides further evidence, via a converging operations approach, that relatively concrete task demands can be enabled by rostral PFC regions and do so in positive relations to the difficulty of task demands.

Implications for a functional hierarchy within the frontal lobes

Results from these two experiments contribute some understanding regarding several questions on the abstractness of action rules, or the degree to which a rule depends on how specified that relationship is between conditions which are met and appropriate actions are executed. Critically, these experiments demonstrated that rostral regions of the PFC are sensitive to the difficulty task demands independent of the flexibility for inputs which prompt an action rule. The results lend support that tasks which independently assess flexibility for inputs and difficulty hold potential for answering basic questions about cognitive flexibility. Furthermore,

tasks which assess flexibility for action rules hold potential for exploring novel approaches to clinical populations which have demonstrated deficits in cognitive flexibility. For example, cognitive impairment associated with aging and Alzheimer's disease have been implicated in both studies of cognitive flexibility and atypical PFC functioning (Addis, Giovanello, Vu, & Schacter, 2013; Mimura & Yano, 2006).

A second important result in the current study was the finding that differences in the degree of flexibility for such action rules were associated with a lateral to medial dissociation across the entire rostro-caudal axis. This conclusion is limited based on the current findings, given that abstractness was only compared on a scale of two factors (abstract versus concrete rules). Additional manipulations, similar to varying the degrees of rule abstractness examined by Badre and D'esposito (2007), which could potentially assess the interaction of action rule abstractness and difficulty on a continuous scale would provide such a further assessment of lateral-medial hierarchy within the entirety of this PFC region network.

Regardless of this limitation, the findings of these two experiments serve to partially reconcile the conflicting reports from previous studies (Bunge et al., 2003; Badre & D'esposito, 2007; Crittenden and Duncan, 2014), which contribute evidence differentially in favor of either the rostro-caudal hierarchy model and the MDA model of frontal lobe functioning. On one hand, the current study demonstrated functional differences between abstract and concrete rule use which may arise from a hierarchical organization within the regions of the PFC. This finding was consistent with notions put forth by Badre and D'Esposito (2009) for a hierarchical organization of the frontal lobes. Given that studies reviewed as evidence for a rostro-caudal organization did not directly assess increased task difficulty for the concrete task demands, it is not surprising that only rostral activations were observed for the relatively more complex and difficult task demands

in these conditions. Unlike the assumptions made by the rostro-caudal hierarchy model, the results of the current study suggest that such an organizational hierarchy does not appear to manifest in a rostral-to-caudal direction.

Conclusion

Throughout these experiments, a running theme is that the number of item-specific action rules can come to require an increased amount of resources and lead to greater difficulty for executing action rules in a continuous manner. This notion is consistent with the utility for use of abstract action rules, in which fewer specific rules must be memorized in order to operate successfully in one's environment. This reduction comes at some cost, with abstract action rules requiring greater flexibility, which can also increase the expenditure of neural resources. The data from these experiments suggest that when memory load for highly specified rules becomes too effortful, abstract rules can serve with less difficulty and potentially fewer resources within the frontal lobes of the brain. One question which remains unclear is whether other tasks and cognitive domains would demonstrate similar functional relationships and lateral-to-medial PFC dissociations which were observed in the current study. A potential approach to this question would be to utilize the BrainMap database (brainmap.org) and Meta-Analytic Connectivity Modeling (MAMC; Robinson, personal communication, November, 2014) to examine whether archival studies reflect a lateral-to-medial functional segmentation of the PFC.

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