INHIBITORY CONTROL IN MALE AND FEMALE ADOLESCENTS WITH AUTISM

SPECTRUM DISORDER (ASD)

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Master of Arts

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By

MACKENZIE N. CISSNE

Dr. Shawn E. Christ, Thesis Supervisor

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The undersigned, appointed by the dean of the Graduate School, have examined the thesis entitled

INHIBITORY CONTROL IN MALE AND FEMALE ADOLESCENTS WITH AUTISM SPECTRUM DISORDER (ASD)

presented by Mackenzie N. Cissne,

a candidate for the degree of master of arts,

and hereby certify that, in their opinion, it is worthy of acceptance.

_____

Professor Shawn Christ

_____

Professor Yuyan Luo

_____

Professor Kerri Nowell

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Abstract

Recent research suggests that individuals with autism spectrum disorder (ASD) experience particular difficulty resisting interference from visual distractors (RIVD) relative to other aspects of inhibitory control (e.g., prepotent response inhibition and resistance to proactive interference). The literature further suggests that the ASD-related disruptions in inhibitory control may be age-related, such that RIVD difficulty may be more pronounced in young verses older adolescents. Much less is known, however, regarding potential sex-related differences in the inhibitory profile (i.e., strengths and weaknesses) in individuals with ASD. The present study was designed to further examine potential age- and sex-related differences in inhibitory ability in individuals with and without ASD. A sample of 44 adolescents (25 males, 19 females) with ASD and 45 adolescents without ASD (22 males, 23 females) participated. Participants completed a computerized flanker visual filtering task and a go/no-go task, which assessed RIVD and prepotent response inhibition, respectively. No significant effect of group (ASD, non-ASD) was observed for the flanker task ($F(1,65) < 1$, $p = .34$, $\eta_p^2 = .014$) or the go/no-go task ($F(1,69) < 1$, $p = .90$, $\eta_p^2 < .001$). There were also no significant interactions between sex and group for either task ($F < 1$, $p > 0.43$, $\eta_p^2 < 0.01$, in both instances). However, a significant relationship between flanker performance and age was observed for the ASD group, with the older children showing smaller flanker effects (i.e., better inhibitory ability) as compared to the younger children ($t(25) = 3.24$, $p = .003$, $pr^2 = 0.30$). Consistent with previous research (e.g., Christ et al., 2011), there was no evidence of ASD-related impairment in prepotent response inhibition as measured by the go/no-go task. Also consistent with past findings (e.g., Boland et al., 2019), age-related differences in RIVD ability were evident for the ASD group. Notably, we found no evidence of sex-related differences in the inhibitory profile of individuals with ASD.

Inhibitory Control in Male and Female Adolescents with Autism Spectrum Disorder (ASD)

Autism spectrum disorders (ASD) are a spectrum of developmental disorders characterized by difficulty in social communication and social interaction, as well as restricted and repetitive patterns of behavior, interests, or activities. Deficits in social interaction include difficulty in social-emotional reciprocity, nonverbal communicative behaviors, and developing, maintaining, and understanding relationships. Restricted and repetitive behaviors include an insistence on sameness, fixated interests that may be abnormal or intense, hypo- or hyper-reactivity to sensory input, as well as repetitive motor actions (American Psychiatric Association, 2013). ASD is heterogeneous and considered a spectrum disorder in that the severity and extent of symptoms may vary greatly from person to person. ASD has an estimated prevalence of 1 in 54 children (Maenner, 2020) and is expected to have an annual cost of $461 billion to society by 2025 (Leigh & Du, 2015). These social and communication challenges faced by individuals with ASD are often compounded by additional neurocognitive difficulties.

Past research has helped further describe the neurocognitive profiles of individuals with ASD, including difficulty with emotion recognition and social perspective taking. Individuals with ASD perform significantly worse than individuals without ASD on tasks requiring discrimination between different facial emotions and the rating of emotional intensity (Liu et al., 2019) and often have difficulty expressing and communicating thoughts and emotions (Dritschel et al., 2010). Additionally, this population shows decreased ability for understanding someone else's perspective, which has been linked to social communication symptomology as well as restricted and repetitive behaviors (Jones et al., 2018). Individuals with ASD often demonstrate weak central coherence, which describes a tendency to focus on the details rather than the larger

context when processing information (Happé & Frith, 2006). In addition, ASD is associated

with difficulty in executive function (Friedman & Sterling, 2019; Hill, 2004; Russo et al., 2007).

Executive function (EF) refers to a set of higher-order cognitive processes that allow for

the flexible modification of thought and behavior in response to changing cognitive or

environmental contexts (Stuss & Benson, 1986). Evidence from a diversity of populations and

research approaches suggests that EF may comprise at least three core component processes:

updating (working memory), shifting (cognitive flexibility), and inhibition (inhibitory control)

(e.g., Blakey et al., 2016; Christ et al., 2009; Johann et al., 2020; Miyake et al., 2000). Cognitive

flexibility refers to the ability to proficiently shift back and forth between multiple tasks,

operations, or mental sets (Monsell, 1996). Historically, ASD has been strongly associated with

disruptions in cognitive flexibility; however, more recent studies and reviews have brought this

belief into question (for additional discussion, see Geurts, Corbett, et al., 2009). For example, a

meta-analytic review by Leung & Kakzanis (2014) found no performance measure of cognitive

flexibility that could differentiate between individuals with ASD and typically developing

individuals. The only measure that showed a significant difference in cognitive flexibility

between individuals with and without ASD was a parent-report measure (i.e., *Shift* subscale

from the Behavior Rating Inventory of Executive; BRIEF; Gioia et al., 2000).

Working memory (WM) involves the active maintenance and manipulation of

information over a brief period. Two meta-analytic reviews of studies investigating WM in

individuals with ASD found evidence of a significant WM impairment in individuals with ASD,

and the impairment was not associated with individual differences in overall intellectual ability

(Habib et al., 2019) or age (Habib et al., 2019; Wang et al., 2017). Recent interesting work by

Bodner et al (2019) suggests that individuals with ASD may have intact working memory

capacity; however, under the demands of high memory load, they are not able to efficiently

allocate such capacity.

Inhibitory Control

Inhibitory control can be defined broadly as the ability to suppress activation processing

or expression of information that would otherwise interfere with the efficient attainment of a

cognitive or behavioral goal (Dagenbach & Carr, 1994). Proficient inhibitory control is critical

for efficiently navigating both the physical world and the complexities of our social world.

Competence in social interactions relies on an individual's ability to withhold responses, ignore

distractors, and attend to relevant information (e.g. facial expressions, body posture) while

ignoring or suppressing irrelevant information (e.g., background objects). Barkley (1997)

proposed that proficient inhibitory control is also critical for other cognitive processing including

working memory, self-regulation, internalization of speech, and reconstitution.   From a

theoretical standpoint, inhibitory control can be conceptualized as comprising three subtypes

(Friedman & Miyake, 2004): prepotent response inhibition, resistance to proactive interference,

and resistance to distractor interference.

Prepotent response inhibition involves the ability to withhold a prepotent or dominant

response. As an example, children must inhibit their prepotent response of running into the

street after an errant ball and choose to stop before entering the street. Common tests of

prepotent response inhibition include the Stroop Color-Word test (Stroop, 1935), stop-signal

(Logan, 1994), go/no-go (Drewe, 1975), and antisaccade tests (Everling & Fischer, 1998). In

each of these tasks, participants are prompted to suppress a response tendency. As an example,

in the go/no-go task, participants are presented with a series of stimuli (e.g., shapes) and are

asked to press a button each time a shape is presented (e.g., triangle, square, cross), except when

a designated non-target (e.g., circle) is presented. The target stimuli are presented more

frequently than the non-target stimuli, thus creating a prepotent tendency to respond on the non-

target, which should be inhibited.

Resistance to proactive interference is the ability to ignore previously learned and

competing information while performing a task. For example, when someone is shopping at the

grocery store, the grocery list they wrote last week may compete with their ability to remember

what items to buy at the store that day. The Brown-Peterson (Brown, 1958; Peterson &

Peterson, 1959) paradigm is a common example of this type of inhibitory control. Participants

are first presented with a list of words to remember. Then, participants are asked to complete a

distractor task which prevents them from rehearsing any items on the list. After the distractor

task, participants are asked to recall as many items from the list as possible. With additional

memory trials, it becomes more difficult to ignore previously learned information from

preceding trials.

Finally, resist interference from visual distractors (RIVD) refers to the ability to filter

and resist interference from visual distractors. As an example, when driving on a busy street,

one must ignore or suppress extraneous stimuli (e.g., ad boards, etc.) while focusing on the

traffic signs and other cars. The most common paradigm used to assess RIVD is the flanker

visual filtering task (Eriksen & Eriksen, 1974). In the flanker task, participants are asked to

respond to a centrally located target stimulus while ignoring distracting visual stimuli located

closely to the left and right of the target. As an example, participants might be instructed to press

with the right button when the center stimulus is "H" and press with the left button when the

center stimulus is "S". The distracting stimuli flanking the central target could be compatible

(i.e., the same, SSSSS or HHHHH) or incompatible (i.e., the competing response, HHSHH,

SSHSS). Inhibitory control is assessed by comparing performance between the two trial types.

Inhibitory Control and ASD

Growing evidence suggests that children with ASD may have particular difficulty with

RIVD relative to other aspects of inhibitory control. In a series of studies, Christ et al. (2007,

2011) administered tests of different subtypes of inhibitory control to children with and without

ASD. They found that children with ASD performed comparable to the non-ASD comparison

group on tests of prepotent response inhibition (i.e., card & computer versions of the Stroop test,

go/no-go task, a Stroop-like counting interference test) and proactive interference. However, in

both studies, children with ASD demonstrated impairments in RIVD relative to the non-ASD

group. A subsequent study by Adams and Jarrold (2012) yielded similar findings. They

administered a stop-signal prepotent response inhibition task and a flanker task to 15 children

with ASD, 15 children with moderate learning disabilities, and 15 typically developing children.

Children with ASD performed comparable to the two comparison groups on the prepotent

response inhibition stop-signal task but showed significant impairment on the flanker task.

Taken together, these findings support the notion that RIVD may be disrupted to a greater extent

than prepotent response inhibition and other aspects of inhibitory control in children with ASD.

The literature further suggests that the aforementioned ASD-related disruptions in

inhibitory control may be age-related. Christ et al. (2011) found that impairment in RIVD was

more evident among young children with ASD as compared to older adolescents with ASD.

Consistent with this, in a subsequent study Boland et al. (2019) administered a flanker task to

older adolescents ages 12-20 years with and without ASD and found no evidence of RIVD

impairment among this older ASD sample. Koolschijn (2016) also found no group differences

between individuals with and without ASD in flanker performance within a sample of adults aged 30-74 years. More general support for age-related differences in inhibitory ability in ASD comes from a study by van den Bergh et al. (2014), which found increased parent-reported inhibition problems for young children with ASD (6-to-8-year-olds) compared to older children and adolescents with ASD. In contrast, a meta-analysis by Geurts et al. (2014) reported that age was not a significant moderator of performance on interference tasks in individuals with ASD. However, their findings may have been influenced by the fact that their compilation of interference studies including not only flanker tasks but also Simon tasks (i.e., a different paradigm that does not assess RIVD) for purposes of analysis.

Potential Sex-Related Differences in Inhibitory Control and ASD

As described above, there is a general pattern in the literature suggesting that ASD is associated with impairments in RIVD whereas other aspects of inhibitory control are relatively spared. It is important to note, however, that the majority of past studies on this topic have employed all (or mostly all) male participant samples. Within this context, it remains unclear to what extent the aforementioned profile of inhibitory strengths and weaknesses may extend to females with ASD. Indeed, the available research suggests that the neurobiological and behavioral profile of females may be distinct from that of males (Frazier et al., 2014). For example, recent research suggests females with ASD show greater overall executive function difficulties and poorer daily living skills compared to males (White et al., 2017), including decreased performance in cognitive flexibility (Kiep & Spek, 2017; Memari et al., 2013) and working memory (Kiep & Spek, 2017).

Preliminary support for the notion of different inhibitory profiles for males and females with ASD comes from a study conducted by Lemon et al. (2011). A stop-signal task was

administered to assess prepotent response inhibition in a small sample of males and females with

and without ASD. Consistent with previous research, Lemon et al. (2011) found intact prepotent

response inhibition in males with ASD. In contrast, the females with ASD performed more

poorly than the females without ASD.

The Present Study

The present study was designed to further examine potential age- and sex-related

differences in inhibitory ability in individuals with and without ASD, as well as to explore

possible cognitive bases for any observed disruptions. To this end, we administered a flanker

visual filtering task and go/no-go task to a sample of males and females with and without ASD.

Both tasks are well-established and have been used in the past to assess RIVD and prepotent

response inhibition, respectively, in pediatric clinical populations including ASD (see review by

Geurts et al., 2014).

In addition, the flanker task was designed to provide additional insight in the nature of the

neurocognitive disruption underlying any observed group differences. Specifically, we examined

the magnitude of the flanker effect (i.e., the performance difference between compatible and

incompatible trials) observed for distractors presented at different spatial eccentricities from the

target stimulus. In typically developing individuals, the flanker effect is largest when distractors

are located very close to the target, and the effect systematically decreases as the spatial distance

between target and distractors increases. Previous work by Caparos & Linnell (2010) suggests

that disruptions in perceptual level processing may manifest as continuing to see robust flanker

effects even at greater target-distractor eccentricities. (In other words, the flanker effect does not

decrease as much as anticipated when the distance between target and distractor is increased.) In

contrast, disruptions in post-perceptual (response selection) level processing are associated with

a generally larger flanker effect at all target-distractor eccentricities including when they are in very close proximity.

Lastly, our analytical approach to the go/no-go task was also aimed at providing additional insight on the cognitive nature of any observed results. Previous research suggests that the magnitude of the inhibitory demands on a given trial in a go/no-go task are dependent on context, specifically the number of consecutive go trials preceding a no-go trial. For example, in a sample of healthy adults, Durston et al. (2002) found that increased number of preceding go trials before a no-go trial increases response inhibition demands and increases the number of errors. It remains unclear whether ASD-related disruptions in prepotent response inhibition may be evident under higher inhibitory demands (i.e., on no-go trials following many go trials).

Methods

Participants

A sample of 44 individuals (25 males, 19 females) with ASD and a demographically matched comparison group of 45 typically developing individuals (22 males, 23 females) without ASD participated in the present study. Seven participants were ultimately excluded from data analyses (6 ASD; 1 non-ASD) due to overall difficulty with the tasks (as reflected by excessive response time and/or error rate) or computer malfunction. Additional demographic and diagnostic information for the final sample of 82 participants is included in Table 1.

Participants with ASD were recruited using a pre-existing database of previously diagnosed individuals with ASD from the University of Missouri Thompson Center for Autism and Developmental Disorders, Columbia MO. They were diagnosed with ASD by qualified clinical personnel based on diagnostic interviews, caregiver questionnaires, and observation focused on DSM-IV criteria (American Psychiatric Association, 1994). The diagnosis of ASD

was further confirmed using the Autism Diagnostic Observation Schedule (ADOS-G and ADOS-2; Lord et al., 2012). [Note that specific ADOS scores were unavailable for three participants, however, it was noted in their medical records that they met cutoffs for ASD.] Non-ASD participants were recruited via advertisements and word-of-mouth from the Columbia, MO area.

Individuals with color blindness, severe cognitive impairment (FSIQ < 70), or major medical history unrelated to ASD were excluded from the study. Seven ASD participants were prescribed attention-related medications or other medications known to affect cognitive performance (e.g., methylphenidate, amphetamine, Concerta). They were able to safely refrain (per their treating physicians) from taking the relevant medication for 24 hours prior to testing and thus were included in the study. Other medications included serotonin-norepinephrine reuptake inhibitor (SNRI; ASD=7), guanfacine (ASD=2), propranolol (ASD=1), selective serotonin reuptake inhibitors (SSRI; ASD=4, non-ASD=2), buspirone (ASD=2), tetracyclic antidepressant (ASD=1), and/or antipsychotics (2nd generation or atypical; ASD = 3). Because of safety reasons and/or their relatively long half-lives, these medications were not withheld for purposes of the present study.

Procedure

The present study was approved by the University of Missouri Internal Review Board (Review ID 2003107) and was carried out in accordance with the provisions of the World Medical Association Declaration of Helsinki. Informed consent and assent were obtained for all individuals prior to participation. All tasks were administered in a small, quiet room with sufficient overhead lighting. The order of task administration was counterbalanced across participants.

Measures and Questionnaires. Participants were administered the Wechsler Abbreviated Scale Intelligence-2 (WASI-2) to estimate overall intellectual ability. Additionally, the parent-report version of the Social Responsiveness Scale (SRS; Constantino et al., 2003) was administered to assess the severity of a child's autism symptomology, engagement in reciprocal social interactions, understanding of emotional and social cues, and motivation to engage with others.

Flanker visual filtering task. The sequence of trial events is illustrated in Figure 1. Each trial began with a preview display that consisted of a centrally located row of 21 figure-eight placeholders and a small arrow positioned below the center-most placeholder. Each placeholder was 0.87° high and 0.26° wide with an inter-stimulus spacing of 0.17°. (The width of the full row of placeholders was approximately 9°.) Following a 1000 ms delay, two line-segments were removed from the center-most placeholder to reveal the target stimulus (i.e., the letter S or H). At the same time, two of the flanking placeholders located equidistant on either side of the target were similarly changed to reveal distractor stimuli that were either compatible (e.g., S's flanking a S target) or incompatible (e.g., S's flanking an H target) with the target stimulus. Distractor stimuli appeared in the nine closest eccentricities, thus distractor stimuli never appeared in the outermost placeholder. Participants pressed one of two keys as quickly as possible to indicate the target identity. The target/distractor display was presented for 240 ms followed by a blank screen, which remained until a response was made.

Following 24 practice trials, participants completed 576 experimental trials. Trial types (compatible and incompatible) were randomly mixed. Trial presentation was also balanced such that the distractor stimuli were equally likely to appear in 9 possible distances/locations from the

target location. The target-to-response key mapping was counterbalanced across participants. At

intervals of 72 trials, participants were offered a break.

Go/no-go prepotent response inhibition task. The stimuli and procedure were similar to those

used in previous studies by Christ et al. (2006, 2007) to directly compare results. Participants

were seated in front of a computer monitor. Two experimental conditions were administered: go

and no-go. On each trial, one of four stimuli (i.e., ◊, □, Δ, O) subtending approximately 2°

vertically and horizontally was centrally displayed for 750 ms. Prior to beginning the task, one of

the stimuli was designated as the nontarget. Participants were asked to press a response button as

quickly as possible when any stimulus appeared except the nontarget (go trials). Participants

were instructed to make no response when the nontarget appeared (no-go trials). After an

intertrial interval of 750 msec, a new trial was presented.

If a participant failed to respond within 750 msec (an inattentive error), a tone and the

message "Too Slow!" were presented. If a participant responded on a no-go trial (a false alarm

error), a tone and "Error!" were presented.

Following 28 practice trials, participants completed 336 experimental trials. Presentation

was balanced such that each stimulus was equally likely to occur; nontargets were presented on a

minority (25%) of trials. The trial types were mixed randomly. The stimulus designated as the

nontarget was counterbalanced across participants. At intervals of 56 trials, participants were

offered a break.

Data Analysis & Statistical Approach.

For the flanker task, in order to ensure sufficient number of trials in each condition type,

trials with distractor stimuli in the first or second position were collapsed, as were trials with

distractor stimuli in the third and fourth position, and so forth. Preliminary analyses

demonstrated no evidence of flanker effects in the furthest distractor location (9th placeholder)

for individuals with or without ASD. Therefore, data for these trials were not considered further.

Consistent with past studies (e.g., Boland et al., 2019; Christ et al., 2011), median

reaction time (RT) served as the primary dependent variable for the flanker task. Note that error

rates were generally very low ($M = 0.10$), and the analyses described below were repeated with

error rate and did not yield any significant findings ($p > .05$ in all instances).

The flanker effect (incompatible RT minus compatible RT) was computed for each

condition of the task. The resulting data were entered into a mixed model ANCOVA with group

(ASD and non-ASD) and sex (male and female) as the between-subjects factors, and distractor

location (1-4) serving as a within-subject variables, and full-scale intelligence quotient (FSIQ) as

a covariate. Additional analyses using hierarchical linear regression were used to further examine

potential age-related differences in task performance for the ASD and non-ASD groups (e.g.,

Boland et al., 2019; Christ et al., 2011).

In the go/no-go task, the number of go trials preceding a no-go trial was manipulated to

examine the effect of preceding context on inhibition. Consistent with past studies (Christ et al.,

2007; Geurts, Begeer, et al., 2009; Sanderson & Allen, 2013), commission error rate served as

the primary dependent variable for the go/no-go task. The go/no-go task data were entered into a

mixed model ANCOVA with group (ASD and non-ASD) and sex (male and female) as the

between-subjects factors, stimulus condition (number of preceding go trials) as a within-subjects

variable, and FSIQ as a covariate. Note that the analyses were repeated with go-trials response

time (RT) and did not yield any significant findings ($p > 0.05$ in all instances).

Results

Flanker visual filtering task

Analysis of the flanker effect (incompatible RT minus compatible RT) revealed a main effect of distance such that participants showed more robust flanker effects when distractor stimuli were located very close to the target as opposed to further away from the target (closest location: $M = 47$ ms; farthest location: $M=9$ ms; $F(3, 195) = 22.96$, $p < 0.001$, $\eta_p^2 = .26$). There was no significant main effect of group [$F(1,65) < 1$, $p = .34$, $\eta_p^2 = .014$] or sex [$F(1,65) = 2.12$, $p = .15$, $\eta_p^2 = .032$]. In addition, the interaction between sex and group was not significant [$F(1,65) < 1$, $p = .74$, $\eta_p^2 = .002$]. All other two-way or three-way interactions were not significant [$F < 1$, $p > 0.6$, $\eta_p^2 < .01$ in all instances]. Results of these analyses are illustrated in Figure 2.

To further examine potential age-related differences in performance, a hierarchical regression was conducted with flanker effect for the closest distractor location condition serving as the dependent variable (see Figure 3). Age and FSIQ were entered in the first step of the regression, group was entered in the second step of the regression, and finally, group by age was entered into the third step of the regression. A main effect of age [$t(67) = 2.50$, $p = .015$, $pr^2 = .09$] but not group [$t(66) < 1$, $p = .33$, $pr^2 = .01$] was observed. Interestingly, there was a significant interaction between group and age [$t(65) = 2.08$ $p = .04$, $pr^2 = .06$]. Subsequent analyses confirmed that this was driven by a significant age-related improvement in the ASD group [$t(25) = 3.24$, $p = .003$, $pr^2 = 0.30$] but not the non-ASD group [$t(39) < 1$, $p = .50$, $pr^2 = 0.01$].

Go/No-Go Task

As illustrated in Figure 4., analysis of commission error rate (i.e., primary dependent variable for the go/no-go task) yielded a significant main effect of condition [$F(6,414) = 2.67$, $p= 0.015$, $\eta_p^2 = 0.04$]. The magnitude of the effect increases with the number of preceding go trials

until it reaches an asymptote of two preceding go trials, then the effect decreases with additional preceding go trials. There was no significant main effect of group ($F(1,69) < 1$, $p = .90$, $\eta_p^2 < .001$) or sex ($F(1,69) < 1$, $p = .77$, $\eta_p^2 = .001$). There was also no significant interaction between sex and group ($F(1,69) < 1$, $p = .44$, $\eta_p^2 = .009$). All other two-way or three-way interactions were not significant ($F < 1$, $p > 0.4$, $\eta_p^2 < .01$ in all instances).

Similar to the flanker analysis, we conducted a supplementary hierarchical regression to explore potential age-related differences in go/no-go task performance (see Figure 5). As described above, commission error rates were highest in the no-go condition with two preceding go trials, suggesting that this was the most difficult condition. As such, error rate for this condition served as the dependent variable. Age and FSIQ were entered in the first step of the regression, group was entered in the second step of the regression, and finally, the group by age interaction term was entered into the third (and final) step of the regression. There was no significant main effect of age [$t(71) < 1$, $p = .72$, $pr^2 = .002$] or group [$t(70) < 1$, $p = .49$, $pr^2 = .007$]. There was also no interaction between group and age [$t(69) < 1$, $p = .42$, $pr^2 = .009$].

Discussion

Previous research employing primarily male participant samples suggests that ASD is associated with impairments in RIVD whereas other aspects of inhibitory control may be relatively spared (Adams & Jarrold, 2012; Christ et al., 2007, 2011). Evidence of potential age-related differences in RIVD have also been reported, with impairments more evident among younger children with ASD as compared to older adolescents with ASD (Boland et al., 2019; Christ et al., 2011; Koolschijn et al., 2016). To the extent that these past studies have employed primarily male participant samples, it remains unclear whether this profile of inhibitory control may differ between males and females with ASD. Indeed, consistent with this possibility, a

small study by Lemon et al. (2011) found impaired prepotent response inhibition in females but

not males with ASD. In the present study, we administered a flanker visual filtering task and a

go/no-go task to a sample of males and females with and without ASD to examine potential age-

and sex-related differences in two aspects of inhibitory control: RIVD and prepotent response

inhibition, respectively.

As anticipated, participants across both groups (ASD and non-ASD) showed greater

flanker inhibitory effects for distractors located in close proximity to the target stimulus as

compared to more distal distractors. These results are consistent with findings from Caparos &

Linnell (2010), which found flanker effect decreased as the spatial distance between the target

and distractors increased in a sample of typically developing individuals. Importantly, the

magnitude of the flanker effect was comparable for the ASD and non-ASD group, and this was

true even for the closest flanker distractor locations (which were presumably associated with the

largest inhibitory demands). As described above, recent research (Boland et al., 2019) suggests

that ASD-related impairments may be more evident in young compared to older children with

ASD. Consistent with this, we also found age-related improvements in RIVD performance for

the present ASD group.

On the go/no-go task, participants showed increased error rate as the number of

consecutive preceding go trials (and thereby presumably the magnitude of inhibitory demands)

increased. This was true until there were more than two preceding go trials. At that point, error

rate actually *decreased* as the number of preceding go trials increased. It could be speculated

that after more than two preceding go trials, participants began anticipating an upcoming no-go

trial and adjusted their performance accordingly. This finding is somewhat inconsistent with that

of Durston and colleagues (2002), whom also found that error rate on no-go trials increased with

the number of preceding go trials but did not observe a corresponding asymptote and subsequent decrease. Of note, however, the Durston et al study focused on healthy adults and was much slower paced (inter-trial interval: Durston study = 4000 ms; present study = 750 ms). Given the sample and task differences, performance was much higher in the Durston study (mean error rate = 4.5%) as compared to the present one (mean error rate = 31%).   It is possible that the go/no-go task was not challenging enough for participants in Durston et al. (2002), and the participants did not have to adopt a strategy to anticipate an upcoming no-go trial. Consistent with a number of previous studies (Adams & Jarrold, 2012; Christ et al., 2007, 2011), there was no evidence of ASD-related difficulties in prepotent response inhibition, even in the most demanding condition (i.e., the no-go condition with two preceding go trials) (for exception, see Geurts et al., 2014). Unlike the flanker task, no age-related effects were observed for either group in the present study, suggesting that the development of prepotent response inhibition was relatively stable across the current age range (11-15 years of age).

As described earlier, we also examined potential sex-related differences in inhibitory performance. Broadly speaking, previous research suggests that there is a difference in the behavioral and neurobiological profiles of males and females with ASD (Frazier et al., 2014). Research also suggests that there may be sex-related neurocognitive differences as well. For example, females with ASD show greater overall executive function difficulties including poorer performance in cognitive flexibility and working memory (Kiep & Spek, 2017; Memari et al., 2013). Preliminary support for sex-related differences in inhibitory control comes from a study by Lemon et al. (2011), which found impairments in prepotent response inhibition for females but not males with ASD. In contrast, the present study found no evidence of sex-related differences in individuals with ASD in RIVD or prepotent response inhibition.

Methodological differences may have contributed to the apparent discrepancy in findings between the present study and Lemon et al. (2011). Whereas the present study utilized a go/no-go task to assess prepotent response inhibition, Lemon and colleagues used a stop-signal task. In a typical stop-signal task, participants perform a basic speeded discrimination task in which they respond as quickly as possible to the identity of a centrally presented target stimulus. On a subset of trials, a stop signal (e.g., a sound) is presented that alerts participants to withhold their response on the current trial. The delay between onset of the target and stop signal stimuli (i.e., stop signal delay; SSD) is systematically varied. Based on a participant's performance at different SSDs, an inhibitory performance measure called the stop signal reaction time (SSRT) is calculated for that individual. Importantly, by varying the SSD (and thereby task difficulty) based on trial-by-trial performance, task difficulty in the stop-signal task is optimized for each individual participant. In contrast, in the go/no-go task, task difficulty is held constant across participants (i.e., the task is designed with a certain percentage of go trials and specific inter-trial intervals). While the present go/no-go task was challenging for many participants (overall error rate = 31%), self-adjusting tasks such as the stop-signal task may optimize measuring prepotent response inhibition for all participants (not just most). This may have contributed to the discrepancy in findings between the present study and Lemon et al. (2011). Future research studies should consider implementing multiple measures of prepotent response inhibition to provide insight into this possibility.

The participant sample in the Lemon et al. (2011) study also included children as young as six years old. (The age range for the present study was 11-15 years.) Although speculative, another potential explanation for the discrepancy in findings is that sex-related differences in prepotent response inhibition are more evident at earlier ages (i.e., early childhood) - much like

the previously described pattern of age-related changes in RIVD (Boland et al., 2019, Christ,

2011). An important avenue for future research is to extend this line of research to examine

potential sex-related differences in inhibitory control in a younger sample.

        Additional Limitations and Future Directions. Although the present sample size

compared favorably to that employed in previous studies (e.g., Boland et al., 2019; Christ et al.,

2007, 2011) it may be the case that a larger sample size would provide additional statistical

power to detect more subtle sex-related differences. An increased sample size would also

increase the confidence with which the results could be generalized to the broader population of

children with ASD. As discussed earlier, a critical next step in the present line of research will

be to examine potential sex-related differences in inhibitory ability in younger children with and

without ASD. Similarly, it will be important to also extend this work to the other end of the

lifespan. Whereas a few studies have begun to focus on differences in other aspects of executive

function (e.g., working memory) in males and females with ASD (e.g., Kiep and Spek, 2017),

little is known regarding potential sex-related differences in inhibitory control in older adults

with ASD. Lastly, future studies involving functional neuroimaging may provide additional

insight into potential sex-related differences in inhibitory control in individuals with ASD.

Despite males and female adolescents with ASD sharing a common behavioral phenotype (in

terms of inhibitory performance), they may differ in the neurocognitive processes that are

engaged during task performance.

Summary and Conclusions

        Proficient inhibitory control is a fundamental skill for navigating the demands of school,

work, social interactions, and relationships with others. A necessary component of day-to-day

functioning involves attending to relevant information and being able to ignore irrelevant

information. The present study found no evidence of impairment or sex-related differences in inhibitory performance in adolescents with ASD. This was true even during the most demanding condition of each inhibitory task. Previous studies have found that inhibitory impairments are more evident in younger as compared to older children with ASD (Boland et al., 2019; Christ et al., 2011; Koolschijn et al., 2016). Consistent with this, we did find age-related improvements in RIVD performance for the ASD group. Future research focusing on younger ages (e.g., early childhood) will be critical in further elucidating potential age- and sex-related differences in inhibitory control. The results may help inform clinical interventions, specifically identifying particular aspects of inhibition and developmental epochs (e.g., early childhood vs adolescence) that are optimal clinical targets.

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Table 1

Sample Characteristics

Variable	ASD (n = 38)		Non-ASD (n = 44)		t value[a]	p value
	M (SD)	Range	M (SD)	Range		
Age (years)	12.9 (1.4)	11-15	13.1 (1.4)	11-15	<1	.53
Sex (M/F)	23/15		22/22			
FSIQ[b]	103 (17.2)	63-134	107 (13.2)	81-140	1.1	.26
VIQ[b]	103 (16.3)	71-136	107 (11.6)	83-134	1.4	.18
PIQ[b]	102 (18.8)	58-139	105 (14.4)	74-140	<1	.47
SRS T Score	76 (10.5)	55-90	46 (5.6)	38-70	16.6	<.001
ADOS-G (n = 2)[c]						
Social	8.5 (0.7)	8-9	---	---		
Communication	1.5 (0.7)	1-2	---	---		
ADOS-2 (n = 26)[c]						
Social Affect	8.9 (3.0)	5-19	---	---		
Restricted, Repetitive Behavior	3.7 (1.5)	1-6	---	---		

Note. FSIQ = Full Scale Intelligence Quotient; VIQ = Verbal Intelligence Quotient; PIQ = Performance Intelligence Quotient; SRS = Social Responsiveness Scale; ADOS = Autism Diagnostic Observation Schedule.

[a]Degrees of Freedom = 80

[b]Estimated based on the WASI-2 (Wechsler, 2011)

[c]Note individual ADOS scores were unavailable for three participants and ADOS sub-scores were unavailable for seven participants; however, it was noted in their medical charts that they met ASD cutoffs.
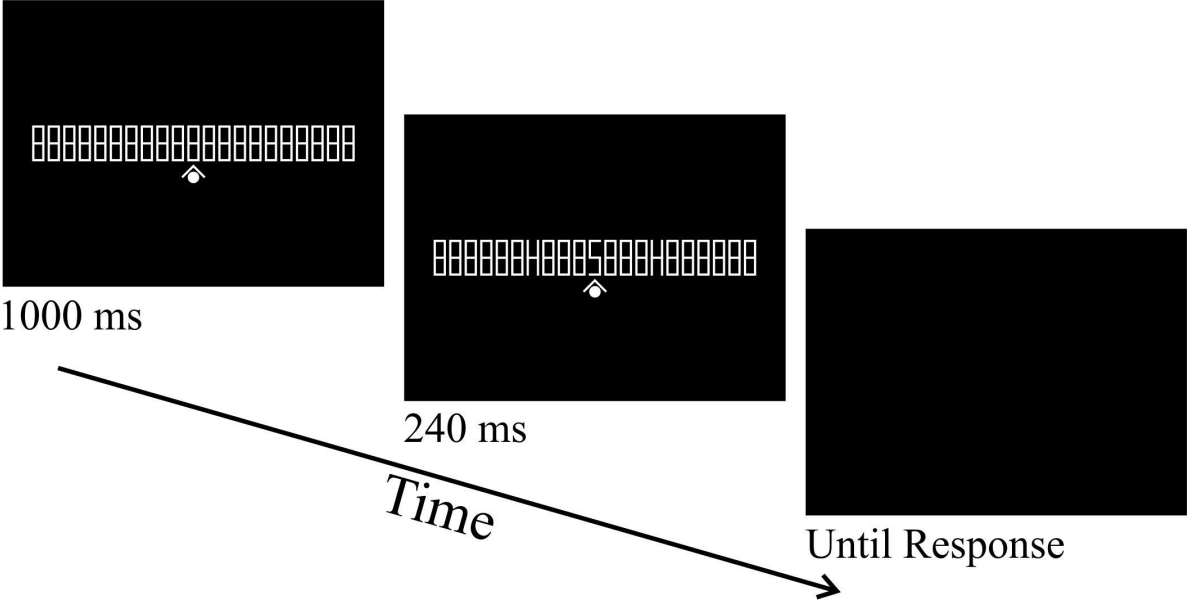
Figure 1. Sequence of events on an incompatible trial of the flanker task. The relative size of the stimuli has been enlarged for illustrative purposes.
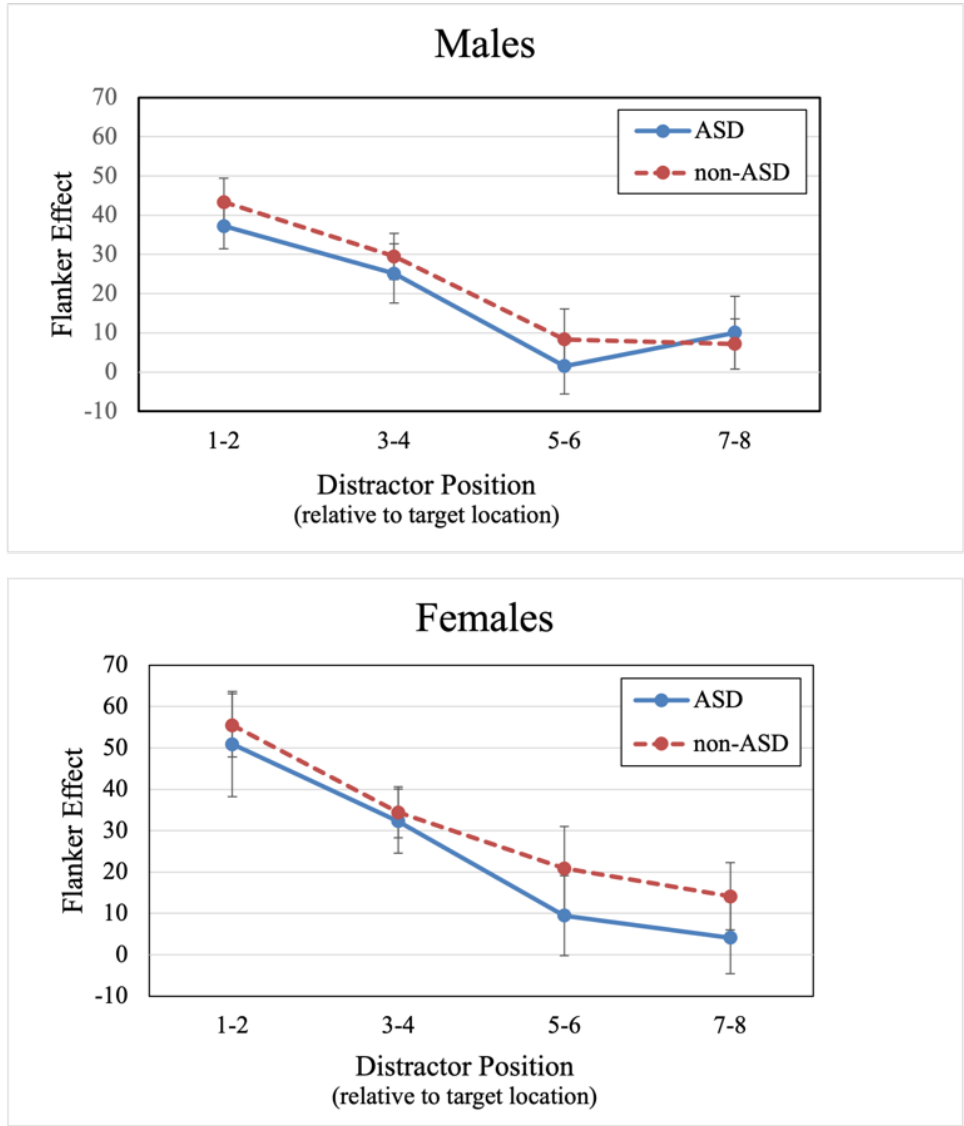
Figure 2. Mean flanker effect (incompatible RT minus compatible RT) for the flanker task, shown separately for each distractor eccentricity/position (relative to target location), group (ASD and non-ASD), and sex (males and females). Error bars represent standard of the mean.
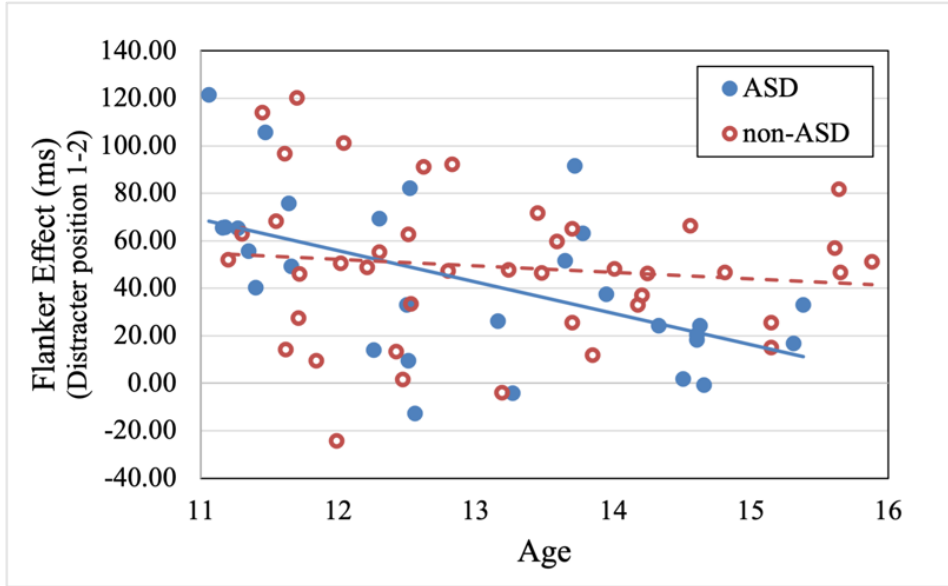
Figure 3. Scatterplot showing the relationship between age and flanker effect for the closest distracter position/eccentricity (relative to the target location). Data and the corresponding linear regression lines are shown separately for group (ASD and non-ASD).
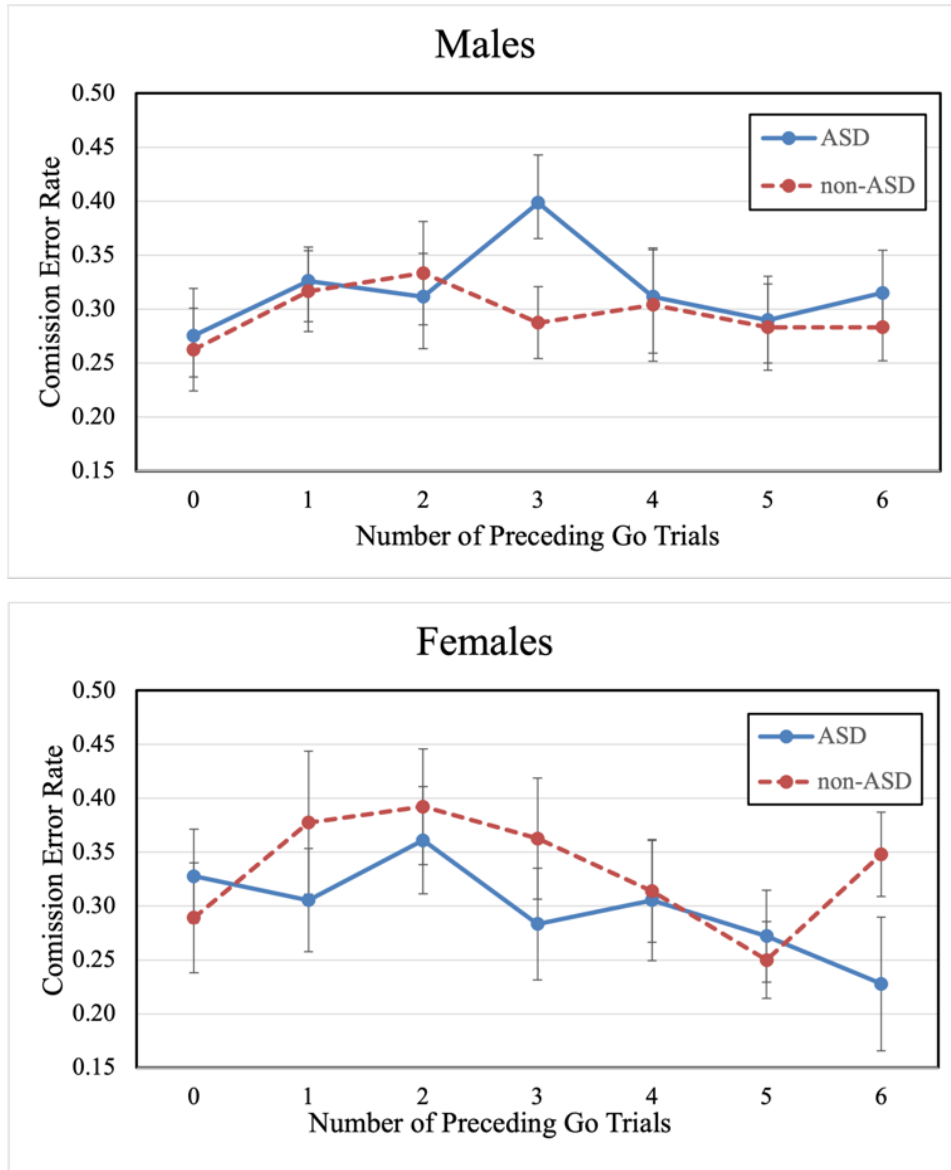
Figure 4. Commission error rate for the go/no-go task, shown separately for condition (i.e., number of preceding go trials), group (ASD and non-ASD), and sex (males and females). Error bars represent standard of the mean.
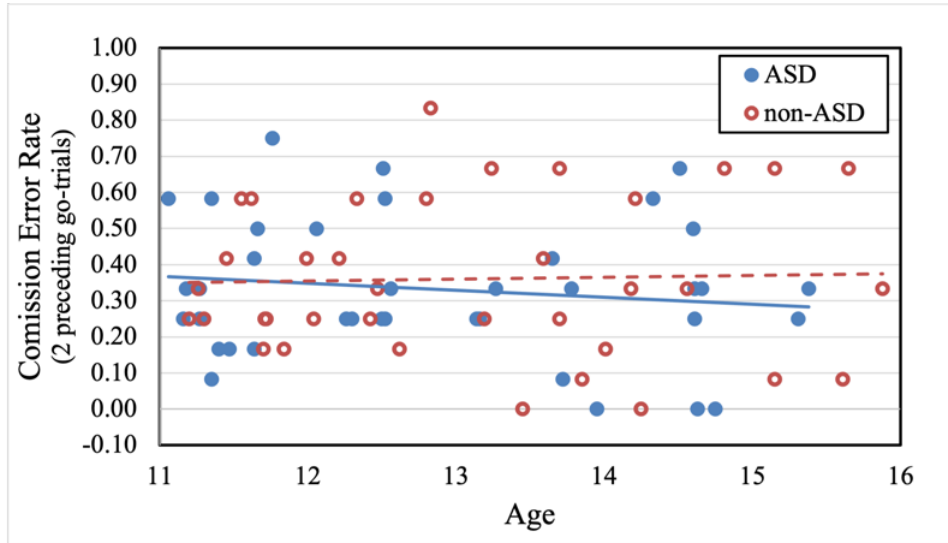
Figure 5. Scatterplot showing the relationship between age and commission error rate for the most difficult task condition (two preceding go-trials). Data and the corresponding linear regression lines are shown separately for group (ASD and non-ASD).