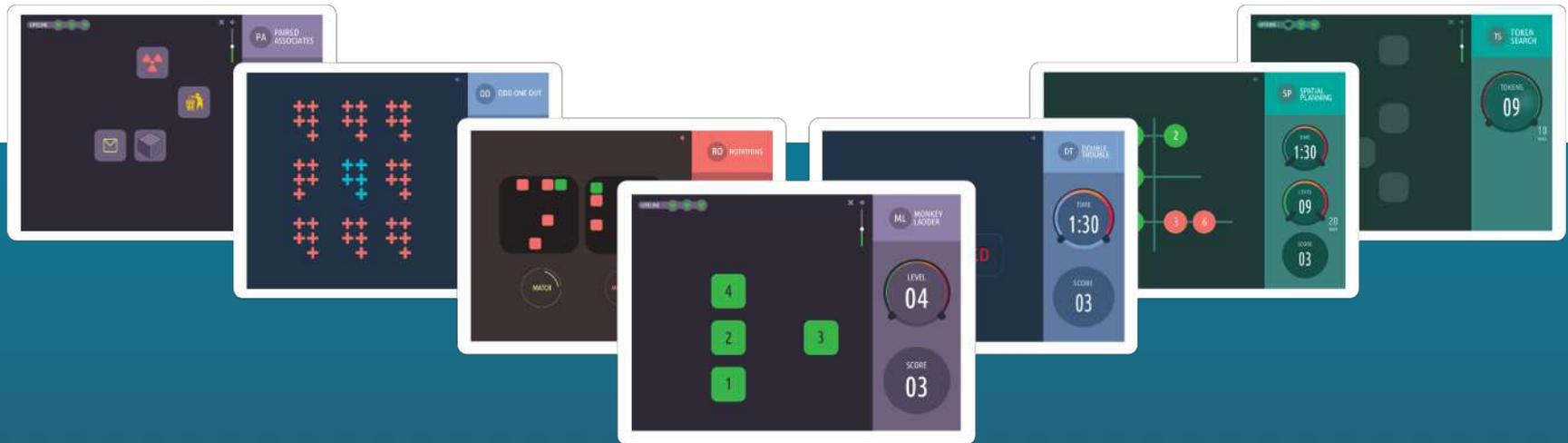


# Creyos Brain Regions Guide

Explore the areas of the brain associated with each Creyos cognitive task.



## Brain Regions Associated with the Creyos Tasks

- A. Document Overview
- B. Brain Networks Behind the Creyos Tasks
- C. Summary Table of the Brain Regions Specific to Each Task
- D. Detailed Supporting Data
- E. References

## A. Document Overview

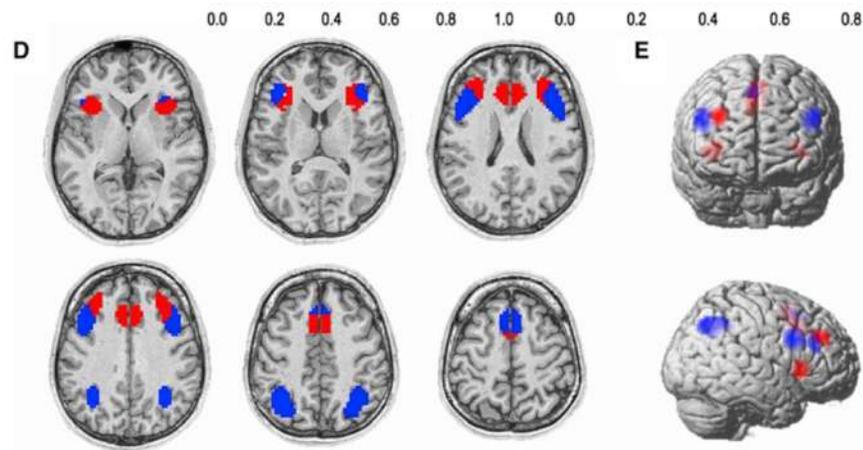
**This document identifies the brain regions that have been linked with performance on each Creyos (formerly Cambridge Brain Sciences) cognitive task. The information comes from studying how performance on the tests is affected by factors such as injuries or disease, as well as studying healthy brains using functional brain imaging technologies like functional magnetic resonance imaging (fMRI) and positron emission tomography (PET).**

When evaluating the core cognitive abilities measured by the Creyos tests, brain regions are recruited to perform a specific task (e.g. manipulate items in memory), rather than deal with a specific type of information (e.g. words vs. numbers), ensuring that our abstract computerized tests are suited to target particular cognitive abilities that apply across a wide range of contexts. Furthermore, all tests (and indeed, most behaviors) require more than one function, such that performance requires a network of brain regions rather than a single region. “It is simply very hard to be precise about the function of a region when that region is important in such a diversity of behavior” (Duncan & Owen, 2000). Nonetheless, research has revealed brain regions that are associated with the cognitive abilities targeted by each test.

## B. Brain Networks Behind the Creyos Tasks

In a landmark study published in *Neuron* (see Hampshire et al., 2012), we found that not only did performance tend to cluster into three cognitive domains—reasoning, short-term memory, and verbal ability—but each domain recruited distinct brain networks.

These networks within the frontal, parietal, and temporal cortices contribute to multiple tests. That is, any given test can recruit from multiple networks to varying degrees—it is not the case that any test or real-world activity activates one specific brain region, but rather, mixes and matches from brain regions suited to the various requirements and stages of a complex task.



The short-term memory (STM) network (red) and reasoning network (blue).

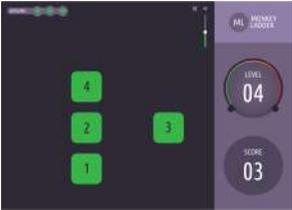
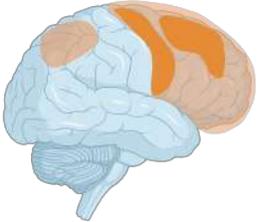
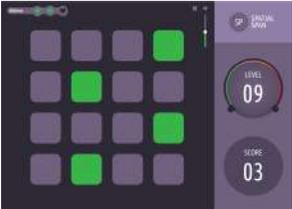
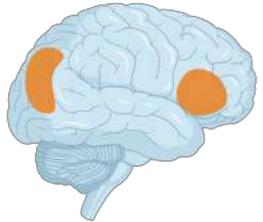
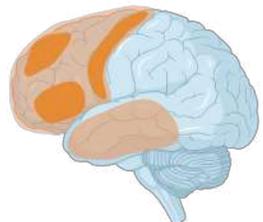
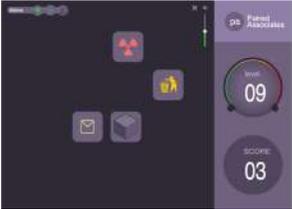
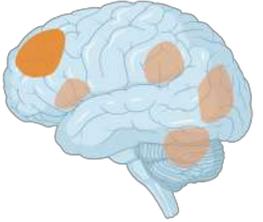
**Table 2. Task-Component Loadings from the PCA of Internet Data with Orthogonal Rotation**

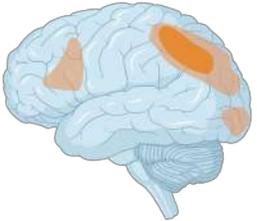
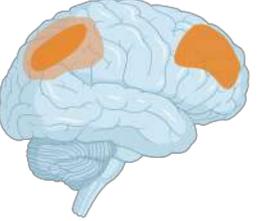
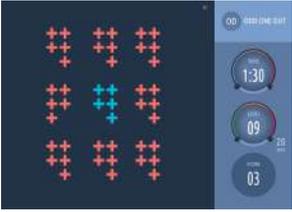
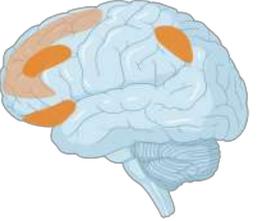
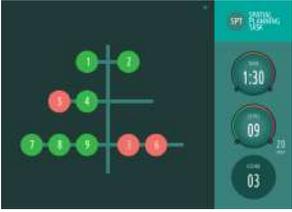
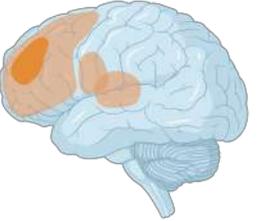
	1 (STM)	2 (Reasoning)	3 (Verbal)
Spatial span	0.69	0.22	
Visuospatial working memory	0.69	0.21	
Self-ordered search	0.62	0.16	0.16
Paired associates	0.58		0.25
Spatial planning	0.41	0.45	
Spatial rotation	0.14	0.66	
Feature match	0.15	0.57	0.22
Interlocking polygons		0.54	0.3
Deductive reasoning	0.19	0.52	-0.14
Digit span	0.26	-0.2	0.71
Verbal reasoning		0.33	0.66
Color-word remapping	0.22	0.35	0.51

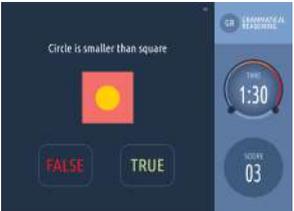
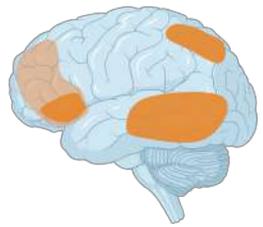
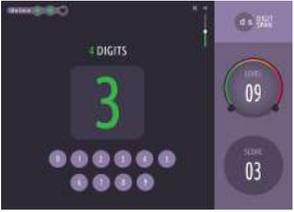
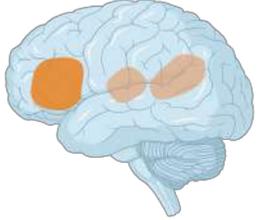
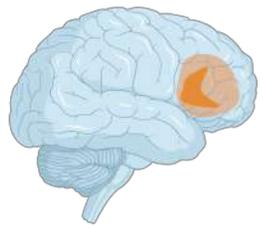
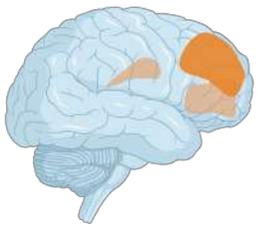
The mapping of each test to each network, based on performance data. The numbers are called factor loadings, and indicate the correlation between the observed test score and the latent “cognitive domain” score associated with a specific brain network.

## C. Summary Table of the Brain Regions Specific to Each Task

Brain regions that correspond with each task. See Section D for detailed explanations.

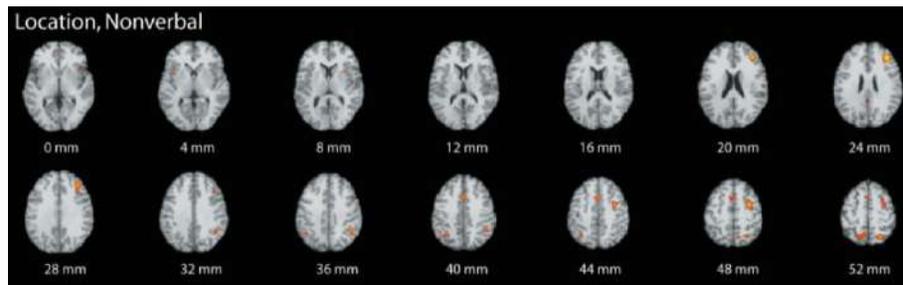
Domain	Task	Outcome	Associated Brain Regions	Example Brain Region Images	
MEMORY		Monkey Ladder	Visuospatial Working Memory	<ul style="list-style-type: none"> <li>• Prefrontal cortex / mid-dorsolateral prefrontal cortex</li> <li>• Premotor cortex</li> <li>• Posterior parietal cortex</li> </ul>	
		Spatial Span	Spatial Short Term Memory	<ul style="list-style-type: none"> <li>• Right mid-ventrolateral area</li> <li>• Parieto-occipital regions</li> </ul>	
		Token Search	Working Memory	<ul style="list-style-type: none"> <li>• Frontal and temporal lobes</li> <li>• Amygdalo-hippocampal region</li> <li>• Mid-ventrolateral frontal cortex</li> <li>• Mid-dorsolateral cortex</li> <li>• Premotor cortex</li> </ul>	
		Paired Associates	Episodic Memory	<ul style="list-style-type: none"> <li>• Left dorsolateral prefrontal cortex, ventral and anterior left prefrontal cortex</li> <li>• Ventral region of the parietal cortex</li> <li>• Occipitotemporal region</li> <li>• Cerebellum</li> </ul>	

Domain	Task	Outcome	Associated Brain Regions	Example Brain Region Images	
<b>REASONING</b>		Rotations	Mental Rotation	<ul style="list-style-type: none"> <li>• Intraparietal sulcus</li> <li>• Medial superior precentral cortex</li> </ul>	
		Polygons	Visuospatial Processing	<ul style="list-style-type: none"> <li>• Intraparietal sulcus</li> <li>• Right dorsolateral prefrontal cortex</li> <li>• Right hemisphere</li> </ul>	
		Odd One Out	Deductive Reasoning	<ul style="list-style-type: none"> <li>• Anterior frontal cortex, anterior cingulate</li> <li>• Anterior insula / frontal operculum</li> <li>• Inferior frontal sulcus</li> <li>• Presupplementary motor area</li> <li>• Intraparietal sulcus</li> </ul>	
		Spatial Planning	Planning	<ul style="list-style-type: none"> <li>• Frontal lobe</li> <li>• Mid-dorsolateral frontal cortex</li> <li>• Caudate nucleus and thalamus</li> <li>• Lateral premotor area</li> <li>• Anterior cingulate</li> </ul>	

Domain	Task	Outcome	Associated Brain Regions	Example Brain Region Images	
VERBAL ABILITY		Grammatical Reasoning	Verbal Reasoning	<ul style="list-style-type: none"> <li>• Frontal operculum</li> <li>• Posterior temporal lobe</li> <li>• Superior parietal lobe</li> <li>• Dorsal prefrontal cortex</li> <li>• Ventral prefrontal cortex</li> </ul>	
		Digit Span	Verbal Short Term Memory	<ul style="list-style-type: none"> <li>• Mid-ventrolateral prefrontal cortex</li> <li>• Left temporo-parietal lobe</li> <li>• Basal ganglia</li> </ul>	
CONCENTRATION		Feature Match	Attention	<ul style="list-style-type: none"> <li>• Mid-ventrolateral frontal cortex</li> <li>• Right inferior frontal gyrus</li> </ul>	
		Double Trouble	Response Inhibition	<ul style="list-style-type: none"> <li>• Right prefrontal cortex</li> <li>• Dorsolateral frontal cortex</li> <li>• Left inferior frontal gyrus</li> <li>• Dorsal striatum</li> </ul>	

## D. Detailed Supporting Data

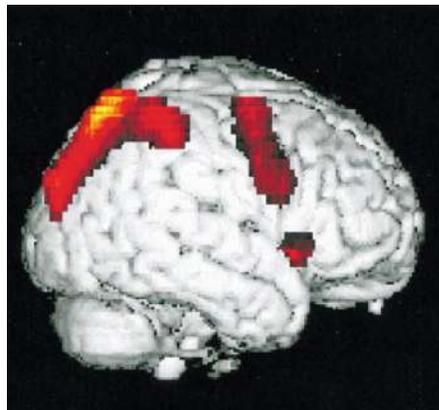
### Monkey Ladder



*Brain regions activated by nonverbal, location-based working memory tasks.  
(Owen et al., 2005)*

Monkey Ladder involves the cognitive function of working memory, but also requires visuospatial functions. Imaging data has revealed the brain regions involved in working memory using nonverbal stimuli with a spatial component. Across studies using tasks of this type, the **prefrontal, premotor, and posterior parietal cortex** are found to be involved (see Owen et al., 2005, for further details). The **mid-dorsolateral prefrontal cortex**, in particular, plays a role in working memory regardless of whether or not there is a spatial component (Owen et al., 1998).

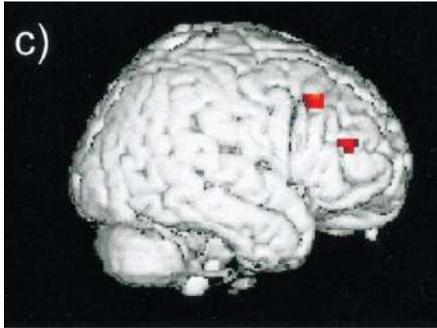
### Spatial Span



*Areas of the brain activated by spatial span,  
compared to simple visuomotor control.  
(Owen et al., 1999)*

Spatial Span is a spatial short-term memory task that requires holding a spatial sequence in memory for a short time. An early imaging study (Owen et al., 1999) using Spatial Span found increased blood flow in the **right mid-ventrolateral** area during the task. In Spatial Span, information does not need to be manipulated in memory, so additional brain regions involved in similar working memory tasks (e.g., Token Search) are not involved in this simpler task. Damage to the **parieto-occipital regions** of the brain causes impairment in visuospatial tasks like Spatial Span, but those with frontal lobe damage tend to be more impaired if there is a planning component, rather than pure memorization.

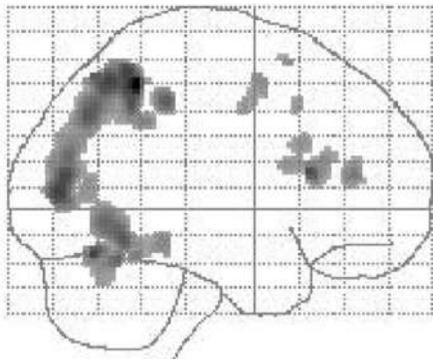
## Token Search



Unique areas of the brain activated by a complex spatial working memory task, in comparison with a simpler Spatial Span task. (Owen et al., 1999)

Token Search combines several cognitive abilities: short-term memory, working memory, and a strategy / planning component. Patients with damage to the **frontal lobe** are impaired even on easy puzzles, despite performing well on simpler short-term memory tests. This implies that the frontal lobe is particularly important for the strategy component of Token Search. Patients with lesions in the **temporal lobe** or **amygdalo-hippocampal region**, on the other hand, are impaired only on more difficult puzzles, implying that these regions are more responsible for the memory component of the task. Imaging studies confirm that the **mid-ventrolateral frontal cortex**, **mid-dorsolateral cortex**, and **premotor cortex** are all activated during this complex task (Owen et al., 1996).

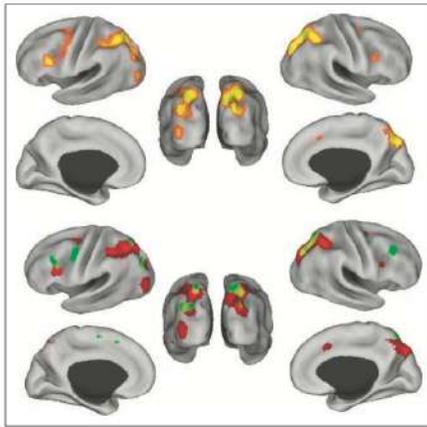
## Paired Associates



Brain regions showing activation during encoding of two object locations compared to a resting baseline (Gould et al., 2006).

Paired Associates is an episodic memory task in which two items—such as object identity and location—must be paired in memory, then later recalled. The **left dorsolateral prefrontal cortex** is related specifically to encoding memories and using executive processes to create an organizational structure, which is required for performance in Paired Associates, and has also been observed in realistic recall of object locations (Hayes et al., 2004). More **ventral and anterior left prefrontal cortex regions** appear to be recruited for general episodic memory encoding (Fletcher, Shallice, & Dolan, 1998a). During retrieval of the encoded memories, the **ventral prefrontal cortex** and the **ventral region of the parietal cortex** are activated specifically during tasks with cued recall (as in Paired Associates; Fletcher et al., 1998b). Furthermore, Gould et al. (2006) confirmed that **lateral and medial prefrontal and parietal cortices, as well as occipitotemporal and cerebellar regions**, were associated with encoding and retrieval of object-location pairs in Paired Associates in both healthy controls and people with Alzheimer's disease.

## Rotations

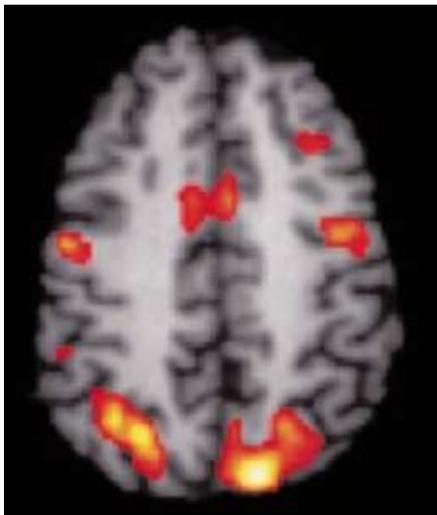


Areas of the brain activated during mental rotation. (Zacks, 2008)

The Rotations test requires visuospatial processing, and specifically the ability to mentally rotate objects. A review of the literature (Zacks, 2008) found that mental rotation activates the **intraparietal sulcus** and adjacent regions—areas that contain spatially mapped representations, implying that a representation of objects is simulated and rotated in the brain in an analog manner.

However, the **medial superior precentral cortex** is also activated—this is a motor area, implying that at least in some cases, a simulation of moving the object occurs in the brain. Damage to the brain can impair mental rotation; for example, patients with Parkinson’s disease perform poorly, which extends to real-world difficulty with tasks such as learning and navigating routes (Uc et al., 2007).

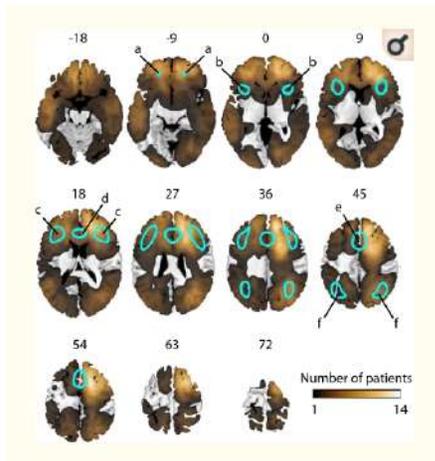
## Polygons



Areas of the dorsolateral prefrontal cortex activated by visuospatial orienting. (Pollman & von Cramon, 2000)

In general, visuospatial tasks activate the frontoparietal network, and particularly the **intraparietal sulcus region** of both hemispheres. Disruptions to the right parietal cortex specifically may have consequences for visuospatial function, such as visual judgement about angles (Sack et al., 2007). Polygons requires quick visuospatial processing, object recognition, and reasoning to determine if the shapes are the same. Compared to some similar tasks, memory is less applicable to Polygons, as there is no delay between presentation of the shape and making a judgment. One study (Pollman & von Cramon, 2000) found the **right dorsolateral prefrontal cortex** activated when performing goal-directed visual search, but was not related to memory, suggesting this area is unique to visuospatial processing. Damage to the brain can impair visuospatial function and attention, leading to poor Polygons performance. In one study (Lee et al., 2008), nearly half of patients with acute **right hemisphere** strokes were impaired in an interlocking polygons task, and extreme cases can lead to neglect of one side of the visual field, leading to failure to attend to one side of the shape.

## Odd One Out

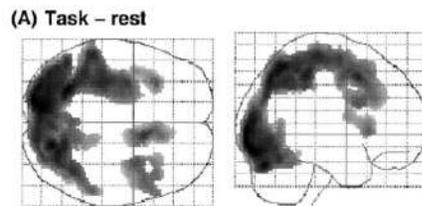


Brain regions involved in deductive reasoning.  
(Woolgar et al., 2010)

Odd One Out is a test of deductive reasoning—a core cognitive ability often included in tests of fluid intelligence. Engaging in difficult deductive reasoning results in a characteristic pattern of activity in several regions of the brain, including the **anterior frontal cortex**, **anterior insula / frontal operculum**, **inferior frontal sulcus**, **anterior cingulate**, **presupplementary motor area**, and **intraparietal sulcus**.

One study (Woolgar et al., 2010) verified that these specific areas play a role in fluid intelligence by confirming that damage to these regions—but not outside of them—predicts poor performance in reasoning tests, including items similar to Odd One Out.

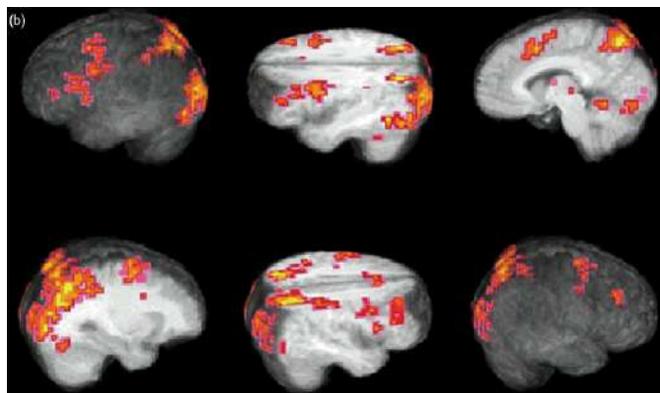
## Spatial Planning



Areas of the brain activated by spatial planning,  
compared to a brain at rest.

Spatial Planning requires the brain's reasoning and forward-thinking abilities. Spatial working memory is also required in order to hold plans in memory long enough to execute. The **frontal lobe** is known for its involvement in these higher executive functions. Early imaging studies (e.g. Owen et al., 1996) found that the **mid-dorsolateral frontal cortex** was activated in various versions of Spatial Planning. The **caudate nucleus** and the **thalamus** were involved only in more difficult puzzles. A subsequent study (Dagher et al., 1999) added the **lateral premotor** and **anterior cingulate** areas to the network responsible for the visual processing and anticipation of movement required for spatial planning.

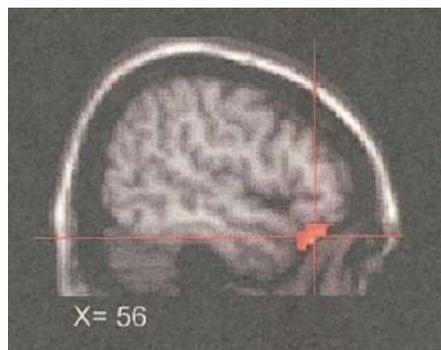
## Grammatical Reasoning



Regions activated by difficult problems in a grammatical reasoning task. (Drummond et al., 2003)

Grammatical Reasoning primarily involves two cognitive processes: verbal-based reasoning to determine what the sentence should be describing, and comparison of this internally-generated answer with the image on the screen. One study (Drummond et al., 2003) found that engaging in these tasks recruited brain regions associated with rehearsal and language processing within the **frontal operculum and posterior temporal lobe** language areas, and the **superior parietal lobe** visuospatial processing region was also active. In more difficult problems, additional brain regions in the **dorsal and ventral prefrontal cortex** are recruited. Interestingly, regions associated with working memory do not seem to be involved, as previously thought. This reliance on verbal and reasoning abilities over working memory is confirmed by imaging and behavioral data in the context of the other eleven tests (Hampshire et al., 2012).

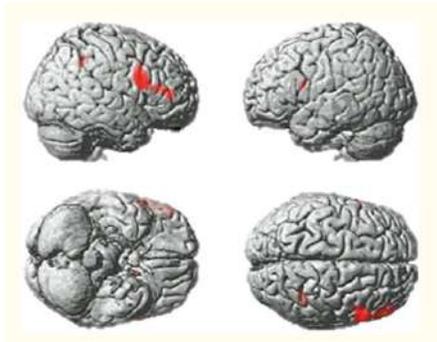
## Digit Span



Averaged PET subtraction image of activation in the right hemisphere during forward digit span performance vs. control. (Owen et al., 2000)

Digit Span requires verbal (versus spatial) short-term memory. The frontal cortex is involved in tasks that require memorizing and recalling verbal information. More specifically, the **mid-ventrolateral prefrontal cortex**, primarily in the right hemisphere, is activated during verbal short-term memory tasks (Owen et al., 2000). This area of the brain is involved in tasks that require active, conscious retrieval and reproduction of stored information. Because Digit Span is a straightforward memorization task that does not require manipulation of items in memory (as in backwards digit span tasks and Croyos working memory tasks, such as Token Search), it does not recruit additional brain regions involved in more complex tasks, such as the dorsolateral prefrontal cortex. Rather, the ventrolateral frontal cortex's general role is to enable the low-level encoding strategies required in Digit Span, such as rehearsal and initiation of intentional retrieval of information from memory. Furthermore, a study of stroke survivors (Geva et al., 2021) indicated that damage to the **left temporo-parietal** and **basal ganglia** structures consistently disrupts performance on Digit Span.

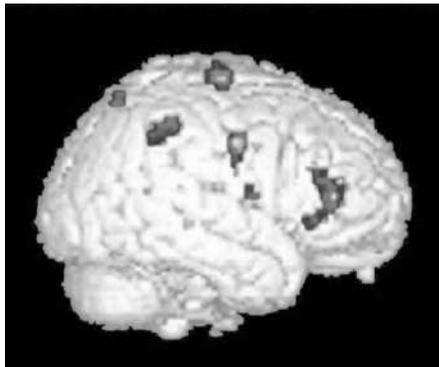
## Feature Match



Activation in the inferior frontal gyrus and right inferior parietal cortex when a target (among distractors) is found. (Hampshire et al., 2010)

Feature Match is a perceptual test that requires the cognitive ability of tuning attention and monitoring for differences. The **mid-ventrolateral frontal cortex** is involved in functions targeted by Feature Match, such as deliberate, focused control of thought and action (Owen & Hampshire, 2009). Within this network, the **right inferior frontal gyrus (IFG)** in particular responds when a desired feature that is being monitored for (such as a difference) is found (Hampshire et al., 2009). This region adapts to activate in response to currently-relevant information— that is, it responds selectively to items that are most relevant to the task at hand, rather than any specific stimulus.

## Double Trouble



Regions of the brain involved in attention, particularly in an unchallenging sustained attention task. (Manly et al., 2003)

Double Trouble is a test of focused attention and response inhibition. The **right prefrontal cortex**, and in particular the **dorsolateral region**, is involved in tests that require sustained focused attention, such as Double Trouble. Damage to these regions, common in cases of traumatic brain injury, may be responsible for the problems with attention that often follow injury, and impair performance on tasks like Double Trouble (Manly et al., 2003; Dimoska-Di Marco, 2011). In addition to attention, Double Trouble involves the cognitive ability of response inhibition—the ability to suppress making responses to task-irrelevant information (e.g., the meaning of a word, rather than its colour). This can be differentiated from simple attention or effort. Brain regions involved in this function, which is particularly prominent in Double Trouble’s double-Stroop design, include the **left inferior frontal gyrus** (Taylor et al., 1997). The **dorsal striatum** has also recently been implicated as important for cognitive control, but not cognitive effort (Robertson et al., 2015).

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*Note: brain regions are approximate, based on available research using tasks identical to or similar to Creyos tasks. Research may refer to the tasks under the previous company name, Cambridge Brain Sciences. Brain illustrations created with [BioRender.com](https://www.biorender.com).*