The Pennsylvania State University

The Graduate School

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A NOVEL GO/NO-GO GRIP FORCE TASK IN THE EXAMINATION OF INHIBITORY CONTROL IN ADULTS WITH AND WITHOUT ADHD

A Thesis in

Kinesiology

by

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ABSTRACT

Inhibitory control is the ability to suppress thoughts or actions that are inappropriate in a given context. Button-press Go/No-Go (GNG) reaction time tasks are traditionally used to measure inhibitory control. Such GNG tasks report commission error (CE) rates based on the presence or absence of a single key press, and therefore may not provide a thorough understanding of motor inhibition. The goal of this study was to employ a continuous grip-force based GNG task to capture subtle but important behavioral differences in motor inhibition. To that end, we employed a traditional button-press GNG task and a grip force variant of the task with identical parameters to examine inhibitory control in adults aged 18 – 25 (N = 171, 84 female) with and without Attention-Deficit/Hyperactivity Disorder (ADHD). ADHD is characterized by poor inhibitory control and can introduce heterogeneity in motor inhibition into the sample. The current study hypothesized that the force GNG task would provide more information regarding inhibitory control than the button-press task. Results suggest that adults with ADHD generated greater peak force and increased trial-by-trial variability of force in No-Go trials of the force task than adults without ADHD. Continuous force outputs were dichotomized to create CE rates. Regardless of group, the force task detected more CEs compared to the button-press task (*p*s < .001). These findings suggest that the force GNG task is a reliable task in quantifying inhibitory control, and the force task excels the button-press task at capturing subtle behavioral characteristics during motor inhibition.

TABLE OF CONTENTS

LIST OF FIGURES

LIST OF TABLES

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Chapter 1

Introduction

Inhibitory control

Inhibitory control is the cognitive ability to suppress thoughts or actions that are inappropriate in a given context. For example, in the game of 'Whac-A-Mole', the goal of the game is to hit "moles" as quickly as possible as they pop up. However, on occasion a rabbit will pop up instead of a mole. In this circumstance, a player has to refrain from hitting the rabbit. This act of restraint – to withhold a response when a rabbit pops up – requires inhibitory control. The ability to exhibit inhibitory control is fundamental for effective execution of functions including working memory, self-regulation of affect, internalization of speech and reconstitution (Barkley, 1997). Poor inhibitory control characterizes many psychiatric disorders such as ADHD (Barkley, 1997; Nigg, 2001), substance use disorder (Jentsch & Taylor, 1999), schizophrenia (Gut-Fayand et al., 2001), and obsessive–compulsive disorder (Chamberlain, Blackwell, Fineberg, Robbins, & Sahakian, 2005).

Inhibitory control can be measured by behavioral tasks in a laboratory setting. Such behavioral tasks depend on creating a prepotency to respond and then an infrequent cue to inhibit the prevailing response that would otherwise be automatically elicited by external stimuli. These tasks are referred to as response inhibition tasks, wherein responses that are inappropriate or irrelevant to goal-directed behaviors are suppressed. One such laboratory task is the Go/No-Go task (GNG task) (Donders, 1969), in which participants respond to one of two stimuli, usually by pressing a button. The "Go" stimulus instructs participants to respond rapidly, and the "No-Go" stimulus instructs them to withhold from responding. Rapid presentation of Go stimuli fosters a

pre-potency to respond to a stimulus. As a result, when less frequent No-Go stimuli are presented, it requires inhibitory control in order to successfully withhold that response, so called response inhibition.

The GNG paradigm was first used as an investigation of reaction time (Donders, 1969) and was later adopted and refined to study response inhibition in individuals with psychological disorders. The GNG task can be altered by changing the type of stimuli (e.g. shapes, letters, pictures), duration of stimuli, relative proportion of Go and No-Go trials, level of similarity between Go and No-Go stimuli, and rule-based associations (e.g., if the stimulus is identical to the previous one, then it is a No-Go stimulus). Dependent measures of GNG task performance include commission errors, omission errors, and reaction time. These measures are derived from trial outcomes. Specifically, there are four possible trial outcomes: successful Go trials (a button is pressed), failed Go trials (no button-press), successful No-Go trials (no button-press), and failed No-Go trials (a button is wrongly pressed). Commission error rate is the proportion of failed No-go responses to all No-go trials. Omission error rate is the proportion of failed Go responses to all Go trials. A high commission error rate indicates poor response inhibition, whereas high omission error rate indicates poor sustained attention (Wright, Lipszyc, Dupuis, Thayapararajah, & Schachar, 2014).

Limitations of Go/No-Go tasks

The GNG paradigm has been an important tool in the investigation of inhibitory control. It is important to note that the dependent variables of the GNG task are derived from button-press data, which means that all utilized information comes from the presence or absence of a single button press. Although every button-press outcome is an actual description of motor inhibition, it lumps together cognitive, sensory, and motor processes into one dichotomous response. As a result,

important aspects of inhibitory control may be overlooked. To address this issue, the current study measured inhibitory control using a specially designed GNG task to record continuous and precise force produced by the thumb and index finger. The advantage of this task is the continuous evaluation of motor output instead of discrete button-press events. In this paradigm, participants viewed two bars a screen: one bar moved up and down with increasing and decreasing force and the second bar served as the target. In Go trials, participants produced force as quickly and accurately as possible, moving the movable bar toward the target. Trials were presented rapidly to create a prepotency to respond. In No-Go trials, participants were to refrain from producing any force. The novel contribution of this task is that the entire time course of motor inhibition was recorded as continuous force. Importantly, analyses of force output enable examination of performance on both within- and between-subject levels. We hypothesized that the continuous nature of this task would reveal subtle behavioral characteristics that the classic button-press task overlooks.

To examine the effectiveness of this continuous GNG task to quantify inhibitory control, a large and heterogeneous sample is required. Most importantly, response inhibition tasks measure errors – responses that should be but are not inhibited. Therefore, we have to make sure erroneous responses are induced in this task. Other than manipulating task parameters to increase task difficulty, we need to include individuals that are more prone to make a response, or are suggested to have deficits in inhibitory control. To this end, we elected to study young adults with and without Attention Deficit/Hyperactivity Disorder (ADHD). It is well established that individuals with ADHD have executive function deficits that include inhibitory control (Epstein et al., 2003; Malloy-Diniz, Fuentes, Leite, Correa, & Bechara, 2007; Murphy & Barkley, 1996), and individuals with ADHD perform poorly on GNG tasks (Malloy-Diniz et al., 2007; Muller et al., 2007).

ADHD and inhibitory control

ADHD is a developmental disorder that begins in childhood and persists into adulthood for up to 65% of individuals (Faraone, Biederman, & Mick, 2006). ADHD has a prevalence of 2.9%-5.2% in adults in the United States (Faraone & Biederman, 2005; Fayyad et al., 2007; Kessler et al., 2006). Adult ADHD is diagnosed by persistent and impairing symptoms characterized by inattention and/or hyperactivity-impulsivity in multiple settings including school, work, and/or home (American Psychiatric Association, 2013). Adults with ADHD have adverse outcomes, such as lower academic and professional achievements (Barkley & Fischer, 2010; Murphy & Barkley, 1996), impaired social functioning (Kessler et al., 2006), higher risk for stressful life events (Friedrichs, Igl, Larsson, & Larsson, 2012) compared to adults without ADHD. ADHD is related to poor physical health (Ebejer et al., 2012) and is confounded with comorbid conditions (Kessler et al., 2006; Murphy & Barkley, 1996), such as substance use disorder (Sibley et al., 2012; Wilens, 2007), anxiety and mood disorders (de Zwaan et al., 2012; Friedrichs et al., 2012), and depression (Biederman, 2005; de Zwaan et al., 2012; Friedrichs et al., 2012; Murphy & Barkley, 1996). Furthermore, ADHD in adults is correlated with higher level of unemployment (Kessler et al., 2006). Therefore, ADHD is a significant public health issue that is characterized by educational, occupational, and social impairment.

Individuals with ADHD make more commission errors and omission errors on the GNG task compared to individuals without ADHD (Barkley, Murphy, & Kwasnik, 1996; Epstein et al., 2003; Losier, McGrath, & Klein, 1996; Malloy-Diniz et al., 2007). Further, individuals with ADHD demonstrate greater variability in reaction time (Barkley et al., 1996; Epstein et al., 2003). However, not all previous work reports differences in GNG task performance for individuals with and without ADHD. For example, McGee and colleagues (2000) failed to find performance differences in children with and without ADHD. In a neuroimaging study, no differences were

found for commission or omission error rates between youths with ADHD and controls aged 16 to 18 years old, although youths with ADHD showed attenuated activity in fronto-striatal regions (Epstein et al., 2007). The above described discrepancies could be attributed to different task parameters such as duration of stimuli and relative proportion of Go and No-Go trials. It could also be that the discrete nature of the button-press GNG task may not be sensitive enough to capture subtle but important behavioral differences, as behaviors are oversimplified in the button-press task to be either hit or miss. In this study, we proposed that the novel force-variant GNG task is better positioned to capture subtle individual differences in inhibitory control.

The current study employed a novel continuous grip-force based GNG task to examine inhibitory control. In the force task, the output is continuous force generated by pressing on force sensors using the index and thumb finger. In this manner, the complete movement profile is recorded during the task. In addition, this task included an amplitude manipulation such that force was to be generated at two different levels: low amplitude level corresponded to 15% of maximum grip force; high amplitude level corresponded to 60% of maximum grip force. This amplitude manipulation enabled examination of differences in movement planning.

The current study examined inhibitory control using a traditional button-press GNG task and a grip force variant of the task with identical parameters in a large sample of young adults with and without ADHD. Given the precise and continuous nature of the GNG force task, it is hypothesized to provide more information regarding inhibitory control than the button-press task. To demonstrate this, GNG performance in the force task was quantified by three different outcome measures: mean force, standard deviation of force, commission errors. Measures from the button-press task, commission errors and reaction time, were also used as dependent variables. It was anticipated that the force task would outperform the button-press task such that it either captured ADHD characteristics that the button-press task failed to capture, or detected larger magnitude of group differences than the button-press task.

Chapter 2

Methods

Participants

Participants were 171 adults (89 males, 82 females) aged 18 to 25 years. Participants were recruited through advertisement in the State College, Pennsylvania area. We recruited two groups of participants: those who self-identified as having a diagnosis of ADHD persisting into adulthood and those who self-identified as having never been given a diagnosis of ADHD. All participants were provided a unique web link to a set of questionnaires completed at their convenience. The online data collection session was approved by the Institutional Review Board at The Pennsylvania State University. The first page of the Qualtrics-based (Qualtrics, Provo, UT) web form contained the informed consent. The forms included the following neuropsychological, cognitive, and clinical measures: a brief medical history, alcohol, nicotine, and substance use information, the long form of the Conners Adult ADHD Rating Scales (CAARS-S:L), the Achenbach Adult Self Report (Achenbach, 2003), the Barratt Impulsiveness Scale (Patton, Stanford, & Barratt, 1995), and the Edinburgh Handedness Inventory (Oldfield, 1971). Responses were reviewed by the study team to determine eligibility for enrollment. Participants were excluded from participation if they indicated: (1) a history of psychiatric disorder involving psychosis, (2) previous diagnosis of a musculoskeletal or neurological disorder, (3) previous diagnosis of seizures, epilepsy, encephalitis, meningitis or an autism spectrum disorder, (4) previous concussions that resulted in a loss of consciousness for longer than 10 minutes or (5) color blindness.

Participants who were eligible for the study were invited to participate in a laboratory session. The experimental tasks reported here were completed as part of a larger battery of experimental and standardized measures that took place in one 3-hour session. Participants gave written informed consent after receiving a complete description of the study. All procedures were approved by the Institutional Review Board at The Pennsylvania State University, and were consistent with the Declaration of Helsinki. All participants received monetary compensation for their participation in the study.

Adults taking any psychostimulant medication (N = 33) completed the testing session after a 24-hour washout period. During the laboratory session, participants completed a semi-structured interview, the Conners' Adult ADHD Diagnostic Interview (CAADID; Multi-Health Systems Inc.), which we updated to reflect the criteria of The Diagnostic and Statistical Manual of Mental Disorders (DSM-5; American Psychiatric Association, 2013). Other tests conducted at this visit included the Digit Span, Matrix Reasoning, and Vocabulary portions of the Wechsler Adult Intelligence Scale-Fourth Edition (Wechsler, 2008) to estimate full-scale intelligence quotient (FSIQ), the Purdue Pegboard Test (Buddenberg & Davis, 2000) to assess motor coordination, a grip dynamometer test to measure maximum pinch grip strength of the dominant - hand. In addition, all participants completed the classic button-press GNG task and force GNG task.

Participants were divided into three groups based on the results of the CAADID diagnostic interview. The ADHD group (ADHD, N = 53, 29 females) met DSM-5 criteria of having ADHD as an adult, such that they had five or more symptoms of inattention or hyperactivity, and symptoms were impairing in at least two settings (e.g. family, school and work). The control group (CTRL, N = 73, 29 females) met the criteria of having less than three total symptoms and two or less symptoms in either of inattention or hyperactivity. The borderline clinical range group (BCR, N = 45, 21 females) did not meet the criteria for CTRL or ADHD.

Procedure

Go/No-Go Force Task

Firstly, maximum voluntary contraction (MVC) was obtained by having participants pinch a grip dynamometer (Lafayette Hydraulic Pinch Gauge, Model J00111, Lafayette, IN) with the thumb and index finger of their dominant hand. MVC was calculated as the average peak force produced across three five-second trials. MVC was then used to create target force amplitudes for each participant.

Visual Stimuli were presented on a 102 cm Samsung TV monitor (Samsung Electronics America Inc., Ridgefiled Park, NJ) with 1920 × 1080 resolution and 120 Hz refresh rate. Participants were comfortably seated in a chair (JedMed Straight Back Chair, St. Louis, MO) facing the center of the TV screen at a horizontal distance of 127 cm. Participants rested their dominant arm at approximately 100 degrees of elbow flexion on a height-adjustable table positioned to the side of the participant's dominant hand. As shown in Figure 2-1, participants used their thumb and index finger to form a pinch grip against a custom designed grip apparatus composed of two identical button load cells (Measurement Specialties, Hampton, VA). Total force was the sum of forces applied to both load cells. Voltage outputs were sent to a force transducer coupler to be amplified (Coulbourn Instruments, Holliston, MA), transmitted via a 16-bit A/D converter (National Instruments, Austin, TX), and digitized at 62.5 Hz. Digitized voltage signals were transformed into Newtons with a resolution of 0.0016 N. The force output from the load cells was presented on the television screen in real time as visual feedback to the participant. Voltage data acquisition, voltage-to-force transformation, stimuli presentation, and real-time visual feedback were conducted using customized programs written in LabVIEW (National Instruments, Austin, TX).

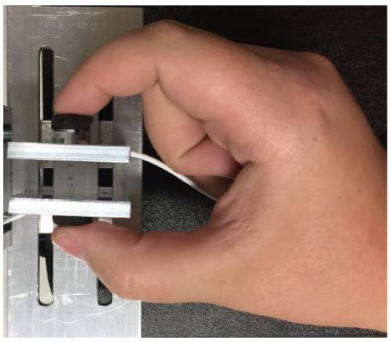

Figure 2-1 Customized grip apparatus for force Go/No-Go task.

Participants produced pinch grip force with the thumb and index finger. Force sensors are mounted onto the top surface of a desk. Participants rested the hand and arm on the desk.

As shown in Figure 2-2, The visual display consisted of two rectangular bars on a black background. A stationary, white target bar represented the target amplitude. A second bar moved up with increasing force and down with decreasing force. The distance moved by the bar was proportional to the amount of total force produced by the participant. When no force was produced, the moveable bar was stationed at a baseline level below the target bar.

Each participant completed two runs of 100 trials (25% No-Go) at low (15% MVC) and high (60% MVC) amplitude conditions for a total of 400 trials. Each run started and ended with 12.5s of rest, during which the movable bar was red, indicating to the participant that they should rest and not press on the load cells. As shown in Figure 2-2, Go trials were signaled by the colors green, aqua, orange, or yellow. No-Go trials were signaled by the color blue. Go and No-Go trials were presented randomly within each run. On Go trials, participants were instructed to press on the load cells as quickly and accurately as possible to match the movable bar to the target bar, and to release when the movable colored bar disappeared. However, on No-Go trials, participants were to refrain from pressing the load cells. Trials were 750 ms in duration, followed by a 500 ms inter-trial-interval, during which only the white target bar was visible. This rapid trial presentation induced a prepotency to respond. All participants practiced the task and had an opportunity to ask questions before completing the four experimental runs.

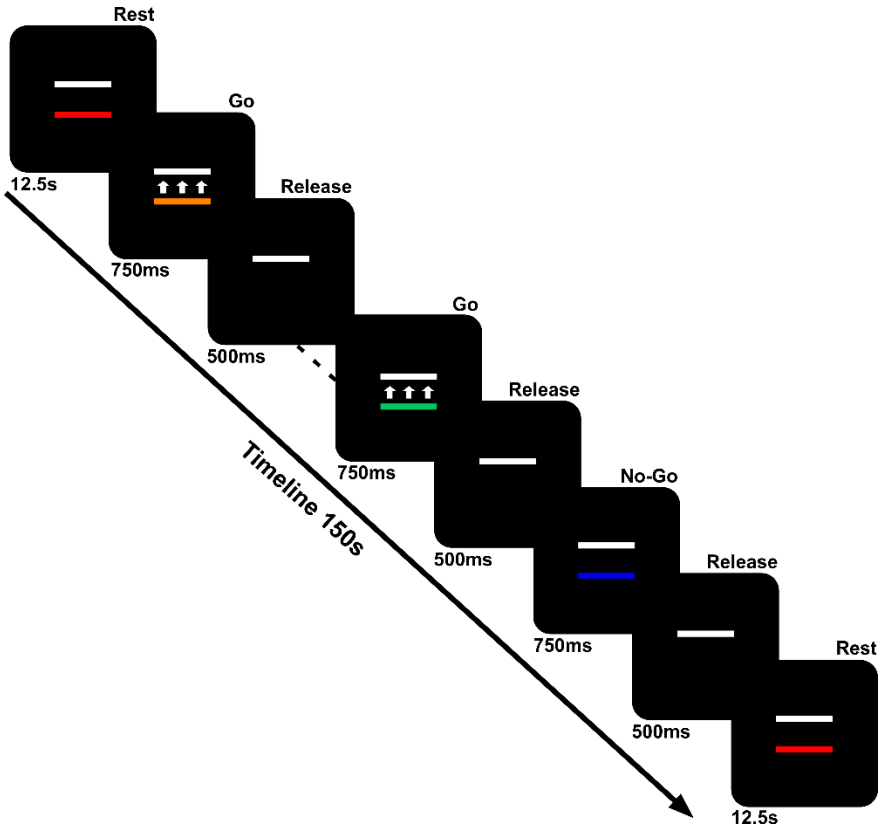

Figure 2-2 Experimental timeline for the force Go/No-Go task.

The task started and ended with the color bar being red, indicating that participants rest their fingers on the sensors and not producing force. When the colored bar turned from red to colors other than dark blue (Go trials), participants produced grip force and the colored bar would move up and down according to applied force. When the colored bar disappeared, participants released their force. When the colored bar turned blue (No-Go trials), participants were to refrain from producing force.

Force data analysis

Force data were analyzed using custom written Matlab® (MATLAB 2015b, The MathWorks Inc., Natick, MA) programs. For each individual, force data, in Newtons, were normalized into percent MVC by dividing by the MVC of that individual. After normalization, each trial output was visually inspected (Figure 2-3). By visual inspection, data from three participants were removed from following analysis because task instructions were violated (2 ADHD and 1 CTRL). After this stage of processing, total sample size was 168 (72 CTRL, 45

BCR, 51 ADHD). Force data were digitally filtered using a 10th-order low-pass Butterworth filter with a 15 Hz cut-off frequency before post-prosessing.

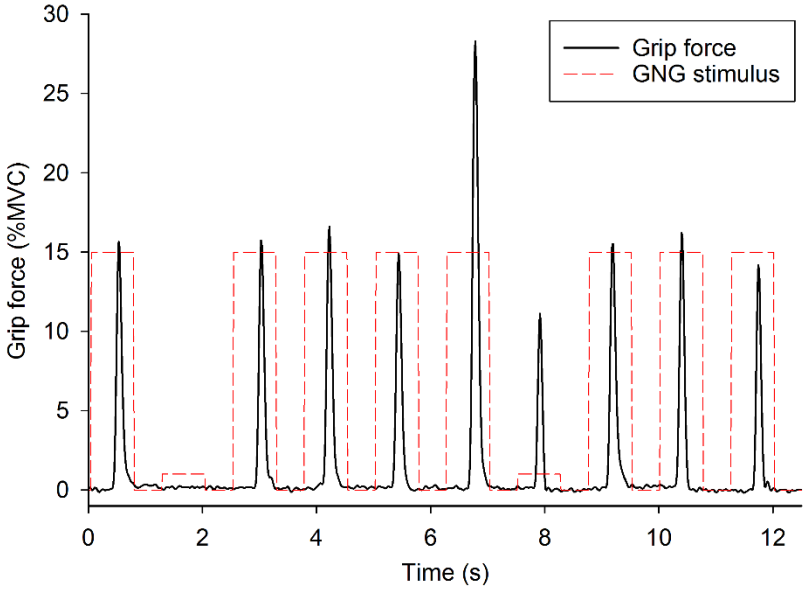

Figure 2-3 An example of raw force data for 10 trials from an exemplar participant.

Red dotted line indicates trial type, trial onset and offset. High rectangle bars suggest Go trials; low rectangle bars suggest No-Go trials. The black line is the actual continuous force data by the participant. Force data were normalized to percentage of maximum voluntary contraction (%MVC).

For each force trial, four time points were selected to capture the characteristics of force production. Because the trial duration was short (i.e., 750 ms), force data were generated in the form of a quick pulse instead of a boxcar. As shown in Figure 2-3, four points were marked on each trial corresponding to the start of rising force (1), end of rising force (2), start of falling force (3) and end of falling force (4). For No-Go trials in which the force pulse was not visually identifiable, the four points were evenly placed within the trial interval. For each trial, individual force amplitude was calculated by taking the average of the force output between points 2 and 3, which was often equal to maximum force of that trial. Mean force was the mean of force amplitudes across all trials of the same type. Standard deviation was computed as the mean deviation of individual force amplitudes from the mean force amplitude. For both the low

amplitude and the high amplitude condition, mean force and standard deviation of force were separately computed for Go trials and No-Go trials.

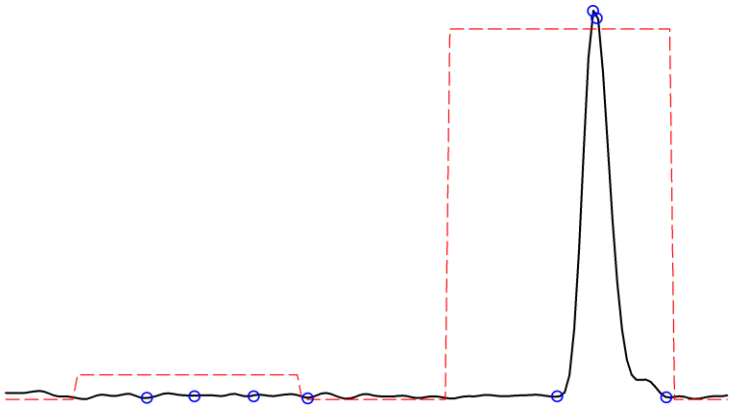

Figure 2-4 Force data processing.

Four points were marked for each trial (blue circles), regardless of trial type. For Go or No-Go trials with a clear force pulse, point 1 marked the start of rising force; point 2 marked the end of rising force; point 3 marked the start of falling force; point 4 marked the end of falling force. For a successful No-Go trial, in which no force pulse was visible, the four points were evenly marked along the course of a trial.

Mean force and standard deviation of force were analyzed using separate three-way mixed-design analysis of variance (ANOVAs) with trial type (Go, No-Go) and amplitdue (low, high) as within-subjects factors, and group (CTRL, BCR, ADHD) as a between-subjects factor.

Go/No-Go Button-press Task and Analysis

The GNG button-press task was identical to the GNG force task, with the exception that only the colored bar was presented on the screen. Specifically, the colored bar was stationary in the middle of the screen and provided the Go or No-Go cue. Stimulus mapping was identical to the force task: go trials were signaled by a bar of either green, aqua, orange, or yellow; whereas

No-Go trials were signaled by a blue bar. Visual stimuli were presented on a 23-inch computer screen (Dell, Round Rock, TX) using E-Prime 2.0 (Psychology Software Tools, Pittsburgh, PA). E-prime provides millisecond precision in timing. Participants were instructed to press the space bar on a keyboard in Go trials as quickly as possible, and to refrain from pressing the space bar in No-Go trials. No feedback about task performance was provided. Participants completed four runs of 100 trials and 25% of all trials were No-Go trials. Each trial was 750 ms in duration and the inter-trial-interval was 500 ms.

Reaction time (RT) for each trial type and commission error (CE) rate for No-Go trials were computed as outcome measures. Reaction time was computed as a within-subject mean of all reaction times in successful Go trials and failed No-Go trials. Reaction time data were submitted to a two-way mixed-design ANOVA with trial type (Go, No-Go) as a within-subjects factor and group (CTRL, BCR, ADHD) as a between-subjects factor. The Commission error rate was computed as the ratio of number of failed No-Go trials to the total number of No-Go trials. The analysis of Commission error rate is described in the next section.

Comparison between force and button-press Go/No-go task

To compare the force GNG task with the button-press GNG task, force output of each No-Go trial was dichotomized as a either successful or failed trial to derive commission error rate. In order to determine the threshold for classifying No-Go trials into successes or failures, the control group was used as the "gold standard" for performance. Firstly, outliers in the CTRL group were identified by applying Tukey's (1977) method on mean forces generated in No-Go trials. Individuals whose mean force exceeded the upper fence were regarded as extreme outliers and eliminated before the determination threshold was calculated. A total of five control participants were removed from the dataset during this process. Two individuals were outliers in

both the 15% and 60% No-Go conditions. Two participants were outliers only in the 15% No-Go condition, and one participant was an outlier in only the 60% No-Go condition. After these outliers were removed, the total sample size was 164 (68 CTRL, 45 BCR, 51 ADHD).

The determination threshold to classify successful and failed No-Go trials was based on mean force output from the control group. Specifically, for each amplitude condition, mean force outcomes in No-Go trials for the control group were regarded as a univariate distribution. The determination threshold was set at three absolute deviations above the median of the distribution. The median absolute deviation method was used because it is resistant to outliers and is robust at estimating parameters from a non-normal distribution (Leys, Ley, Klein, Bernard, & Licata, 2013). The mean force output that was considered a No-Go success was defined as values that fell within three absolute deviations of the median of this distribution. For every No-Go trial, if the force output was larger than the determination threshold, the trial was coded as a No-Go failure; whereas if the mean force was less than the determination threshold, the trial was coded as a No-Go success. Based on this coding strategy, a Commission error rate was computed for both the 15% MVC and 60% MVC force tasks as a ratio of the number of No-Go failures to the total number of No-Go trials (n = 50).

Commission error rates of the three GNG tasks were analyzed using a two way mixed-design ANOVA with a within-subjects factor of task (button-press, low amplitude force, and high amplitude force) and a between-subjects factor of group (CTRL, BCR, ADHD).

Chapter 3

Results

Participants

Table 3-1 reports the demographics of the final sample included in the statistical analysis. As reported in Table 3-1, independent univariate ANOVAs for group demonstrated there were no between-group differences for age, $F(2, 161) = 0.97$, $p = 0.381$, MVC, $F(2, 161) = 1.66$, $p = 0.194$, or FSIQ, $F(2, 161) = 2.62$, $p = .076$. As expected, between-group differences were revealed for ADHD symptoms as measured by the CAADID. Specifically, a main effect of group was found for the number of inattention symptoms endorsed in adulthood, the number of hyperactivity/impulsivity symptoms endorsed in adulthood, and the total number of symptoms endorsed in adulthood, Fs(2, 161) = 253.33, 135.01, and 334.13, respectively, ps < .001. Tukey's post hoc analysis demonstrated that all three CAADID measures increased from CTRL to BCR to ADHD (all ps < .001).

Table 3-1. Participant characteristics

Note. Values are means and standard deviations (in parentheses).

***** CTRL < BCR < ADHD, *ps* < 0.001**

Variables	Group		
	Control	**BCR**	**ADHD**
Sample size	68	45	51
Females	29	21	29
Right-handed	56	39	44
Mixed-handed	6	4	4
Age, yrs	21.28 (2.04)	20.89 (1.68)	21.10 (1.81)
FSIQ	109.91 (12.08)	107.78 (8.38)	105.25 (11.49)
MVC	41.64 (13.43)	47.15 (15.33)	42.81 (16.37)
CAADID			
Number of inattention symptoms endorsed in adulthood ***	0.04 (0.27)	2.29 (2.06)	6.45 (1.95)
Number of hyperactive/impulsive symptoms endorsed in adulthood ***	0.09 (0.33)	2.02 (1.69)	4.90 (2.33)
Total number of symptoms endorsed in adulthood ***	0.13 (0.42)	4.31 (2.92)	11.35 (3.16)

GNG Force Task

Mean force

Mean force was analyzed using a three-way mixed-design ANOVA with trial type (Go, No-Go) and amplitude (low, high) as within-subjects factors, and group (CTRL, BCR, ADHD) as a between-subjects factor. For mean force, there was a significant three-way interaction for trial type by amplitude by group, $F(2, 161) = 3.11$, $p < .047$. To further examine this three-way interaction, a two way ANOVA was run at each level of trial type. The interaction between amplitude and group is altered by trial type, such that the interaction was present for No-Go trials ($F(2,161) = 23.14$, $p < .001$), but not for Go trials ($F(2,161) = 1.03$, $p = .358$). Follow-up one way ANOVAs with group as factor were run in the No-Go trials for each amplitude. As shown in Figure 3-1, the results showed main effects of group for low and high amplitudes, $F(2,161) = 16.54$, $p < .001$, $\eta_p^2 = .170$; $F(2,161) = 38.82$, $p < .001$, $\eta_p^2 = .325$, respectively. Tukey's HSD post-hoc tests revealed that ADHD produced force that was 5.5% MVC higher than CTRL ($p < .001$) and 3.6% MVC higher than BCR ($p = .002$) in the low amplitude condition, and that ADHD produced force that was 15.4% MVC higher than CTRL ($p < .001$) and 13.3% MVC higher than BCR ($p < .001$) in the high amplitude condition.

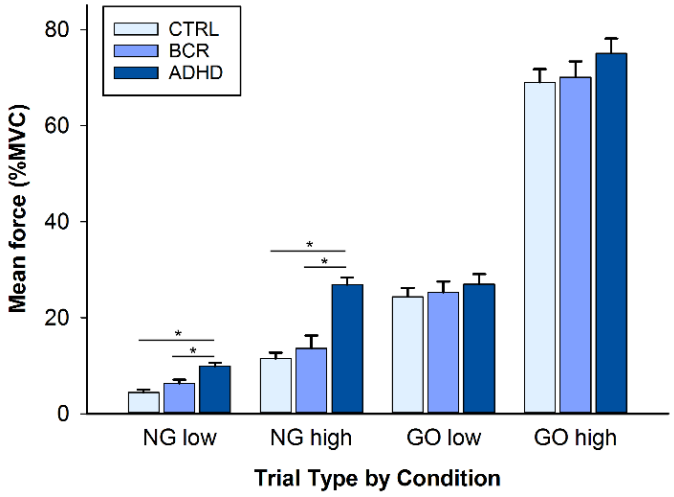

Figure 3-1 Mean force for the three groups of participants across different trial types and amplitudes.

ADHD produced more force in No-Go trials compared to CTRL and BCR but comparable force in Go trials. There was an interaction effect for amplitude by group in the No-Go trials, such that the difference in mean force between ADHD and the other two group was significantly larger in the high amplitude condition than in the low amplitude condition. NG = No-Go trials, GO = Go trials. *p < 0.001.

Standard deviation of force

Similar to the analysis of mean force, standard deviation of force was analyzed using three-way mixed-design ANOVAs with trial type (Go, No-Go) and amplitude (low, high) as within-subjects factors, and group (CTRL, BCR, ADHD) as a between-subjects factor. There was a significant three-way interaction for trial type by amplitude by group, $F(2, 161) = 4.67$, $p < .011$. The interaction between amplitude and group was altered by trial type, such that the interaction is present for No-Go trials ($F(2,161) = 11.32$, $p < .001$), but not Go trials ($F(2,161) = .846$, $p = .431$). For both low and high amplitude tasks, a follow-up one way ANOVA for standard deviations from No-Go trials with group as factor was conducted. The results showed main effects of group for both low and high amplitude, $F(2,161) = 7.00$, $p < .001$, $\eta_p^2 = .080$; $F(2,161) = 19.98$, $p < .001$, $\eta_p^2 = .199$, respectively. Tukey's HSD post-hoc tests revealed that, in No-Go trials, ADHD generated more variable force compared to CTRL (3.7%MVC, $p < .001$),

but not to BCR (2.2%MVC, p = .101) in the low amplitude condition. In the high amplitude condition, however, ADHD generated more variable force compared to both CTRL (8.4%MVC, p < .001) and BCR (7.2%MVC, p < .001).

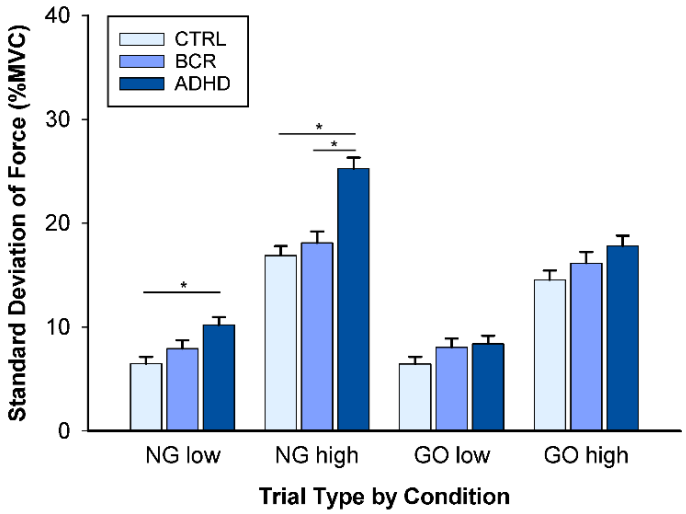

Figure 3-2 Standard deviation of force for the three groups of participants across different trial types and conditions.

ADHD showed increased force variability compared with CTRL, not BCR, in the No-Go low amplitude task, but showed increased force variability compared with both CTRL and BCR in the No-Go high amplitude task. There was not a main effect of group in the Go trials. NG = No-Go trials, GO = Go trials. *p < .001.

GNG Button-press Task

Reaction time data was submitted to a two-way mixed-design ANOVA with trial type (Go, No-Go) as within-subjects factor and group (CTRL, BCR, ADHD) as between-subjects factor. The results demonstrated only a main effect of trial type, $F(1, 161) = 333.11$, $p < .001$, $\eta_p^2 = .674$, such that RTs for No-Go trials (311.76 ms SD 76.96 ms) were faster than RTs for Go trials (351.11 ms, SD 39.56 ms). As shown in Figure 3-3, no main effect of group, or interaction between trial type and group was found, Fs < 1.

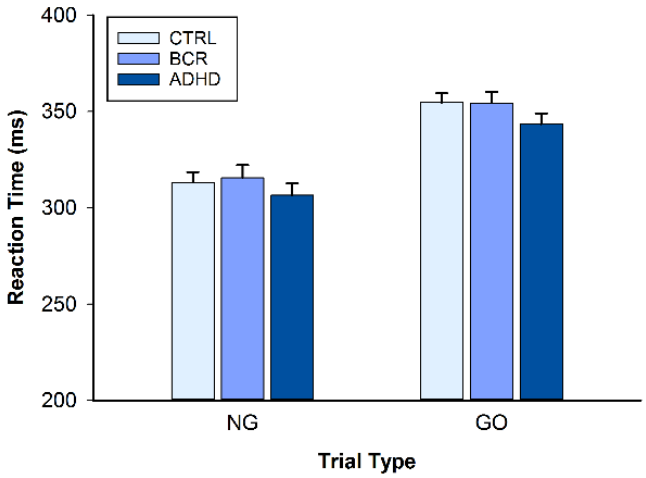

Figure 3-3 Reaction time of different trial types in the button-press task.

No group differences were found, but RTs for No-Go trials (311.76 ms, SD 76.96ms) were faster than RTs for Go trials (351.11ms, SD 39.56ms).

Comparison of tasks

Commission error rates of the three GNG tasks were analyzed using a mixed-design ANOVA with a within-subjects factor of task (button-press, low amplitude, and high amplitude task) and a between-subjects factor of group (CTRL, BCR, ADHD). Mauchly's test indicated that the assumption of sphericity had been violated ($\chi^2(2) = 12.7$, $p < .002$), therefore degrees of freedom were corrected using Huynh-Feldt estimates of sphericity ($\varepsilon = 0.95$). The results demonstrated main effects of task, $F(1.90, 306.21) = 66.8$, $p < .001$, and group, $F(2, 161) = 33.73$, $p < .001$, and an interaction between task and group, $F(3.80, 306.21) = 6.83$, $p < .001$. This interaction was evaluated by three separate repeated measures ANOVAs to compare commission error rate across tasks within each group (CTRL, BCR, ADHD). As shown in Figure 3-4, the results for CTRL showed a main effect of task ($F(2, 134) = 24.3$, $p < .001$). Paired samples t-tests revealed that commission error rate for the button-press task was less than commission error rate for both low and high amplitude tasks (all *p*s < .001). However, commission error rate for the low

and high amplitude tasks were not different (p = .75). The same pattern of results was observed for BCR. The results showed a main effect of task (F(2, 88) = 9.88, p < .001) and paired samples t-tests revealed that commission error rate for the button-press task was less than commission error rate for both the low and high amplitude tasks (all ps < .001). However, commission error rate of the low and high amplitude task were not different (p = .19). The same pattern of results was observed for ADHD. In this analysis, Mauchly's test indicated that the assumption of sphericity had been violated (χ2(2) = 14.2, p < .001), therefore degrees of freedom were corrected using Huynh-Feldt estimates of sphericity (ε = 0.82). The results indicated that commission error rate for the three tasks were different (F(1.64, 82.08) = 38.2, p < .001) and paired samples t-tests revealed that commission error rate for the button-press task was less than commission error rate for both the low and high amplitude tasks (all ps < .001). However, commission error rate for the low and high amplitude tasks was not different (p = .09). In summary, and as shown in Figure 3-4, for all groups, commission error rate for the button-press task was always less than the commission error rate for the force task.

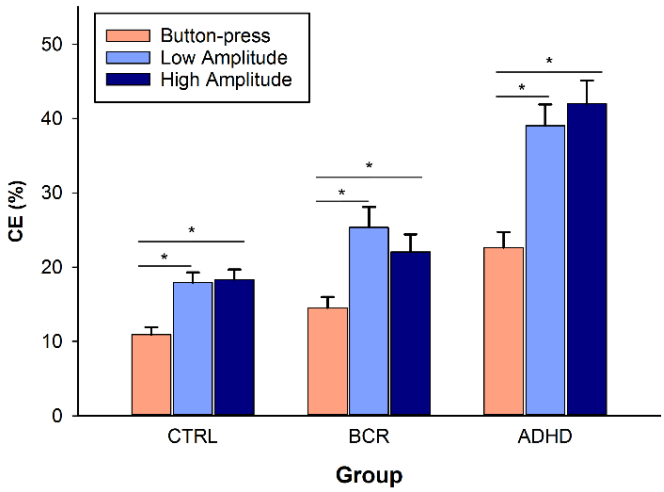

Figure 3-4 Commission error rates detected by the button-press task and the force task.

The force task detected more CEs than the button-press task (colored in orange) across all groups. Two conditions of the force task did not differ in CE.

Chapter 4

Discussion

This study examined inhibitory control using a force GNG task and a traditional button-press GNG task. The goal of the study was to quantify performance in the force and button-press tasks to examine performance differences in adults with and without ADHD. Commission error rates derived from the force task and the button-press task were compared to test if the force task would capture more failed inhibits than the button-press task. The results from the force task demonstrate that the ADHD group produced more force and showed more trial-by-trial variability in force production in No-Go trials compared to the CTRL and BCR groups. In the button-press task, the ADHD group made more commission errors than the other two groups. Finally, when we compared the two tasks, we found that the force task detected more commission errors than the button-press task. These findings suggest that the force GNG task is reliable for quantifying inhibitory control and outperforms the button-press task in that it is more sensitive at detecting performance differences among groups.

Force GNG task

As expected, there was a significant trial type by amplitude by group interaction for both mean force and standard deviation of force. Specifically, for Go-trials, the groups did not differ in mean force nor standard deviation of force. In No-Go trials, however, the ADHD group produced more force and showed more trial-by-trial variability than the CTRL and BCR groups. Here, we interpret the results for Go trials and No-Go trials separately because they represent different aspects of motor control. In Go trials, the goal was to generate and scale force production to

repetitive, rhythmic, and rapid stimuli for two different target amplitudes. Mean force and standard deviation of force have been extensively studied as measures of accuracy and precision. Analyses of mean force and standard deviation of force in Go trials will speak to motor performance. In contrast, in No-Go trials, the goal was to inhibit all force production. Therefore, mean force and standard deviation can be regarded as measures of motor inhibition performance and consistency, respectively.

Force outcomes in Go trials

Lack of group differences for mean force in Go trials regardless of the target amplitude demonstrates that adults with ADHD do not have deficits generating and scaling force production to the goals of the task. This is consistent with previous work from our lab demonstrating that adults with ADHD did not differ from those without ADHD on mean force during visually guided force production, reflecting appropriate response planning for adults with and without ADHD (Neely et al., 2016; Neely et al., 2017). The idea of an internal model suggested by Wolpert et al. (1995) argues that the motor system builds up a clear parameterization of a movement plan to facilitate goal-directed movements. Therefore, these results suggest that adults with ADHD do not have motor deficits creating an internal model of force amplitude.

Variation in force output is regarded as noise in the neuromuscular system (Harris & Wolpert, 1998; Slifkin & Newell, 1999). Specifically, variability of movement is regarded as noised imposed on a control signal (plan of the movement) that results in a certain range of deviation of movement around a target. The minimum variance theory proposed by Harris and Wolpert (1998) proposed that the accuracy of a goal-directed movement is ensured by minimizing variability. Further, studies have shown that greater force production is accompanied by greater trial-by-trial variability (Newell & Carlton, 1985; Poston, Christou, Enoka, & Enoka,

2010). In the current study, standard deviation of force in the high amplitude condition was greater than that in the low amplitude condition for each group. No group differences for standard deviation of force were found for Go trials regardless of target amplitude. This suggests that adults with and without ADHD were comparably precise in producing force to the target amplitude by controlling for variance.

Taken together, the results for mean force and force variability for the Go trials suggests that all participants were able to implement a motor plan that meets the demands of the task and control for noise in the neuromuscular system. That is, the ability to control movement parameters and variability in goal-directed movements was not impaired for adults with ADHD.

Force outcomes in No-Go trials

Mean force in No-Go trials is a measure of inhibitory control. Ideally, complete absence of force production reflects good inhibitory control; likewise, greater force production (i.e., increased mean force) represents poor inhibitory control whereas little force production represents good inhibitory control. This study demonstrated that adults with ADHD produced greater force in No-Go trials is in accordance with previous studies that find more commission errors in button-press GNG tasks in individuals with ADHD (Barkley et al., 1996; Epstein et al., 2003; Losier et al., 1996; Malloy-Diniz et al., 2007). Importantly, there were no group differences in MVC, which means that greater force in No-Go trials cannot be attributed to differences in individual grip strength. This study proposes two explanations for this finding. On the one hand, it could be that on average, ADHD produced more force in the majority of No-Go trials compared to CTRL and BCR. That is, adults with ADHD may have produced more force in each No-Go trial. On the other hand, it could be that adults with ADHD had some trials in which they failed to inhibit their force production as well as CTRL and BCR had, but yet did equally well in the

remaining trials. This explanation relies on the notion that adults with ADHD are less consistent in their performance across trials, despite being able to inhibit their response on several trials. The analysis of standard deviation of force could provide more information in this respect. We will discuss the results of the standard deviation analysis in the following paragraph and provide evidence in support of the latter hypothesis.

The standard deviation of force in No-Go trials is a measure of trial-by-trial variability and therefore reflects consistency in inhibitory control performance. For No-Go trials, standard deviation of force was higher in the high than low amplitude task for all groups. Because the instruction in No-Go trials was to inhibit all force production, instead of to produce force to a target level, differences in force variability across amplitudes could not be simply attributed to that the force/force-variability relationship in the motor system. That is, it might not be that the higher amplitude task requires more force production and thus there was greater variability. It may also be that the high amplitude condition held more room for trial-by-trial variability (up to 60% MVC) in the case of failed motor inhibits than the low amplitude condition (up to 15% MVC). Therefore, it is important to note that, for one individual, greater force variability in the high versus low amplitude condition did not imply worse inhibitory performance in the high amplitude condition. Nor can we conclude that the high amplitude condition is a more difficult condition to inhibit force production. However, as explained below, comparing how the three groups differ in the amplitude-related changes in force variability can be informative.

In No-Go trials, ADHD showed more variable force production than CTRL regardless of amplitude. However, ADHD only showed more variable force production than BCR in the high, not low, amplitude condition. The magnitude of difference among groups was larger in the high amplitude task as shown by the group by amplitude interaction. Comparison of the low and high amplitude results suggests that the high amplitude task has more potential at detecting performance differences between BCR and ADHD, which might be due to the high amplitude

condition having more room for error than the low amplitude condition and thus acting as a magnifier for behavioral differences.

We interpret the increased force variability for adults with ADHD as a manifestation of "poor" inhibitory control. It is important to note that, in No-Go trials, elevated force production by an adult with ADHD was also accompanied by increased variability, and thus results in a wider range of force production across trials compared to force produced by those in the CTRL and BCR groups. That is, adults with ADHD were less consistent at inhibiting force – they successfully inhibited force in some trials (force amplitude comparable to those by CTRL and BCR), but in other trials produced considerably more force (e.g., force amplitude higher than those by CTRL and BCR). This finding suggests that adults with ADHD were able to inhibit their movement in some but not all trials. The current study proposes that this inconsistency in performance might be partly due to poor inhibitory control. Based on the internal model suggested by Wolpert (1995), the ideal parameterization of the pinching movement should be set to zero force in No-Go trials. However, the rapid stimulus presentation of the GNG paradigm builds up a prepotency to respond and thus creates a tendency to keep implementing the Go model. Therefore, it is possible that a No-Go model is overridden by that of a Go model. It is common that participants implement the parameterization of a Go model in a No-Go trial because of this prepotency. As this conflict is detected, the undergoing Go plan should be canceled. As opposed to movement implementation where movement noise should be minimized to ensure accuracy (Harris & Wolpert, 1998), movement cancellation does not implement feedforward control with a parameterized model, and thus motor noise may be less accounted for. Therefore, it is possible that force produced in No-Go trials reflects noise in the system. If this is the case, the elevated variability in No-Go trials could also be attributed to the elevated noise in the biological system in adults with ADHD. Studies examining children with ADHD have shown increased variability in movement trajectory and movement timing in goal-directed movements compared

to children without ADHD (Rommelse et al., 2008; Yan & Thomas, 2002). Further, a study on gait variability (Manicolo, Grob, Lemola, & Hagmann-von Arx, 2016) suggested an age-related decrease in movement variability such that children at a higher age with ADHD walked with lower variability compared children at a lower age, whereas in typically developing children there was no such effect of age. It could be that individuals with ADHD may also adapt to cope with elevated variability during goal-directed movements as they age. However, such elevated motor variability may appear during a No-Go trial where there is not a specific motor plan to minimize variability. Implementation of variants of the Go/No-Go task using other movement types such as reaching and grasping to characterize movement in individuals with ADHD, could test this hypothesis.

Button-press GNG task

In the current work, there were no group differences in reaction time for Go or No-Go trials. Earlier studies have reported no between-group differences in adults (Barkley et al., 1996; Sebastian et al., 2012) and in children (Epstein et al., 2003) with ADHD compared to healthy, age-matched controls. Reaction time is a measure of information processing and assessment of sustained attention. Our results suggests that mean processing speed did not differ between the different groups studied here, and therefore adults with ADHD could adequately integrate information to respond in the GNG task. A consistent finding in the ADHD response inhibition literature is that children and adults with ADHD show increased reaction time variability, also known as intra-individual variability, for Go trials when compared to their counterpart without ADHD (Hervey et al., 2006; Vaurio, Simmonds, & Mostofsky, 2009). This study found elevated intra-subject variability in adults with ADHD in the force GNG task, implied by increased force variability observed in No-Go trials. As shown by the button-press and force task outcomes,

adults with ADHD showed inconsistency in both performance speed and inhibitory control performance. As intra-individual variability in ADHD are typically interpreted as reflecting deficit of sustained attention (Bellgrove, Hester, & Garavan, 2004; Leth-Steensen, Elbaz, & Douglas, 2000; Tamm et al., 2012), we propose that traits of inattention and poor inhibitory control in ADHD might be intertwined with each other.

Comparison of the force task and the button-press task

A primary goal of this study was to determine if a force variant of the traditional GNG task captures subtle differences in motor inhibition that the button-press might overlook. To that end, force output was dichotomized to generate commission errors. There are two important findings. First, both the button-press GNG task and the force task detected more commission errors for the ADHD group than CTRL and BCR group. This outcome was expected because the tasks were designed to be nearly identical in terms of the experimental timeline, visual stimuli, and instruction set. This result demonstrates that the GNG parameters adopted in this study are effective to capture behavioral differences in adults with and without ADHD. We did not observe a difference between the CTRL and BCR groups.

Secondly, for all groups, the force task detected more commission errors than the button-press task. Increased commission errors detected by the force task suggests the force task is able to detect subtle behavioral characteristics that the button-press task overlooks, due to the continuous nature of the force output. Continuous force output enables monitoring motor behavior throughout the entire time course of the inhibitory process, including stimuli detection, motor response (inhibit or not), response adjustment (cancel response or not), and inter-trial rest. In comparison, a discrete button-press registration only captures a single event where the fingertip force exerted on a button exceeds a mechanical force threshold. In subthreshold No-Go trials

where no button-press is registered, the level of motor inhibition could vary. That is, the mechanical force threshold that classical button-press task uses to determine the success or failure of one motor inhibition event might not be biologically or psychologically valid to label behavior, especially for a concept such as inhibitory control. In this regard, the threshold used for the force task was determined from the distribution of motor inhibition behaviors of the control group, whom is assumed to exhibit a range of normative inhibitory behaviors. The threshold was determined by adding three median absolute deviations to the median of mean force in No-Go trials by the control group (Leys et al., 2013). This approach has been used as a method of determination to detect outliers in a non-normal distribution. In this study, this outlier detection method was adopted in this study to label force outcome, because the distribution of forces in No-Go trials is highly right-skewed. Forces in No-Go trials that exceed this threshold were regarded as outliers from normative inhibitory behavior and therefore coded as a failed inhibit. We argue that, in this manner, commission errors derived from the force output could hold more biological validity than the commission errors derived from the button-press task.

Evaluation of amplitude manipulation of the force task

Commission error rates from the low and high amplitude condition were not different for all three groups. This suggests that the two amplitude conditions were equivalent at deriving errors. The fact that commission error rate does not scale with force amplitude for any group indicates that increased force production did not interfere with cognitive performance. However, continuous force output was dichotomized into a binary error rate measure in this analysis, which could result in the high amplitude condition losing its advantage over the low amplitude condition. Based on the results from the mean force and standard deviation of force analyses, the high amplitude condition detected larger magnitude of difference between performance of the

ADHD group and the other two groups. Therefore, the high amplitude task can be used as a magnifier of subtle behavior differences among groups. Moreover, since the high amplitude task holds more room for variability, it is better suited to examine individual differences in motor inhibition. The heterogeneity of ADHD is a critical challenge in understanding this disorder. Specifically, intrasubject variability complicates the detection of group differences in neuropsychological dysfunctioning (Mostert et al., 2015; Steinhausen, 2009). The novel force task used in this study could be adopted to different cognitive paradigms, such as the stop-signal task and other dual-task paradigms, to study individual differences in other aspects of cognitive functioning because of its continuous nature and measures of variability provided. A moderate to high amplitude force paradigm is better than a lower amplitude one because of the aforementioned magnifier effect on subtle behaviors.

Study limitations and future directions

This thesis aimed at examining inhibitory control, a psychological concept, by a grip force GNG task and tried to compare the force task with the classic button-press task. There are several limitations to this study.

One limitation is the lack of temporal characteristics of force output as performance measures to the GNG task. Temporal metrics, such as reaction time, constitute an important aspect of movement, as well as that of a GNG task. As mentioned in the methods section, force data for each trial was visually inspected and marked by choosing four points that characterize the start, peak and end of a force pulse. However, marking No-Go force output with no visible force production was challenging. To ensure the capture of force amplitude, the four points were placed out evenly on the force trajectory, which as a compromise weakens the interpretation of reaction time. Without temporal metrics, comparison between reaction time of the force and button-press

task is lacking. In future investigations, a method to quantify reaction time in No-Go trials should be developed. Since the force task is sensitive to subtle force differences, advantageous over the button-press task that can only detect force above the mechanical threshold of the keyboard, it could capture sub-threshold forces that represents the start of a response, equivalently a shorter reaction time in theory. Reaction time in the force GNG task would answer an interesting question – will increased intra-subject reaction time variability still hold in the force task for adults with ADHD, and if so, will the reaction time variability increase or decrease compared to the button-press task. Answers to such questions would deepen our understanding of inhibitory control and motor control for ADHD.

The findings presented in this study on inhibitory control should be tempered with the fact that the population we studied is also characterized by inattention. Inattention is a core feature of ADHD. Therefore, performance may be confounded by a participant's attentiveness to the task. Analysis of trial effect on No-Go performance could provide insights into this matter, because the requirement for attention is stronger during the later part compared to the start of a task block. Also, to study the effect of preceding trial type (Go versus No-Go) on No-Go performance could speak to the effect of attention in that a preceding No-Go cue can raise the awareness of participant to pay attention to the next trial.

Lastly, it should be addressed that derivation of commission errors from the force output was to enable comparisons with the button-press task, rather than to provide a means to evaluate performance. Admittedly, there are other methods of determination to calculate a threshold to label normalize behavior, but the method used in this study is qualified at illustrating the difference between tasks.

Conclusion

This thesis employed a continuous grip-force based GNG task at examining inhibitory control in adults with and without ADHD, and proposed that the force task would outperform the classic button-press task at capturing subtle behaviors. Results suggest that while adults with ADHD were able to control movement parameters as well as adults without ADHD, they generated larger force and increased trial-by-trial force variability in No-Go trials of the force task, demonstrating a manifestation of poor inhibitory control. This finding suggests that the force GNG task is a reliable task in quantifying inhibitory control.

Continuous force outputs were dichotomized to create commission errors to facilitate comparison with the button-press task. Expectedly, regardless of group, the force task detected more commission errors compared to the button-press task. This finding demonstrates that the continuous force task captured subtle behavioral characteristics to a larger extent compared to the discrete button-press task. The force variant GNG task could be implemented in future investigations on inhibitory control. Further, the continuous and precise nature of the force apparatus also makes it a good candidate to be adopted to use for other cognitive tasks and for association studies.

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