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APPLYING MENTAL BRAKES: AN FMRI INVESTIGATION OF PREPOTENT MOTOR RESPONSE SUPPRESSION

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ABSTRACT

The utilization of fMRI research has become essential in studying the regions of the brain responsible for motor inhibition. Despite the wealth of published research on the locations for motor inhibition control, little to no data describes how motor inhibition proficiency influences the activation within motor control regions. This study examines the effect of individual differences in inhibition proficiency on the neural regions activated during a Go/No-go task to investigate how individual motor inhibition skill correlates with increased or decreased neural activity. The results revealed five areas of the brain that show increased activation as individual performance improves, including the bilateral superior frontal gyrus and the bilateral middle frontal gyrus, regions known for their role in motor inhibition. In addition, the activity in the putamen, a region responsible for neural connectivity during motor inhibition, narrowly escaped threshold for increased activation (12 voxels). This information will contribute to the concept of the brain-behavior relationship of inhibition control.

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Chapter 1

Introduction

The notion of "stop" remains as innate to the human mind as the concept of "go". While the idea of "go" incites associations with action, "stop" provokes the opposite: the halting of action or lack of motion. For years psychologists have tried to measure the cognitive and behavioral reactions to stop commands; however, the real conundrum of the field derives from the issue of how one measures the absence of a tangible process. After much research, several tasks have been developed as tools to successfully investigate this concept; many of them function by measuring rates of inhibition success as compared to initiation success. New information on the neural aspects of stop processes have emerged as the advent of neuroimaging technology has revealed glimpses into the inner functioning of the brain. Such studies have shown that inhibition of action relies more heavily on active cognitive and neurological functions than previously hypothesized. While many researchers have looked at behavior and neural networking separately during investigations into the "stop" paradigm, none to date have investigated how behavioral success impacts neural activity. The current study will use fMRI to investigate the role of individual differences in inhibitory function on motor inhibition using the Go/No-go task.

Since the early days of psychology, researchers have defined and categorized types of human behavior. In 1929, E.B. Skaggs produced an article describing and itemizing the concept of inhibition, or the interference of one mental process on another (Skaggs, 1929). By inhibiting or blocking the progress and fruition of any sort of action or thought, the brain can exert control upon the domains of cognition and behavior. Skaggs splits inhibition into voluntary and

involuntary inhibition and further divides each into categories of learning, thought, sensation, and movement. The key consideration for each type of inhibition involves whether the action developed with or without active, effortful cognitive processes (voluntary inhibition as the former and involuntary as the latter).

Considering the bifurcation of inhibition, motor inhibition exists as motor reflexes and active (prepotent) motor suppression. Reflexes fall under Skaggs' category of involuntary motor inhibition and are characterized as unwilled responses to the environment resulting in the termination of action (Skaggs, 1929). Contrastingly, voluntary motor inhibition, termed prepotent motor response suppression, involves the operative interference of an act already in motion such as the cessation of laughter or walking. Prepotent motor response suppression also applies to inhibitions upon the impulse to act (Skaggs, 1929). Although prepotent motor response suppression and response selection are often equated (Rubia et al, 2001), real differences exist between the two cognitive-motor processes (Bedard et al, 2002). Response selection involves the choice between two different movements, while motor response suppression involves the choice between action and no movement; individuals utilize response selection to determine the type of action required and motor response suppression to determine if action is required at all (Kawashima et al, 1996).

Barring response selection tasks, researchers currently use two main tasks to study prepotent motor inhibition: the stop signal task and the go-no/go task. The stop signal reaction task (SSRT), developed by Lappin and Eriksen in 1966, works to determine a person's ability to withhold a reaction or inhibit a motion already in progress. Within the task, participants constantly receive "go" stimuli and occasionally receive "stop" stimuli right after the "go" signal. Although the participant may not have initiated the motion response to the "go" stimuli,

they have already started the cognitive response. The SSRT measures how quickly one can inhibit both cognitive and motor responses. The Go/No-go task (GNG) has a much more simplistic way of accessing motor inhibition competency. The GNG, developed by Mishkin and Pribram in 1955, assesses an individual's ability to successfully inhibit or initiate an action based on stimuli cues. If the "go" stimulus appears, the participant responds with a designated action, and if the "no-go" stimulus appears, the participant withholds the action. Because the majority of the trials present "go" stimuli, the "go" response becomes the participant's habitual or baseline action. The sudden "no-go" signals force the participant to inhibit the ingrained "go" motor response, and the success rate of inactivity during the "no-go" signals demonstrates the individual's prepotent motor suppression skills.

Early Go/No-go Studies

Before modern technological advancements such as fMRI, researchers relied on more basic methods of investigating neural activity. Some of the first studies investigating motor inhibition relied on lesion methodology on a variety of primate subjects. These studies showed that lesions located in parts of the frontal cortex cause the most hindrance in performing the GNG task (Mishkin & Pribram, 1955; Drewe, 1975; Petrides, 1986). Mishkin and Pribram (1955) isolated the anterolateral frontal cortex and found that macaques without this brain region took much longer to train to complete the GNG task and exhibited decreased accuracy in inhibition performance. Supporting this research, rhesus monkeys with lesions in the periarcuate cortex of the frontal lobe, specified as Brodmann areas (BA) 6 and 8, took more time to train for the GNG task than monkeys without lesions or lesions in other areas of the brain; some of the

monkeys with periarcuate lesions were completely unable to perform the GNG task (Petrides, 1986).

While the early lesion studies found specific brain regions associated with motor inhibition, the advent of electroencephalography (EEG), magnetoencephalography (MEG), and positron emission tomography (PET) allowed researchers to see exactly when and where the brain activates in response to stimuli. Although the names given to the regions activated during the GNG task vary across researchers, the general consensus agrees that control of motor inhibition resides in the prefrontal cortex (PFC; Eimer, 1993; Kawashima et al, 1996). A series of PET and MEG studies specifies the frontal association cortex as the primary region for the decision- making component of inhibiting a motor response (Tsujimoto et al, 1997; Sasaki et al, 1993). As the part of the frontal association cortex that has the strongest control over motor inhibition, the primary sulcus within monkey subjects correlates to BA 9 and 46 in the human brain (Tsujimoto et al, 1997). Researchers suggest that a connection exists between the frontal association cortex and the premotor cortex to control movements (Sasaki et al, 1993); the prefrontal cortex regions involved in inhibition are activated before the premotor cortex neurons (Falkenstein et al, 1999). While connectivity impacts the success of inhibition, EEG studies have suggested that the amplitude of neural activity increases as the GNG task difficulty increases (Jodo & Kayama, 1992).

Recent fMRI Studies

Over the past few years, functional magnetic resonance imaging (fMRI) has become one of the most utilized techniques for observing the neural activity of motor inhibition. Although

researchers do not always use the same labeling system for reporting the areas of the brain activated, a closer examination of the data reveals two main areas involved in motor inhibition: the inferior frontal cortex (IFC) and the pre-supplementary motor area (pre-SMA) (Aron et al, 2004; Bedard et al, 2002; Duann et al, 2009; Rubia et al, 2001).

In GNG and other research designs, the inferior frontal cortex (IFC), considered part of the prefrontal cortex, serves as one of the most highly studied areas associated with motor inhibition. Formed from BA 44, 45 and 47, the IFC is one of the last brain regions to develop both ontologically and phylogentically (Aron et al., 2004). For this reason, children tend to perform worse on motor inhibition tasks than adults (Casey et al., 1997). As one of the most heavily connected areas of the prefrontal cortex (Aron et al., 2004), the IFC is believed to serve as the control center for initiating a motor inhibition event (Aron et al., 2004; Rubia et al., 2001; Casey et al., 1997).

The IFC connects to areas of the middle frontal gyrus, including the pre-supplementary cortex (pre-SMA), to control motor inhibition (Duann et al., 2009; Watanabe et al., 2002; Rubia et al., 2001). Bilateral activation of the middle frontal gyrus occurs across all different types of motor inhibition tasks, indicating its use is not specific to the GNG task (Watanabe et al. 2002; Rubia et al., 2001). Additionally, comparisons of children and adults demonstrate that children recruit greater volumes of neural activation in this region during prepotent motor suppression tasks (Casey et al., 1997). This may serve as a compensation mechanism for underdevelopment of the IFC during childhood. Within the middle frontal gyrus, the pre-SMA is defined as the rostral component of BA 6 (Watanabe et al., 2002). While the mesial and dorsolateral areas of the prefrontal cortex activate during the inhibition of reflexes, the pre-SMA control the initiation and suppression of voluntary movements (Rubia et al., 2001). In a stop-signal reaction time (a

type of motor inhibition task) experiment, Duann *et al.* (2009) demonstrated that pre-SMA neural activity increases with improved ability and speed of initiating a motor suppression event.

In order for successful motor inhibition to occur, the separate regions of the brain controlling the response must neurologically connect and create a decisive behavioral output. To study the synaptic or cortical influence of one system over another, one must analyze neural connectivity during the intended event (Friston, 1994). Within the literature for motor inhibition using the GNG task, two regions have received disputed attention as the area that connects the IFC with the pre-SMA: the anterior cingulate cortex and the basal ganglia (Aron et al., 2004; Duann et al., 2009; Rubia et al., 2001; Watanabe et al., 2002). Most research analyzing neural activation contends that the right anterior cingulate acts as the region that connects the pre-SMA and IFC (Watanabe et al., 2002; Rubia et al., 2001). Additional research found a correlation between failed motor inhibition and faulty anterior cingulate activation (Casey et al., 1997). Other studies that use a connectivity analysis design support the idea of the basal ganglia as the site for neural connectivity (Aron et al., 2004; Duann et al., 2009). In particular, Duann *et al*. (2009) suggest that the IFC forms a direct neural route to the subthalamic nucleus, a component of the basal ganglia. While either or both structures may influence motor inhibition networks, more research is needed to verify the source of neural connectivity during motor inhibition.

Motor Inhibition and Developmental Connections

Many investigators have studied how motor inhibition changes across the lifespan and varies between individuals. One of the primary findings of studies comparing children to adults shows that the capacity for motor inhibition develops as one ages (Casey et al., 1997; Bedard et

al., 2002). Although children and adults have similar mean reaction rates to responding to GNG tasks, children exhibit much higher false alarm rates or failing to inhibit the motor movement (Casey et al., 1997). Additionally, children use much larger neural areas to control inhibition. The delayed development of the IFC may account for these neural and behavioral differences (Aron et al., 2004). Despite changes in inhibition performance across the lifespan, an individual's relative motor inhibition performance remains stable through life (Bedard et al., 2002). Therefore, individuals with above-average motor inhibition skills early in life should remain above-average relative to his/her aged contemporaries.

These patterns have been detected using both GNG and SSRT tasks. In an fMRI study comparing both tasks, participants use the pre-SMA, the anterior cingulate cortex, and the right inferior parietal lobe (Rubia et al., 2001). The use of the IFC appears across any task assessing motor inhibition (Rubia et al., 2001; Aron et al., 2004; Duann et al., 2009). Because these tasks assess the same process and produce very similar neural responses, they may be used in conjunction or interchangeably to evaluate motor inhibition skills.

Current Study

The current study utilizes motor data from a go/no-go task, focusing on the connections between behavioral success and neural activation. Measurements of behavioral success will involve a proficiency comparison between participants using four inhibition tasks. The assessment of neural activation will involve fMRI data collected during a go/no-go task. Merging the results of the behavioral and imaging components, a regression analysis will reveal the correlations between inhibition success and neural activity patterns in a Go/No-go task.

The investigations will rest upon three hypotheses about the brain behavior relationships of motor inhibition. Rubia et al. (2001) have found that the prefrontal cortex (PFC), specifically the IFC, controls motor inhibition involved in go/no-go tasks. Therefore, we predict that behavioral success (faster and more accurate inhibitory responses) will correlate with increased neural activity: specifically, participants will recruit more neurons in the IFC to support improved task performance. In addition to the IFC, the activation of the pre-supplementary motor area (pre-SMA), the neural correlate for inhibiting movement, will be investigated. We predict that participants with comparatively increased performance in the go/no-go task will display increased usage of the pre-SMA. Finally, I will analyze the activity of the basal ganglia to inspect the inhibitory signal connectivity from the IFC to the pre-SMA. I predict that, as the IFC increases, the strength of the inhibitory signal sent to the pre-SMA, thus increasing basal ganglia activity, participants should experience enhanced task performance. While previous research has already discovered the neural correlates of prepotent response suppression, this study's research contributes to the knowledge of motor inhibition by incorporating behavioral performance into an fMRI study.

Chapter 2

Methods

Participants

Participants included twenty-five undergraduate students from Penn State University between the ages of 18-24 (M = 21.0 years, SD = 1.73 years; 19 females). Due to scanner malfunctions, the data of two participants were lost, leaving 23 participants in the final analysis. All participants were right-handed, healthy, English speakers. Each student received monetary compensation for their time and provided informed consent, approved by the Pennsylvania State University Institutional Review Board, for biomedical research with human participants.

Behavioral Data Collection

In addition to conducting the fMRI based portion of the experiment, behavioral data was analyzed to create a proficiency comparison of general inhibition skills. Participants completed two memory and two motor inhibition tasks. The tasks included a Go/no-go task, a Stop Signal Task, a Think/No-think task, and a Directed forgetting task. For task designs, look at the procedure written above, Logan, Schachar, & Tannock, Anderson et al., and Rizio & Dennis, respectively (Logan et al., 1997; Anderson et al., 2011; Rizio & Dennis, 2013). After scaling the participants' results for each task, the z-scores of each participant were averaged to create an overall inhibition proficiency score.

Procedure

The experiment primarily utilized a traditional Go/No-go task within the scanner. Refer to Figure 1, in Appendix A, for a pictorial representation of the Go/No-go paradigm. A randomized trial type appeared on the screen for 500 milliseconds (msec). The appearance of green pound signs indicated a go signal, while red pound signs signified a no-go cue. If the participant saw a go signal, they were instructed to press a button with their thumb. If the participant saw a no-go signal, they were instructed to not press anything and cease movement. The go cues occurred for 75% of the trials. A jitter fixation cross appeared between key press cues and lasted an average of 2000 msec.

Scanning

Imaging data was collected utilizing a 3-T Siemens Magnetom Trio MRI scanner (Siemens, Erlangen, Germany). Obtained in five 5.60 min runs, each consisting of 165 volumes. The Go/No-go task was collected using an EPI sequence with a 2-sec repetition time (TR), 30-msec echo time, 240-mm field of view, and a 70° flip angle. Thirty-four slices were acquired per TR, with a slice thickness of 3.8 mm, resulting in 3.8 mm^3 isotropic voxels. Structural images were acquired using a T1-weighted magnetization prepared rapid gradient echo (MP RAGE), with a TR of 2300 msec, an echo time of 3.41 msec, a 230-mm field of view, and a voxel size of 0. 9 mm^3.

Processing

Preprocessing and statistical analysis were performed using SPM software in MATLAB (SPM 8; Wellcome Department of Cognitive Neurology, London, United Kingdom). First, the time-series data received corrections for differences in slice acquisition time. Images were then spatially realigned to the first functional run and checked for movement artifacts using a time-series diagnostic function TSDiffAna (Freiburg Brain Imaging, Freiburg, Germany) in MATLAB (MathWorks). Because no individual moved more than 3 mm in any direction on any run, no data were removed due to motion artifacts. The functional images were normalized using the Montreal Neurological Institute template and converted to Talairach space (Talairach & Tournoux, 1988). Finally, the images were smoothed using an 8-mm Gaussian smoothing kernel to reduce high frequency noise and account for anatomical differences.

fMRI Analyses

For each participant, trial-related activity was modeled with a stick function corresponding to stimulus onsets, convolved with a canonical hemodynamic response function within the context of the general linear model, as implemented in SPM8. Confounding factors (head motion, magnetic field drift) were also included in the model. By applying linear contrasts with the parameter estimates (beta weights) of the events of interest, statistical parametric maps were identified for each participant resulting in a *t* statistic for every voxel.

Regression analysis was performed to reveal the correlations between general inhibition task performance from our behavioral measures and neural activation due to motor inhibition

during a Go/No-go task. Individuals' averaged z-scores from the four behavioral tasks served as the independent variable upon which the regression was based.

To obtain results that were corrected for multiple comparisons, Monte Carlo simulations (www2.bc.edu/slotnics/scripts.htm) were used to define individual voxel and cluster extent thresholds (eg., Garoff-Eaton et al., 2007; Slotnick & Schecter, 2004; Slotnick et al., 2003; Forman et al., 1995). For this study, an individual voxel threshold of $p < 0.005$ was used in combination with a cluster extent threshold of 18 resampled voxels (486 mm^3), which yielded results corrected for multiple comparisons at $p < 0.05$.

Chapter 3

Results

Behavioral Results

For a report of participants' average z-score as well as scores for individual tasks, refer to Table 1 in Appendix A.

Neuroimaging Results

A general analysis yielded several cerebral loci that increase activation during the Go/No-go task. Further analysis using a regression model indicated that five regions of the brain are associated with better performance in the task. Table 2 in Appendix A displays the specifics of these five regions. Individuals with increased performance on the inhibition tasks displayed increased activation in both right and left hemispheres of the superior and middle frontal gyri as well as right hemisphere activation of the putamen. The left superior frontal gyrus showed the largest area of activation with a cluster size of 36 voxels. For images of the activated areas, view Figure 2. After correcting the voxel size for multiple comparisons, the area activated within the putamen did not have a large enough voxel size for inclusion in the data set statistically significant below a 0.005 p-value. This area does reach significance with a p-value less than 0.01. With the partial exception of the right putamen activity, increased inhibition performance in Go/No-go tasks is significantly associated with stronger bilateral activation of the frontal orbital.

Chapter 4

Discussion

The objective of this thesis involves the analysis of the brain-behavior relationship involved in prepotent motor suppression during a Go/No-go (GNG) task. While the study initially intended to investigate the correlations between motor inhibition performance and the activation of the IFC, pre-SMA, and basal ganglia, the results revealed additional areas of the brain which produce stronger activation as motor inhibition skills increase.

The activity detected in Brodmann's Area (BA) 6 supports the pre-SMA hypothesis. The regression analysis tested and found that as inhibitory performance increases, so too does recruitment in regions of BA 6, located in the middle frontal gyrus (view *Table 2*. for details). In particular BA 6 indicates the pre-SMA, the region of the brain involved in planning complex behaviors, such as the initiation and inhibition of movement (Watanabe et al., 2002; Rubia et al., 2001). The evidence for activation is supported by multiple previous works, all suggesting that this area of the brain has a crucial role in inhibiting movement (Casey et al., 1997; Rubia et al., 2001; Watanabe et al., 2002; Duann et al., 2009). As individual motor inhibition skill improves, the brain recruits more neurons in the pre-SMA to gain better control over inhibiting movement.

While the activation of BA 9 in the left middle frontal gyrus was not originally predicted in the hypothesis, previous motor inhibition and neurological data support the evidence for this region. In studies with monkeys the comparative neural area to the human BA 9 provides inhibitory control in motor suppression and attentional selection or attentional focus (Tsujimoto et al., 1997; Dias et al., 1996). This area is also activated when the use of executive control is required to override automatic responses (Kübler et al., 2006). Within the GNG task, the

utilization of this area most likely correlates with the brain recognizing that the No-go signal has appeared and the subsequent override of the conditioned Go response to press the key. Individuals with above-average inhibition skills recruit more activation in BA 9, allowing them to inhibit the automatic motor movement.

The bilateral activation of the superior frontal gyrus in BA 8 was also unanticipated. The majority of literature designates BA 8 as the frontal eye field or the region of the brain that controls saccadic eye movements (Schall et al., 1995; Sato et al., 2001). This region also processes visual and auditory information to produce consequent eye movements in response to the stimuli. Recently, BA 8 has been attributed to processes other than those controlled by the frontal eye field; efforts in executive control and decision making during events producing uncertainty and doubt correlate with this region (Kübler et al., 2006; Volz et al., 2005). One known study has connected BA 8 to motor inhibition. In a study comparing children with and without ADHD, the children without ADHD showed stronger activation in BA 8 during the inhibition task (Rubia et al., 1999). If other studies have shown that individuals with ADHD have poor motor inhibition skills (Logan et al., 1997; Chambers et al., 2006) and Rubia *et al* has found that those with ADHD have weaker BA 8 activation, then this provides support to the evidence of increased BA 8 activation in individuals with exceptional motor inhibition skills. Additionally, this area may have increased activation due to the situation of uncertainty before each stimulus in whether or not to make a Go response.

Although this area did not officially reach significance at $p<0.005$ and 18 voxel size, the putamen still showed increased activation during the GNG task. When the voxel threshold was lowered to 10 voxels at $p<0.005$, the putamen was the only region that appeared within this less stringent criteria for inclusion. This area links back to the basal ganglia vs. anterior cingulate

cortex debate among scholars as discussed in the Introduction. Although previous papers have indicated that the anterior cingulate cortex provides the neural connection between the IFC and the pre-SMA (Watanabe et al., 2002; Casey et al., 1997), this study provides evidence for increased activation of the putamen, a region within the basal ganglia, which most probably provides neural connectivity during motor inhibition. This report does not dispute the use of the anterior cingulate cortex during motor inhibition; however, this regression analysis suggests that individuals utilize the anterior cingulate cortex in similar amounts regardless of skill in motor inhibition. Individuals with better motor inhibition skills have improved neural connectivity through the increased neural activation of the putamen.

This research did not find any of the expected neural activity for the IFC. As demonstrated in previous research, the IFC plays a major role in prepotent motor suppression (Aron et al., 2004; Rubia et al., 2001); however, this study demonstrates all individuals regardless of inhibition skill equally activate the IFC in the GNG task. These results may suggest more general conclusions that increased activation in this area does not appear to confer greater skill in motor inhibition.

Some of the limitations of this research provide possible sources of error. The sample may not have represented the adult population properly, as all of the participants were below the age of 25, college educated, and primarily female. In future replications of the experimental design, the participants should comprise a more equally gendered sample with a broader range of adult ages and educational backgrounds. The nature of the inhibition proficiency score created from the behavioral inhibition tasks may produce a slight source of error. Because little variation between participants emerged using only the behavioral Go/No-go data, a composite inhibition score was used with both memory and motor inhibition to create statistically significant

differences between individuals. If only motor inhibition tasks were used to create the inhibition proficiency score, the increased IFC activity may have appeared in the regression analysis. However, the analysis may produce the same results as found in this study regardless of the tasks used to create the inhibition proficiency score.

Several expansions upon this experimental design could aid in the development of future motor inhibition research. An additional connectivity analysis should be conducted with this data to elucidate the path of activation in a time wise fashion. This may provide greater detail on the use of the putamen in the connectivity of the pre-SMA and the superior frontal gyrus. A localized analysis of the putamen should also be conducted to find a more specified statistical power for the putamen activation. The putamen remains a relatively small structure compared to other brain regions. This study's threshold of 18 voxels at a total of 486 mm^3 may be overly conservative for a structure of a small size. This continuation of the analysis may support the full inclusion of the putamen as one of the structures contributing to improved motor inhibition. Although research has been conducted investigating children's motor inhibition skills (Casey et al, 1997), very little documents motor inhibition in elderly populations. Future studies could analyze if inhibition performance decreases with age and if older adults utilize different areas of the brain than young adults during the Go/No-go task.

The outcome of this study provides several new conclusions about the neural activity of motor inhibition. While the pre-SMA, superior frontal cortex, and possibly the putamen all contribute to improved skill in motor inhibition, expected areas such as the inferior frontal cortex did not. More generally applied to cognitive neuroscience, this study demonstrates that not all regions contributing to the execution of a task are involved in the individual proficiency differences in task skill.

Appendix A

Tables and Figures

Tables

Table 1: ***Participants' Z-scores for Four Behavioral Tasks***

	GNG	SSRT	TNT	DRFR	Average
y1693	0.221567	0.860032	*	0.691353	0.590984
y1695	0.85857	-1.62302	-1.08223	-1.64196	-0.87216
y1696	0.221567	-0.93478	0.108223	-0.95061	-0.3889
y1706	-2.00795	0.18529	-0.487	-0.4321	-0.68544
y1714	0.85857	0.401208	0.703449	-0.69135	0.317969
y1715	0.85857	-1.62302	0.108223	1.296286	0.160016
y1717	1.177072	1.305361	0.108223	-0.34568	0.561245
y1727	0.85857	0.860032	1.298676	-0.77777	0.559877
y1731	0.221567	-0.04412	-1.67746	3.283926	0.445979
y1743	0.221567	-0.04412	0.108223	0.691353	0.244255
y1780	-1.37094	0.860032	-1.67746	-0.4321	-0.65512
y1801	0.85857	-0.48945	-0.487	0.172838	0.013739
y1802	0.85857	-0.48945	0.703449	-0.60493	0.116909
y1808	0.85857	**	-0.487	**	0.185783
y1809	-2.32645	**	1.298676	**	-0.51389
y1836	0.221567	-1.3936	-0.487	0.086419	-0.39316
y1847	-0.73394	0.860032	0.108223	-0.51851	-0.07105
y1871	0.540068	0.401208	-0.487	-0.17284	0.070359
y1877	-0.73394	1.305361	0.703449	1.2E-16	0.318718
y1936	0.221567	0.401208	0.108223	0.432095	0.290773
y1960	-1.37094	1.305361	-1.67746	0.345676	-0.34934
y1963	-0.73394	-1.61411	1.298676	0.172838	-0.21913
y1972	0.221567	-0.48945	1.893902	-0.60493	0.255271

Key: GNG = Go/No-go; SSRT = Stop Signal Reaction Time; TNT = Think/No-think; DRFR = Directed Forgetting

* Participant fell asleep during task

** Participants did not return for the second day of data collection

Table 2: ***Areas Activated as Inhibition Proficiency Increases in the Go/No-go Task***

	H	BA	Coordinates (T&T)			*t*	voxels
			X	Y	Z		
Superior frontal gyrus	L	8	-15	27	31	4.86	36
Superior frontal gyrus	R	8	24	27	34	3.72	23
Middle frontal gyrus	R	6	42	1	35	4.04	22
Middle frontal gyrus	L	9	-36	3	29	3.12	20
Putamen	R		27	-1	5	3.61	12

Key: H = hemisphere; BA = Brodmann's area; Coordinates= Talairach and Tournoux coordinates; *t* = statistical *t*-value; L = left; R = right

Figures

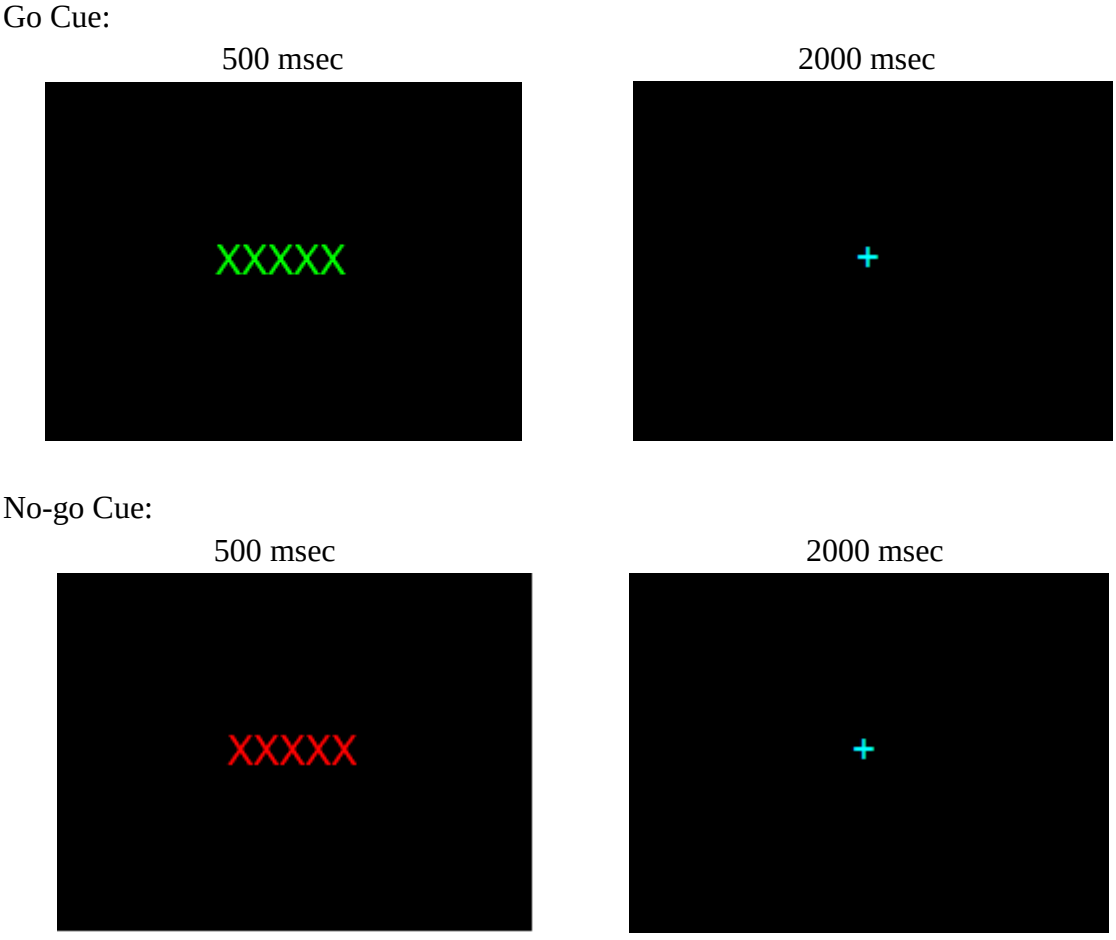

Figure 1: Visual Summary of the Go/No-go Task-The participants were instructed to press a key when given a go cue (green) and instructed not to press any keys when given a no-go cue (red).

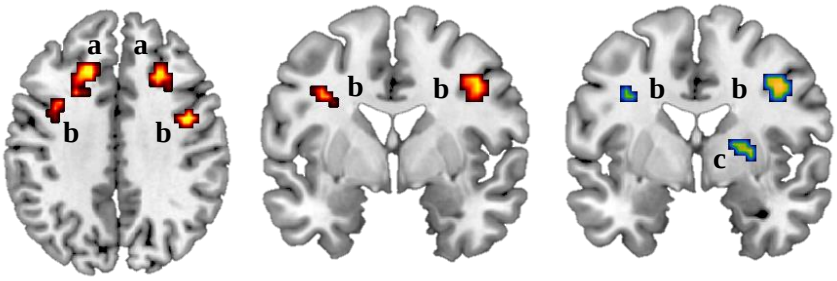

Figure 2: The Go/No-go task with a Regression Analysis showing the neural regions with increased activation as individual inhibition proficiency score increases- Significant activation seen in a) bilateral superior frontal gyrus activation at Z Talairach coordinate of 37 b) bilateral middle frontal gyrus activation at Y Talairach coordinate of 0 c) right putamen activation at Y Talairach coordinate of -1 *The putamen activation was obtained by dropping the cluster extent threshold from 18 to 12 voxels.

BIBLIOGRAPHY

Anderson, M.C., Reinholz, J., Kuhl, B.A., Ulrich, M. (2011). Intentional suppression of unwanted memories grows more difficult as we age. *Psychology and Aging, 26*(2), 397-405

Aron, A. R., Robbins, T. W., & Poldrack, R. A. (2004). Inhibition and the right inferior frontal cortex. *Trends in Cognitive Sciences, 8*(4), 170-177. doi: 10.1016/j.tics.2004.02.010

Bedard, A. C., Nichols, S., Barbosa, J. A., Schachar, R., Logan, G. D., & Tannock, R. (2002). The development of selective inhibitory control across the life span. *Developmental Neuropsychology, 21*(1), 93-111. doi: 10.1207/S15326942dn2101_5

Casey, B. J., Trainor, R. J., Orendi, J. L., Schubert, A. B., Nystrom, L. E., Giedd, J. N., . . . Rapoport, J. L. (1997). A developmental functional MRI study of prefrontal activation during performance of a Go-No-Go task. *Journal of Cognitive Neuroscience, 9*(6), 835-847. doi: 10.1162/jocn.1997.9.6.835

Chambers, C. D., Bellgrove, M. A., Stokes, M. G., Henderson, T. R., Garavan, H., Robertson, I. H., . . . Mattingley, J. B. (2006). Executive "brake failure" following deactivation of human frontal lobe. Journal of Cognitive Neuroscience, 18(3), 444-455. doi: 10.1162/089892906775990606.

Dias, R., Robbins, T.W., & Roberts, A.C., (1996). Dissociation in prefrontal cortex of affective and attentional shifts. *Nature, 380,* 69-72. doi: 10.1038/380069a0.

Drewe, E. A. (1975). Go - no go learning after frontal lobe lesions in humans. *Cortex, 11*(1), 8-16.

Duann, J.R., Ide, J.S., Luo, X., & Li, C.R. (2009). Functional connectivity delineates distinct roles of the inferior frontal cortex and presupplementary motor area in stop signal inhibition. *The Journal of Neuroscience, 29*(32), 10171-10179.

Eimer, M. (1993). Effects of attention and stimulus probability on ERPs in a Go/Nogo task. *Biological Psychology, 35*(2), 123-138.

Falkenstein, M., Hoormann, J., & Hohnsbein, J. (1999). ERP components in Go Nogo tasks and their relation to inhibition. *Acta Psychologica, 101*(2-3), 267-291. doi: 10.1016/S0001-6918(99)00008-6

Forman, S.D., Cohen, J.D., Fitzgerald, M., Eddy, W.F., Mintun, M.A., & Noll, D.C., 1995. Improved assessment of significant activation in functional magnetic resonance imaging (fMRI): use of a cluster-size threshold. *Magnetic Resonance in Medicine, 33*, 636-647.

Friston, K.J. (1994). Functional and effective connectivity in neuroimaging: A synthesis. *Human Brain Mapping, 2*, 56-78.

Garoff-Eaton, R.J., Kensinger, E.A., Schacter, D.L., 2007. The neural correlates of conceptual and perceptual false recognition. Learn. Mem. 14, 684-692.

Jodo, E. & Kayama, Y. (1992). Relation of a negative ERP component to response inhibition in a Go/No-go task. *Electroencephalography and Clinical Neurophysiology*

Kawashima, R., Satoh, K., Itoh, H., Ono, S., Furumoto, S., Gotoh, R., . . . Fukuda, H. (1996). Functional anatomy of GO/NO-GO discrimination and response selection--a PET study in man. *Brain Research, 728*(1), 79-89.

Kübler, A., Dixon, V., & Garavan, H. (2006). Automaticity and reestablishment of executive control-An fMRI study. *Journal of Cognitive Neuroscience, 18*(8), 1331-1342.

Lappin, J.S. & Eriksen, C.W. (1966). Use of a delayed signal to stop a visual reaction time response. *Journal of Experimental Psychology, 72*, 805-811.

Logan, G. D., Schachar, R. J., & Tannock, R. (1997). Impulsivity and inhibitory control. *Psychological Science, 8*, 60–64.

Mishkin, M., & Pribram, K. H. (1955). Analysis of the Effects of Frontal Lesions in Monkey .1. Variations of Delayed Alternation. *Journal of Comparative and Physiological Psychology, 48*(6), 492-495. doi: 10.1037/H0040318

Petrides, M. (1986). The effect of periarcuate lesions in the monkey on the performance of symmetrically and asymmetrically reinforced visual and auditory go, no-go tasks, *Journal of Neuroscience, 6*, 2054-2063.

Rizio, A.A. & Dennis, N.A. (2013). The neural correlates of cognitive control: Successful remembering and intentional forgetting. *Journal of Cognitive Neuroscience, 25*(2): 297-312.

Rubia, K., Overmeyer, S., Taylor, E., Brammer, M., Williams, S.C.R., Simmons, A., & Bullmore, E.T., (1999). Hypofrontality in attention deficit hyperactivity disorder during higher-order motor control: A study with functional MRI *American Journal of Psychiatry, 156*(6), 891-896.

Rubia, K., Russell, T., Overmaeyer, S., Brammer, M. F., Bullmore, E.T., Sharma, T…& Taylor, E. (2001). Mapping motor inhibitions: conjunctive brain activations across different versions of go/no-go and stop tasks. *NeuroImage, 13*(2), 250-261. doi: 10.1006/nimg.2000.0685.

Sato, T., Murthy, A., Thompson, K.G., & Schall, J.D., (2001). Search efficiency but not response interference affects visual selection in frontal eye field. *Neuron, 30*(2), 583-591.

Schall J. D., Morel A., King D. J., Bullier J. (1995). Topography of visual cortex connections with frontal eye field in macaque: convergence and segregation of processing streams. *Journal of Neuroscience, 15,* 4464–4487.

Skaggs, E. B. (1929). The major descriptive categories of inhibition in psychology. *Journal of Abnormal and Social Psychology, 24,* 310-317. doi: 10.1037/H0073411

Slotnick, S.D., Moo, L.R., Segal, J.B., & Hart Jr., J., 2003. Distinct prefrontal cortex activity assoctiated with item memory and source memory for visual shapes. *Brain Research: Cognitive Brain Research, 17,* 75-82.

Slotnick, S.D. & Schacter, D.L., 2004. A sensory signature that distinguishes true from false memories. *Natural Neuroscience, 7,* 664-672.

Talairach, J., & Tournoux, P. (1988). Co-planar stereotaxic atlas of the human brain. Stuttgart, Germany: Thieme.

Tsujimoto, T., Ogawa, M., Nishikawa, S., Tsukada, H., Kakiuchi, T., & Sasaki, K. (1997). Activation of the prefrontal, occipital and parietal cortices during go/no-go discrimination tasks in the monkey as revealed by positron emission tomography. *Neuroscience Letters, 224*(2), 111-114. doi: 10.1016/S0304-3940(97)13480-2

Volz, K.G., Schubotz, R.I., & Yves von Cramon, D., (2005). Variants of uncertainty in decision-making and their neural correlates. *Brain Research Bulletin, 67,* 403-412. doi: 10.1016/j.brainresbull.2005.06.011.

Watanabe, J., Sugiura, M., Sato, K., Sato, Y., Maeda, Y., Matsue, Y.,… & Kawashima, R. (2002). The human prefrontal and parietal association cortices are involved in NO-GO performances: An event-related fMRI study. *NeuroImage, 17* (3), 1207-1216.

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Education

The Pennsylvania State University
Schreyer Honors College
College of the Liberal Arts
B. S. Psychology with Honors (Neuroscience Option), expected May 2015
Eberly College of Science
B. S. Science (Biological and Health Science Option), expected May 2015
Honors Thesis: *Applying mental brakes: An fMRI investigation of prepotent motor response suppression*
Honors Thesis Supervisor: Dr. Nancy A. Dennis

Honors and Awards

- Schreyer Honors College 2011 – Present
- Schreyer Honors College Academic Excellence Scholarship 2011 – 2015
- Dean's List Award 2011 – 2014
- Undergraduate Discovery Research Grant Summer 2014
- Richard J. and Lela A. Nestler Scholarship 2011 – 2012

Research Experience

Cognitive Aging and Neuroimaging Lab at Penn State 2012 – Present
Undergraduate Research Assistant
Adviser: Dr. Nancy Dennis, The Pennsylvania State University

- Analyze, interpret, and report behavioral and fMRI data in adults for an honors thesis.
- Participant recruitment (younger and older adults)
- Administration and scoring of neuropsychological tests to older adults including the MMSE and subtests from the WAIS III and WMS
- Administration of participant health screenings for fMRI experiments
- Conduct literature searches for background information on studies
- Stimuli development, creation, norming, and quality assessment
- Experimental/behavioral testing including subsequent data collection and analysis of results
- Analysis of fMRI data with SPM8 implemented in MATLAB
- Present experimental data informally in graduate lab meetings, and formally at university-wide poster presentations.
- Train new undergraduate research assistants in lab policies, and data collection and analysis.

Research Presentations

Manbeck, A.B. & Dennis, N.A. (2015, April) *Applying mental brakes: An fMRI investigation of prepotent motor response.* Poster presented at Penn State Undergraduate Exhibition in University Park, P.A.

Ross, A.-S. M., Manbeck, A.B., Spielvogel, B.L., & Li, J.F. (2014, April). *What types of Americans are prejudiced against Muslims?* Poster presented at annual Psi Chi National Honor Society Undergraduate Research Conference in University Park, PA.

Skills and Qualifications

- **Software:**
  SPSS Statistical Analysis Software, E-Prime, MATLAB, SPM8 fMRI analysis, MRIcroN2, Microsoft Excel, Microsoft PowerPoint, Microsoft Access, Photoshop, Microsoft Word
- **Research Training:**
  Clinical assessments: Mini Mental State Examination (MMSE), Wechsler Adult Intelligence Scale IV (WAIS-IV), Wechsler Memory Scale (WMS-IV), Beck Depression Inventory II (BDI-II), Geriatric Depression Scale (GDS)
  MRI Safety Trained
- **Languages:**
  English, Spanish proficiency

Other Experience

- **Schreyer Honors College Office of Student Programming**
  Schreyer Honors Orientation Mentor: Backstage and Logistics Team Leader 2014 – 2015
  Schreyer Honors Orientation Mentor: Backstage Coordinator/Photographer 2013 – 2014
  Schreyer Honors Orientation Mentor: Service Team Leader 2012 – 2013
- **Education Abroad- Schreyer Honors College India Program** 2013
  Attended Sri Ram College of Commerce, New Delhi, India and India International School, Jaipur, India
  Volunteered at Udayan Children's Village, Jaipur, India
  Researched Aging and the Elderly in Indian Society
- **Member of Newman Catholic Student Association** 2011 – Present
  2013 – 2014 Position: Fundraising Chair
- **Member of Ambitions Dance Organization** 2012 – Present
  2013 – 2014 Position: Historian
- **Pennsylvania State University Football Concessions**
  Volunteer- Cashier, Food Production Manager 2011 – 2014
  Stand Manager- Labor Control, Funds Director, Inventory, Recruitment 2013
- **American Red Cross**
  Blood Drive Volunteer 2011 – Present
  PSU-MSU Donor Challenge and Alpha Epsilon Delta Blood Cup Committee 2012 – 2014