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# A split-brain case study on the hemispheric lateralization of inhibitory control

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ABSTRACT

Understanding the neurobiological mechanisms underlying inhibitory control is crucial given its role in various disease states and substance abuse/misuse. Neuroimaging research examining inhibitory control has yielded conflicting results on the relative importance of the left and right hemisphere during successful inhibition of a motor response. In the current study, a split-brain patient was examined in order to assess the independent inhibitory capabilities of each hemisphere. The patient's right hemisphere exhibited superior inhibitory ability compared to his left hemisphere on three inhibitory control tasks. Although inferior to the right, the left hemisphere inhibited motor responses on inhibitory trials in all three tasks. The results from this study support the dominance of the right hemisphere in inhibitory control.

## 1. Introduction

The ability to inhibit inappropriate thoughts, emotions, and behaviors is a critical component of executive functioning and cognitive control. Humans must continuously adapt to changing environments and circumstances, filter out irrelevant information, and evade danger and harm, all of which require inhibitory control. Deficits in inhibitory control contribute to clinical conditions including Parkinson's disease (Gauggel et al., 2004), attention deficit hyperactivity disorder (ADHD; Casey et al., 1997; Slaats-Willemse et al., 2003), and obsessive-compulsive disorder (OCD; Bannon et al., 2002; Penades et al., 2007). Additionally, sub-clinical impairments in inhibitory control are associated with impulsivity and risk-taking behaviors evident in substance misuse (Helfinstein and Poldrack, 2012; Nigg et al., 2006; Whelan et al., 2012).

Two task paradigms commonly used to assess inhibitory control are the Go/No-Go task and the Stop Signal Task (SST). Both tasks require rapid behavioral responding to a go signal on a majority of trials, and a withholding of the response on a subset of "no-go" and "stop" trials. In the Go/No-Go paradigm, an individual must inhibit the prepotent go response when presented with an infrequent stimulus, the no-go signal (Bokura et al., 2001; Eimer, 1993; Menon et al., 2001). In the SST, an individual must inhibit an already initiated response when presentation of a go signal is followed by the presentation of a stop signal, which occurs on a minority of trials (Logan, 1994; Logan and Cowan, 1984).

Neuroimaging studies that use the SST and the Go/No-Go task have found conflicting results as to the lateralization of inhibitory control. A large body of research has identified the right inferior frontal gyrus (rIFG) as a key area for successful response inhibition. Functional neuroimaging studies have found increased activation in the rIFG during successful inhibition of a motor response in both the Go/No-Go and the SST (Aron et al., 2004; Garavan et al., 1999; Hampshire et al., 2010; Rubia et al., 2001). Further, patients with damage to the rIFG show decreased performance in the SST compared to healthy controls (Aron et al., 2003) and inhibition is temporarily impaired in individuals who were exposed to Transcranial Magnetic Stimulation (TMS) that was directed at the rIFG (Chambers et al., 2007; Siebner and Rothwell, 2003).

However, there is also compelling research suggesting a role of the left inferior frontal gyrus (lIFG) in response inhibition. Much of this research describes the activation of the lIFG in conjunction with rIFG activation during successful inhibition in Go/No-Go and SST (Hirose et al., 2012; Li et al., 2006; McNab et al., 2008; Rubia et al., 2001; Rushworth et al., 2001). Results from these studies suggest that as the difficulty of inhibition increases, the lIFG is recruited to supplement the rIFG (Hirose et al., 2012). However, Swick et al. (2008) found that individuals with lesions in the lIFG performed worse on a Go/No-Go task compared to healthy controls, suggesting that the lIFG plays a critical, rather than a supplemental role, in response inhibition. Taken together, previous research highlights the importance of both the left and right hemispheres in response inhibition, and therein the lateralization of the neural mechanisms underlying inhibitory control

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remains unclear.

In addition to left and right prefrontal systems, subcortical structures, namely the basal ganglia and the subthalamic nucleus (STN), have been implicated in response inhibition as well. Research examining the role of the STN in response inhibition has found increased activation in the STN during successful inhibition (Aron and Poldrack, 2006), and surgical lesions of the STN in rodents result in a significant loss of inhibitory abilities (Eagle and Robbins, 2003). Interestingly, Van den Wildenberg et al. (2006) found that stimulation of the STN in patients with Parkinson's Disease improved inhibitory control deficits that are a primary characteristic of the disease. Thus, researchers have proposed a neural circuit involving both the prefrontal cortex and the basal ganglia for response selection and response inhibition (Nambu et al., 2002).

Examining an individual who has undergone a corpus callosotomy provides a unique approach to address the hemispheric lateralization of response inhibition. Complete resection of the corpus callosum results in near total loss of communication between the right and left hemispheres at the cortical level, which includes the transfer of perceptual, sensory, cognitive, and motor information (Gazzaniga, 2005). Split-brain patients have been studied extensively to expose the independent functions of each hemisphere (Gazzaniga, 2000, 2005; Springer and Deutsch, 1998). Due to the neural architecture of the visual system, a stimulus can be presented laterally in the visual field such that the visual information is only processed in one hemisphere (Brindley, 1960). Split-brain patients lack commissural fibers for inter-hemispheric communication, and therefore the hemisphere that processes a visual stimulus must complete the task indicated by the stimulus. Thus, presenting a task in the lateral visual field of a split-brain patient can isolate the function of a single hemisphere.

The goal of the present study is to explore the lateralization of inhibitory control using a corpus callosotomy patient. We test the patient using both Go/No-Go and Stop Signal Tasks in which only one hemisphere is probed at a time for each stimulus. We hypothesize that the right hemisphere will possess superior inhibitory abilities compared to the left hemisphere during both Go/No-Go and Stop Signal Tasks.

## 2. Materials and methods

### 2.1. Participant

The participant in the current study was patient J.W., a 48-year-old, right-handed male of average intelligence. Handedness was assessed using the Edinburgh Handedness Inventory (Oldfield, 1971). At the age of 25, J.W. received a two-stage surgical resection of his corpus callosum as treatment for medically intractable epilepsy. Post-surgical MRI confirmed complete resection of the corpus callosum with no additional brain damage. Patient J.W.'s medical details and cognitive profile have been previously described (Gazzaniga et al., 1984).

### 2.2. Divided visual field

The current study examines previously collected data from a one day visit in which J.W. participated in an assessment of response inhibition. These data were not a part of a larger test battery. J.W. completed three motor inhibition tasks: one Go/No-Go task, a single choice Stop Signal Task, and a forced choice Stop Signal Task, in this order. Breaks were provided as needed. For all three tasks, the divided visual field technique was employed on all stimuli presented. The technique is designed to target only one hemisphere per stimulus. The visual system is organized such that the medial hemiretina of the eye projects to the contralateral hemisphere and the lateral hemiretina projects to the ipsilateral hemisphere. Thus, a stimulus presented lateral to midline will be perceived by the contralateral hemisphere. For example, if the image is presented left of midline, the left medial retina and the right lateral retina will detect the image, and both will project to the right hemisphere.

### 2.3. Experimental design

J.W. was seated 57 cm from the computer screen and was instructed to fixate on a midline fixation cross. Stimuli were presented for 150 ms. 150 ms stimulus presentation has been used in previous work using the divided visual field design with split brain patients (Corballis et al., 2002; Colvin et al., 2005), and a report by Funnell et al. (2007), which used eye-tracking software, reported this stimulus length to not produce saccadic movements. The medial edges of the stimuli were at least 3 cm lateral to midline, which fall outside the field of nasotemporal overlap. These parameters ensure that only the hemisphere contralateral to the visual field of stimulus presentation perceives the stimuli.

Responses to stimuli were made via key press on a standard Macintosh keyboard with the hand ipsilateral to the visual field of presentation. Therefore, the hemisphere receiving the visual stimuli was the same hemisphere generating the motor response. Four keys, two for left hand responses (A and Z) and two for right hand responses (“ and /), were marked with stickers to indicate the correct response keys. On the Go/No-Go and single choice Stop Signal Task, one key for each hand was used for a response to the go signal. On the forced choice Stop Signal Task, there were two possible key responses for each hand corresponding to the two possible go signals.

### 2.4. Go/No-Go task

A series of the letters X and Y were presented in a ratio of 15:1, pseudorandomly. The letters were presented equally often in both the left visual field and the right visual field. J.W. was instructed to make a key press as quickly as possible with his left hand when the letter X appeared on the left side of the screen, a key press with his right hand as quickly as possible when the letter X appeared on the right side of the screen, and to make no response when the letter Y appeared on either side of the screen. There were 256 trials in each session, with 128 stimuli presented in each visual field. Trials were presented randomly in each visual field and J.W. was asked to maintain fixation on the center of the screen. J.W. completed 5 sessions, each session lasted approximately four and a half minutes.

### 2.5. Single choice Stop Signal Task

The first Stop Signal Task was a single-choice task (Fig. 2). J.W. was presented with a series of X's (go signal) and instructed to respond via key press, as quickly as possible with the hand ipsilateral to the side of the screen the X was presented. Following 25% of the X's, a stop signal flashed on the screen, signaling to J.W. to no longer respond to the X. The onset of the stop signal presentation varied from 50 to 250 ms delay at 50 ms intervals. Each stop signal delay (SSD) was presented equally often. There were 96 total trials in each session, with 48 stimuli presented in each visual field. Trials were presented randomly in each visual field and J.W. was asked to maintain fixation on the center of the screen. J.W. completed 16 sessions of the task, each session lasted just under three minutes.

### 2.6. Forced choice Stop Signal Task

The second stop signal task required J.W. to choose between two possible response keys on the go signal. In this task, J.W. was presented with either an X or an O as the go signals (Fig. 2). J.W. responded as quickly as possible with the appropriate key on all go trials with the hand ipsilateral to the stimuli presentation. There were four possible keys for go responses: one key for the O stimuli in the left visual field, a key for the O stimuli in the right visual field, a key for the