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Journal

Journal of Psychopathology and Clinical Science, 129(5)

ISSN

2769-7541

Authors

Krug, Marie K
Elliott, Matthew V
Gordon, Andrew
et al.

Publication Date

2020-07-01

DOI

10.1037/abn0000527

Peer reviewed

HHS Public Access

Author manuscript

J Abnorm Psychol. Author manuscript; available in PMC 2021 July 01.

Published in final edited form as:

J Abnorm Psychol. 2020 July ; 129(5): 517–527. doi:10.1037/abn0000527.

Proactive Control in Adolescents and Young Adults with Autism Spectrum Disorder: Unimpaired but Associated with Symptoms of Depression

Marie K. Krug[1,2], **Matthew V. Elliott**[3], **Andrew J. Gordon**[1,2], **Jeremy Hogeveen**[4], **Marjorie Solomon**[1,2,5]

[1]Department of Psychiatry and Behavioral Sciences, University of California, Davis

[2]University of California, Davis MIND Institute

[3]Department of Psychology, University of California, Berkeley

[4]Department of Psychology, University of New Mexico

[5]Imaging Research Center, University of California, Davis

Abstract

Although autism spectrum disorder (ASD) is characterized by deficits in cognitive control, our previous work suggests that preparatory, goal-directed cognitive processing (proactive control), may be preserved in children with ASD. We investigated whether proactive control is intact in adolescents and young adults with ASD, as well as how symptoms of ASD (repetitive behaviors) and psychopathology (depressive, anxiety, and attention-deficit/hyperactivity problems) are related to proactive control. Participants were adolescents and young adults with ASD (N=44) and typical development (TD) (N=44). Proactive control was assessed using a picture-word Stroop paradigm where participants named animals depicted in drawings while ignoring a superimposed written animal word. Interference effects (reaction time differences between more difficult incongruent trials, where animal pictures and words prompted different responses, and simpler congruent trials, where animal pictures and words prompted the same response) were calculated for two versions of the Stroop Task: a mostly congruent (MC) block, where the majority of trials were congruent, and a mostly incongruent (MI) block, where most trials were incongruent. Proactive control is calculated as the reduction in interference in the MI block in comparison to the MC block. Proactive control did not differ between groups, indicating that proactive control is not impaired in adolescents and young adults with ASD. In ASD, depression symptoms were associated with reduced proactive control. Future research should investigate the effects of interventions targeting depression as well as interventions targeting proactive control processes in individuals with ASD and comorbid depression.

General Nonscientific Summary

Autism spectrum disorder (ASD) is characterized by deficits in cognitive control, which is defined as goal-directed cognition and behavior. This study showed that proactive control, a type of

Corresponding author: mkkrug@ucdavis.edu.

cognitive control characterized by sustained, preparatory maintenance of task goals, is unimpaired in adolescents and young adults with ASD. However, increasing symptoms of depression in individuals with ASD were associated with reduced proactive control. Treatment of comorbid depression and/or cognitive interventions may help adolescents and young adults with ASD function optimally.

Keywords

autism spectrum disorder; cognitive control; proactive control; adolescence; depression

Autism spectrum disorder is a neurodevelopmental disorder defined by pervasive deficits in social communication and restricted, repetitive behaviors or interests (American Psychiatric Association, 2013). In addition, deficits in executive function or cognitive control are often present in affected individuals (Hill, 2004; Solomon, Hogeveen, Libero, & Nordahl, 2017; van den Bergh, Scheeren, Begeer, Koot, & Geurts, 2014; Vogan et al., 2018).

Cognitive control is a cognitive system that orchestrates thoughts and behavior in accordance with goals and intentions (Miller & Cohen, 2001). According to the Research Domain Criteria Project (RDoC: https://www.nimh.nih.gov/research/research-funded-bynimh/rdoc/index.shtml), cognitive control includes diverse functions such as goal selection (including updating, representation, maintenance, and task switching), response selection (including inhibition), and performance monitoring. In one prominent model of cognitive control, the Dual Mechanisms of Control framework, cognitive control processes operate under two distinct modes: proactive or reactive control. Proactive control is defined as active, sustained, and preparatory maintenance of goal-relevant information, whereas reactive control, which is a late correction or a “just in time” mode of cognitive control, is implemented at the moment in which it is needed (Braver, 2012; Braver, Gray, & Burgess, 2007). For example, if one always turns left at an intersection coming home from work, but hears about traffic congestion on that route, they may implement proactive control by actively reminding themselves to turn right during the entire drive, prior to arriving at the intersection. Alternatively, they might implement a reactive control strategy, whereby arriving at the intersection triggers the memory of the need to turn right to avoid the traffic. This “in the moment” reactive control is less resource demanding than proactive control, but may be more error-prone and disruptive.

Typical Development of Proactive Control

Variations of cognitive control paradigms such as the AX Continuous Performance Task (AX-CPT) and the Stroop Task have been designed to specifically assess implementation of proactive control strategies (Gonthier, Braver, & Bugg, 2016; Gonthier, Macnamara, Chow, Conway, & Braver, 2016; Gonthier, Zira, Cole, & Blaye, 2019). In the AX-CPT, participants are presented with a cue followed by a probe. If an A cue is followed by an X probe, then participants are required to make a “target” response. The remaining cue-probe sequences (AY: A cue followed by a non-X probe; BX: non-A cue followed by X; BY: non-A cue followed by a non-X probe) require a “non-target” response. AX trials occur more frequently than the other trials (70%, relative to 10% for each non-target condition). If the A

cue is adequately maintained via proactive control processes, AY trials will be slow while BX trials will not be difficult because the non-target response is prepared, resulting in a quick “non-target” response to the X probe.

In standard Stroop tasks, participants are asked to name the ink color of a written color word (Stroop, 1935). The word can be congruent (e.g. the word “red” written in red ink) or incongruent (e.g. the word “red” written in blue ink). Because word reading is automatic, for incongruent trials the word causes interference, leading to a slow reaction time (RT) in comparison to congruent trials. Increasing the frequency of incongruent trials increases the demand for proactive control; when incongruent trials occur often, a proactive control strategy of focusing attention away from the word should be implemented to speed performance on these trials. Congruent trials, however, would become slower, as the congruent word would no longer facilitate a quick response. Interference effects, calculated by subtracting congruent trial RT from incongruent trial RT, would be reduced (Braver et al., 2007; Gonthier, Braver, et al., 2016; Lindsay & Jacoby, 1994; Logan & Zbrodoff, 1979; Tzelgov, Henik, & Berger, 1992).

Chatham, Frank, & Munakata (2009) found that typically developing 3.5 year olds use a reactive control strategy while 8 year olds utilize a proactive control strategy during performance of the AX-CPT. By investigating AX-CPT performance in a large sample of young children (age 4 to 7 years), Gonthier et al. (2019) determined that children begin to switch from a reactive control strategy (more difficulty on BX trials) to a proactive control strategy (more difficulty on AY trials) by age 5.5. Others have shown that proactive control continues to develop throughout adolescence and into adulthood (Lorsbach & Reimer, 2008, 2010).

Cognitive Control and Internalizing Psychopathology

Cognitive control impairments can be clinically significant, as illustrated by their association with major depressive disorder (MDD) which is characterized by difficulties concentrating, inhibiting intrusive negative thoughts, or making decisions required for goal-directed behavior (American Psychiatric Association, 2013). Major depressive disorder is associated with impairments in cognitive control processes such as updating, shifting, and inhibition (Joormann & Tanovic, 2015) as well as impairments in proactive control more specifically. In a longitudinal study Vijayakumar et al. (2016) assessed participants for MDD during early (age 12), mid (age 16) and late (age 18) adolescence using a color-word Stroop Task, and found that adolescents diagnosed with MDD during early adolescence (age 12) had greater proactive control-related interference compared to adolescents who did not develop MDD until late adolescence. Depression is also associated with impairment in sustained attention, a cognitive process essential for successful proactive control, with depressed children showing greater RT variability, slower RT, and more errors of omission on the Continuous Performance sustained attention task compared to controls (Cataldo, Nobile, Lorusso, Battaglia, & Molteni, 2005).

Finally, depression-related impairments in cognitive control may be associated with rumination, which is defined as repetitive negative thinking about one’s own shortcomings,

distress, and sadness (Nolen-Hoeksema, 1991; Smith & Alloy, 2009). For example, rumination is associated with impaired sustained attention (Wagner, Alloy, & Abramson, 2015) and impaired set-shifting and inhibition (Yang, Cao, Shields, Teng, & Liu, 2017), while repetitive negative thinking more generally is associated with difficulty removing irrelevant information from working memory (Zetsche, Burkner, & Schulze, 2018).

Impairments in cognitive control have also been associated with anxiety in typical development. According to Eysenck, Derakshan, Santos, & Calvo's attentional control theory (2007), individuals high in anxiety have impaired cognitive control (particularly in inhibition and shifting) because they rely more on automatic, salience-driven, bottom-up attentional processes as opposed to top-down, goal-relevant attentional processes. These impairments often manifest when distracting stimuli are threat-related, (Williams, Mathews, & MacLeod, 1996), although Eysenck et al. (2007) emphasize that threat-related distracters can be internally generated, as would occur when an anxious individual is worrying or ruminating while concurrently trying to achieve a goal or perform a task. They also reference evidence that individuals high in anxiety self-report that they have problems with cognitive control (Broadbent, Cooper, FitzGerald, & Parkes, 1982; Derryberry & Reed, 2002) and that the effects of anxiety on cognitive control are worsened when task demands are high (Calvo & Eysenck, 1996; Eysenck & Graydon, 1989; Wood, Mathews, & Dalgleish, 2001). Krug & Carter (2012) found that trait anxiety was associated with behavioral impairment in an emotional Stroop paradigm designed to elicit proactive control specifically. Forster, Nunez Elizalde, Castle & Bishop (2015) attempted to disentangle the relationship between trait anxiety and worry, a defining feature of anxiety disorders (Meyer, Miller, Metzger, & Borkovec, 1990), on proactive control during a sustained attention paradigm. They found that trait anxiety was associated with slower performance, while both trait anxiety and worry were associated with the neural signatures of mind-wandering.

Autism Spectrum Disorder and Proactive Control

Individuals with ASD have historically shown deficits on neuropsychological measures of executive function (Hill, 2004; Ozonoff et al., 2004). Both parent-report (van den Bergh et al., 2014; Vogan et al., 2018) and self-report (Johnston, Murray, Spain, Walker, & Russell, 2019) data indicate deficits in executive functioning in daily life. Specific behavioral deficits on cognitive control paradigms, including cue/context maintenance, response inhibition, and task switching, as well as structural and functional differences in brain regions that underlie these processes have also been demonstrated (Solomon et al., 2017; Solomon, Ozonoff, Cummings, & Carter, 2008; Solomon et al., 2009). More recent work, however, suggests that proactive control may be intact in middle childhood (Hogeveen, Krug, Elliott, Carter, & Solomon, 2018). In Hogeveen et al., participants with ASD did not show impairments in performance on an AX-CPT designed for children (Chatham et al., 2009). However, for children with ASD, greater attention problems were associated with reduced proactive control, and increased repetitive behaviors (specifically, compulsive behaviors) were associated with increased proactive control. Abu-Akel, Apperly, Spaniol, Geng, & Movorach (2018) showed that higher autism traits in TD individuals were associated with better performance on a face-discrimination task in the presence of a task-irrelevant distractor,

suggesting that autism traits (in TD individuals, and perhaps also in individuals with ASD) may even lead to enhanced proactive control.

Internalizing Psychopathology in ASD

When investigating the development of proactive control in ASD, it is essential to consider comorbid depression and/or anxiety. In TD populations the prevalence of MDD rises during adolescence (Kessler, Avenevoli, & Ries Merikangas, 2001; Thapar, Collishaw, Pine, & Thapar, 2012). Parent-report and self-report measures indicate that children and adolescents (age range 8–18) with ASD have higher symptoms of both anxiety and depression compared to those with TD (Oswald et al., 2016; Solomon, Miller, Taylor, Hinshaw, & Carter, 2012), and a recent longitudinal population based study found that ASD was associated with increased depressive symptoms in comparison to TD beginning at age 10 and persisting until age 18 (Rai et al., 2018). A longitudinal assessment of both depression and anxiety symptoms from age 9–24 years showed that individuals with ASD had 1.6 times greater depression symptoms and 1.4 times greater anxiety symptoms in comparison to a developmentally delayed control group (Gotham, Brunwasser, & Lord, 2015).

Current Study: Goals and Hypotheses

In the current study we investigated proactive control and its association with repetitive behaviors and psychopathology in adolescents and young adults with ASD. We implemented a picture-word Stroop Task (Gonthier, Braver, et al., 2016) which confers an advantage over standard neuropsychological tests in that it is designed to measure a specific cognitive control deficit (proactive control) (MacDonald & Carter, 2002). This paradigm was designed specifically to overcome potential confounds encountered when using standard Stroop tasks to measure proactive control (Gonthier, Braver, et al., 2016).

First, we investigated proactive control in adolescents and young adults with ASD in comparison to those with TD. While Hogeveen et al. (2018) found that proactive control was unimpaired in middle childhood, we made no strong prediction in our older sample, given that proactive control continues to improve throughout adolescence (Lorsbach & Reimer, 2008).

Second, we investigated how implementation of proactive control is related to symptoms of ASD (repetitive behaviors) as well as psychopathology (attention deficit/hyperactivity, depressive, and anxiety problems). We tested whether the relationships between proactive control and repetitive behaviors/attention symptoms found in children (Hogeveen et al., 2018) are also seen in an older sample and predicted that increasing symptoms of depression and anxiety in the ASD group would be associated with impairments in proactive control, as is found in TD (Cataldo et al., 2005; Forster et al., 2015; Krug & Carter, 2012; Vanderhasselt et al., 2014; Vijayakumar et al., 2016; Wagner et al., 2015).

Methods

Participants

Participants in the current study included eighty-eight individuals (44 ASD; 44 TD), who were a subset of the cohort enrolled in Time Point 1 of the Cognitive Control in Autism (CoCoA) Study at the UC Davis MIND Institute. All participants were recruited from the community, physician referrals, or the UC Davis MIND Institute participant database. To qualify for the study, all participants were required to be between 12 and 22 years of age, have a Wechsler Abbreviated Scale of Intelligence (WASI)-II full scale IQ (four-factor) (FSIQ) (Wechsler, 2011) ≥ 70, and not be taking psychotropic medications. Participants with ASD had a community diagnosis of ASD and met diagnostic criteria for ASD on a Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM)-5 Criteria Checklist for ASD (American Psychiatric Association, 2013) and the Autism Diagnostic Observation Schedule 2 (ADOS-2) (Lord et al., 2000), which was administered by a licensed clinical psychologist at the UC Davis MIND Institute. Typically developing participants were required to have no social (pragmatic) communication disorder as assessed by a DSM-5 based symptom checklist, have a score of ≤ 11 on the Social Communication Questionnaire (SCQ) (Rutter, Bailey, & Lord, 2003), have no first-degree family members with a diagnosis of ASD, and no reported Axis 1 psychopathology or neurodevelopmental disorders. To be included in this dataset, participants' parents also needed to complete the Achenbach System of Empirically Based Assessment (ASEBA) questionnaire (Achenbach & Rescorla, 2001, 2003). Participant assent and parental consent or participant consent were obtained. The CoCoA Study protocol was approved by the UC Davis Medical Center Institutional Review Board.

Groups did not differ on age, sex distribution, or WASI measures (including Verbal Comprehension) (Table 1).

Measures

Proactive Control: Stroop Task.—Participants performed a well-validated picture-word Stroop Task, an adaptation of the classic color-word Stroop (Stroop, 1935) designed to measure proactive control (Gonthier, Braver, et al., 2016). The task was adapted from Gonthier et al. (2016), and similar Stroop paradigms have been used in other studies of cognitive control (Bugg & Chanani, 2011; Bugg, Jacoby, & Chanani, 2011).

The Stroop Task was administered on a laptop computer. Each trial consisted of a line drawing of an animal, with an animal word superimposed over the picture. The word could be congruent or incongruent to the animal picture (Figure 1A). Participants were instructed to ignore the word and name the pictured animal as quickly and accurately as possible. The response was spoken into a microphone and recorded in a .wav audio file. Eight animal categories were used (bear, bird, cat, cow, deer, dog, goat, pig) and the same eight animal pictures were presented throughout the experiment. Each stimulus remained on the screen for 2000 ms, after which a blank screen appeared, and the next trial was initiated by the experimenter. Reaction time (RT) for each trial was extracted using a combination of in-house scripts and Chronset, a software tool for automated speech onset detection (Roux,

Armstrong, & Carreiras, 2017). Lab personnel listened to Stroop audio files and coded each trial. Incorrect responses, trials without responses, and "scratch" trials (trials with partial responses and non-task related vocalizations, such as sneezing, mumbling, etc.) were removed prior to analysis. Correct trials faster than 200 ms were also removed. Participants with < 70% scorable trials were removed from the analysis (1 participant with ASD).

In the current study, the Stroop task was divided into 2 blocks: a 'mostly congruent' (MC) block and a 'mostly incongruent' (MI) block. The MC block was performed first. Four of the animals were presented as congruent 75% of the time and as incongruent 25% of the time (MC items) while the other four animals were presented as congruent 50% of the time and incongruent 50% of the time ((PC)-50 items) (Figure 1B). For the MI block, the 4 animals that were previously MC items were presented as MI items (congruent 25% of the time, incongruent 75% of the time) (Figure 1B). Mean RT for correct trials was computed for all trial types. Stroop interference effects (incongruent RT- congruent RT) were calculated for MC items, MI items, and PC-50 items in both blocks. Participants with any interference effects greater than 3 standard deviations from the group mean were removed from the dataset (1 ASD; 1 TD) (Gonthier, Braver, et al., 2016). Lastly, we calculated *proactive control*, which represents the degree to which the difference between incongruent and congruent trials is reduced on the MI block relative to the MC block (larger values=greater proactive control; Figure 1B) (Gonthier, Braver, et al., 2016).

We chose this particular paradigm because inclusion of PC-50 items circumvents a major criticism of block-wise manipulations of proportion congruency; that the same pattern of results could be accounted for by an item-specific control system (Bugg & Crump, 2012; Bugg, Jacoby, & Toth, 2008). For example, if the dog picture is almost always paired with an incongruent word, then the dog picture itself could trigger a reactive cognitive control process at that moment. If all animals in the stimulus set are incongruent most of the time, proportion congruency across the entire block of trials and proportion congruency for each item are confounded, rendering it difficult to distinguish between proactive and reactive control processes. If a global, preparatory proactive control strategy is being used, reduction of interference should extend to PC-50 items presented in the context of the MI block, as has been demonstrated in TD (Bugg & Chanani, 2011; Gonthier, Braver, et al., 2016). Consequently, PC-50 items were the focus of our inferential analyses.

Clinical Measures.—Standard clinical measures for assessing autism symptoms (Autism Diagnostic Observation Schedule 2 (ADOS-2) (Lord et al., 2000), Social Communication Questionnaire (SCQ) (Rutter et al., 2003), Repetitive Behavior Scale-Revised (RBS-R) (Lam & Aman, 2007)), cognitive ability (Weschler Abbreviated Scale of Intelligence Second Edition (WASI-II) (Wechsler, 2011)), and psychopathology (Achenbach System of Empirically Based Assessment (ASEBA) (Achenbach & Rescorla, 2001, 2003)) were administered (see Supplemental Methods).

Statistical Analysis

A two (group: ASD, TD) x two (block: MC, MI) x two (trial type: C, I) ANOVA was conducted on RT data (PC-50 items; correct trials only) to assess group differences in

proactive control. Follow-up repeated measures t-tests were conducted to see if each group individually showed evidence of proactive control. Two (group: ASD, TD) x two (trial type: C, I) ANOVAs were then conducted for the MC and MI blocks individually. Lastly, for participants with ASD, correlations were run to evaluate associations between proactive control and RBS-R subscales, and ASEBA Depressive, Anxiety, and Attention Deficit/Hyperactivity (AD/H) Problems. Because RBS-R and ASEBA data were not normally distributed, non-parametric correlations (Kendall's tau-b [τ_b]) are reported. As a result of our stringent inclusion criteria for TD participants in the CoCoA Study, there was a low incidence of repetitive behaviors and psychopathology with many scores at floor. Results of these correlations for participants with TD are provided but should be interpreted with caution (Supplemental Table 1). Statistical tests were conducted using SPSS (Version 25), JASP (Version 0.11.1) and R Studio (Version 3.6.1). Psych (Revelle, 2018) and apaTables (Stanley, 2018) packages were used to calculate effect size confidence intervals.

Bayes Factors are reported for all statistical tests. Bayes Factors are advantageous in that they indicate strength of evidence for the alternative hypothesis (H1) in comparison to the null hypothesis (H0). Although other interpretations exist, values of 1–3, 3–10, and > 10 typically indicate weak, intermediate, and strong evidence, respectively (Held & Ott, 2018). For Bayes Factors < 1, the reciprocal effect is reported to indicate strength of evidence for H0 in comparison to H1. Evidence in support of H1 is reported as BF_{10} and evidence in support of the null hypothesis is reported as BF_{01} (ie., $1/BF_{10}$). Bayes Factors were computed in R Studio using the BayesFactor package (Morey & Rouder, 2018) for parametric tests and in JASP for non-parametric tests.

Results

Proactive Control: Stroop Task

Proactive Control.—A group (ASD, TD) x block (MC, MI) x trial type (congruent, incongruent) ANOVA was not significant ($F(1, 86)=.163$, $p=.688$, $\eta_p^2=.002$, 90% CI [0, 0.04], $BF_{01}=8.459$), indicating that there were no differences between groups in proactive control. Post-hoc tests showed that each group had a significant reduction in interference for the MI block compared to the MC block (i.e., proactive control): ASD ($t(43)=3.943$, $p<.001$, $d=.594$, 95% CI [.27, .91], $BF_{10}=89.659$); TD ($t(43)=5.230$, $p<.001$, $d=.788$, 95% CI [.45, 1.12], $BF_{10}=3.921 \times 10^3$) (Figure 1C, Table 2)[1]. Proactive control was not associated with age in either group (Supplemental Table 2).

MC Block.—For the MC block, a group (ASD, TD) x trial type (congruent, incongruent) interaction was not significant ($F(1,86)=.150$, $p=.700$, $\eta_p^2=.002$, 90% CI [0, .04], $BF_{01}=6.080$). There was a main effect of group ($F(1,86)=15.355$, $p<.001$, $\eta_p^2=.151$, 90% CI [.05, .26], $BF_{10}=2.674 \times 10^3$), driven by slower RT across all trials in the ASD group, and a significant main effect of trial type, driven by slower RT on incongruent compared to

[1]It is important to note that the proactive control effect was driven by slowing on congruent trials in the MI block compared to the MC block, which is often termed a *congruency cost*. This slowing is a natural consequence of proactive control and serves to decrease interference by reducing facilitation of the word-reading response on congruent trials. Changes in the magnitude of Stroop interference effects are considered the best indicator of cognitive control implementation (see Gonthier, Braver, & Bugg, 2016).

congruent trials (F(1,86)=344.303, p<.001, η_p^2=.800, 90% CI [.74, .84], BF_{10}=6.250 × 10^7) (Figure 1D, Table 2).

MI Block.—For the MI block, a group (ASD, TD) x trial type (congruent, incongruent) interaction was not significant (F(1,86)=.875, p=.352, η_p^2=.010, 90% CI [0, .07], BF_{01}=5.948). Once again there was a main effect of group, driven by slower RT across all trials in the ASD group (F(1,86)=12.521, p=.001, η_p^2=.127, 90% CI [.04, .24], BF_{10}=2.906 × 10^3), and a significant main effect of trial type (F(1,86)=193.271, p<.001, η_p^2=.692, 90% CI [.60, .75], BF_{10}=157.974), driven by slower RT on incongruent compared to congruent trials. (Figure 1D; Table 2).

Trials Removed.—Means percentages of trials removed from RT analyses and statistical analyses on trials removed are reported in Supplemental Table 3 and 4 respectively. An analysis specifically on error trials was not conducted, as it was often difficult to discern whether a trial with a partial vocalization prior to the correct response should be counted as a true error; clear and full vocalizations of an incorrect response were quite rare. Similar to RT analyses, proactive control did not differ between groups for trials removed.

Proactive Control and RBS-R

A Mann-Whitney U test showed (as expected) that the ASD and TD groups differed significantly on all RBS-R subscales (all p's≤.002) (Table 1). None of the RBS-R subscales were significantly correlated with proactive control for individuals with ASD: Stereotypic Behavior (τ_b= .073, 95% CI [−.137, .282], p=.511, BF_{01}=4.021); Self-Injurious Behavior (τ_b= −.034, 95% CI [−.234, .166], p=.772, BF_{01}=4.818); Compulsive Behavior (τ_b= −.110, 95% CI [−.301, .081], p=.338, BF_{01}=2.985); Ritualistic/Sameness Behavior (τ_b= −.164, 95% CI [−.346, .019], p=.130, BF_{01}=1.575); Restricted Interests (τ_b= −.063, 95% CI [−.270, .143], p=.568, BF_{01}=4.251).

Proactive Control and Psychopathology

The group with ASD scored higher than TD on ASEBA Depressive Problems, Anxiety Problems, and AD/H Problems (all p's<.001) (Table 1). For ASD, 13 individuals (29.5%) had a score of 65 or higher on Depressive Problems, indicating depression scores in the borderline to clinical range. Twelve individuals (27.3%) were in the borderline to clinical range for Anxiety Problems and 9 individuals (20.5%) were in the borderline to clinical range for AD/H Problems. Psychopathology was very low in the TD group. Four participants (9.1%) had a score in the borderline to clinical range for Depressive Problems and no individuals had scores of 65 or above for Anxiety or AD/H Problems.

In the ASD group, there was a significant negative correlation between Depressive Problems and proactive control (τ_b= −.217, 95% CI [−.394, −.039], p=.042, BF_{10}=1.589) (Figure 2a), indicating that more symptoms of depression are associated with less ability to implement proactive control. Follow-up analyses showed that MC interference was not associated with Depressive Problems (τ_b= −.056, 95% CI [−.273, .160], p=.598, BF_{01}=4.441), while greater MI interference was significantly associated with greater Depressive Problems (τ_b= .232, 95% CI [.066, .397], p=.030, BF_{10}=2.153) (Figure 2b), indicating that Depressive Problems

are specifically associated with performance in the proactive control-inducing MI block. In a post-hoc analysis we found that overall RT was not associated with Depressive Problems in the ASD group, indicating that our association between Depressive Problems and reduced proactive control cannot be accounted for by a generalized psychomotor slowing effect due to depression (Bennabi, Vandel, Papaxanthis, Pozzo, & Haffen, 2013; Sobin & Sackeim, 1997).

There was no association between Anxiety (τ_b= −.164, 95% CI [−.342, .014], p=.131, BF_{01}=1.539) or AD/H Problems (τ_b= −.073, 95% CI [−.263, .116], p=.496, BF_{01}=4.030) and proactive control.

Lastly, we performed a multiple linear regression with all three ASEBA scales included as independent variables and proactive control as the dependent variable. Results were in accordance with the separate correlation analyses; Anxiety and AD/H Problems were not significant predictors of proactive control (p's>.25), while Depressive Problems showed a (marginally) significant effect (β=−3.459, 95% CI [−7.014, .096], p=.056, BF_{10}=1.425).

Discussion

Adolescents and young adults with ASD and TD performed two versions of a picture-word Stroop task: an MC block, where most trials were congruent, and an MI block, designed to induce a proactive control strategy, where most trials were incongruent. Our index of proactive control was significant for ASD and TD, indicating that both groups engaged proactive control processes. However, there were no significant differences between groups for proactive control, and evidence for the null hypothesis, as revealed by an analysis of Bayes Factors, was moderate, indicating that proactive control is likely *not impaired* in adolescents and young adults with ASD. Proactive control was not associated with repetitive behaviors, Anxiety, or AD/H Problems in the ASD group. However, Depressive Problems were associated with reduced proactive control, suggesting that depression is associated with proactive control impairment in adolescents and young adults with ASD.

It is important to consider whether proactive control would still be intact if measured while performing a cognitive task that is more problematic for individuals with ASD. In a meta-analysis, Geurts, van den Bergh, & Ruzzano (2014) found that individuals with ASD show greater difficulty with response inhibition tasks (such as Stop-Signal) than in interference control tasks (such as Stroop). Schmitt, White, Cook, Sweeney, & Musconi (2018) looked at Strop Signal Task performance in ASD. They found that while the stopping process itself is intact, individuals with ASD show reduced RT slowing on GO trials, suggesting that preparatory, or proactive control processes contribute to impaired task performance. However, a study in children with ADHD and ASD found no impairments in the proactive component of response inhibition (van Hulst et al., 2018). It is also important to consider that our Stroop Task used two distinct stimuli presented simultaneously (a word and a picture); given that individuals with ASD may be biased toward local processing (Happe & Frith, 2006), individuals with ASD may be particularly adept at implementing proactive control when it requires focused attention to a feature of a stimulus. Future studies are needed to fully investigate proactive control in ASD across different types of tasks.

As in TD, children, adolescents, and adults with ASD show an association between repetitive negative thinking such as worry, brooding and rumination and increased anxiety and depression (Bos, Diamantopoulou, Stockmann, Begeer, & Rieffe, 2018; Burns, Irvine, & Woodcock, 2019; Crane, Goddard, & Pring, 2013; Gotham, Bishop, Brunwasser, & Lord, 2014). Assuming that rumination also affects cognition similarly in ASD and TD, our results support the resource-depletion theory of rumination (Hertel, 1998; Levens, Muhtadie, & Gotlib, 2009). Because proactive control is resource-demanding, the rumination characteristic of depression leaves limited cognitive resources for proactive control, resulting in impaired performance. Our follow-up analyses show that depression is significantly associated with poor performance exclusively in the more resource-demanding proactive control condition (MI block).

The attentional scope model of rumination (Whitmer & Gotlib, 2013) proposes that individuals high in trait rumination are characterized by a narrow attentional focus, which confers an advantage on tasks where a participant needs to focus on a task-relevant stimulus and ignore distracters. This model also suggests that when a trait ruminator is in a state of active rumination, performance will be impaired as a narrowed attentional focus may be directed toward active rumination as opposed to the task at hand. The repetitive thinking characteristic of ASD may be associated with a narrow attentional focus, resulting in better proactive control. With concurrent depression, however, this advantage may disappear. Interestingly, Burrows, Timpano, and Uddin (2017) propose that it is the increased self-referential processing and cognitive inflexibility characteristic of individuals with ASD that predisposes them to repetitive negative thinking and increased internalizing psychopathology. Future work should directly investigate associations between repetitive negative thinking such as rumination and worry and proactive control in ASD.

The association between proactive control and depressive symptoms is of potentially high clinical relevance for the treatment of internalizing disorders in individuals with ASD. Cognitive-behavioral therapy (CBT), an evidence-based treatment which aims to alter negative thought patterns to enhance coping and reduce distress (Hollon & Beck, 2013), offers promise in producing significant improvements in depression symptoms for individuals with ASD (Sukhodolsky, Bloch, Panza, & Reichow, 2013; Ung, Selles, Small, & Storch, 2015; Weston, Hodgekins, & Langdon, 2016). A recent clinical trial in TD adults has shown that a rumination-focused CBT may be even more effective than standard CBT in relieving symptoms of depression (Hvenegaard et al., 2019) and could one day be adapted for individuals with ASD. Resolution of depression and amelioration of rumination and worry may free up the resources needed to implement effective proactive control, which is otherwise preserved in individuals with ASD. Improved proactive control may have cascading benefits into other areas of functioning; stronger executive function has been tied to reduction in symptoms of ASD and better overall quality of life (de Vries & Geurts, 2015; Kenworthy, Black, Harrison, della Rosa, & Wallace, 2009). However, because the relationship between depressive symptoms and proactive control is likely complex (and likely not unidirectional), cognitive interventions should also be considered when treating individuals with ASD and comorbid internalizing psychopathology. Joormann & Quinn (2014) review interventions that directly target attentional and cognitive control processes and show promise in alleviating symptoms of anxiety and depression.

It is important to note that the current study did not include participants with ASD and intellectual disability, thus the results described here should not be overextended. Because the picture-word Stroop task requires word-reading and the ability to make a clear verbal response, an alternative paradigm would be required for some populations. The child-adapted AX-CPT (Chatham et al., 2009; Hogeveen et al., 2018), which does not rely upon word-reading or require a verbal response, could be used to investigate proactive control in individuals with limited verbal abilities. The Nonverbal Stroop Card Sorting Test (Koch & Rold, 2016) could potentially be adapted to assess proactive control processes in individuals with intellectual disability and/or impaired verbal functioning.

One limitation is that our TD sample reported very low rates of psychopathology on the ASEBA. Consequently, we are unable to conclude whether the associations we found between Depressive Problems and proactive control are specific to ASD or would also occur in a TD sample with higher rates of psychopathology. Lastly, conclusions regarding associations (or lack thereof) between proactive control and RBS-R and ASEBA scores should be interpreted with caution when the reported Bayes Factors provide only weak evidence in support of H0 or H1. For example, although correlations between Depressive Problems and proactive control and Depressive Problems and MI interference are statistically significant (p's<.05), support for H1 is weak. We did not find the predicted association between Anxiety Problems and proactive control. Our ASD group was a bit lower on Anxiety Problems compared to Depressive Problems, so it is unclear whether the relationship we report between Depressive Problems and proactive control is specific to depression or would also extend to anxiety in a sample with higher symptoms. In a post-hoc analysis, Anxiety Problems did show a weak albeit significant correlation with MI block interference (τ_b= .226, 95% CI [.034, .491], p=.037, BF_{10}=1.914). Unlike Hogeveen et al. (2018), we did not find an association between AD/H problems and proactive control in our ASD group. The relationship found in Hogeveen et al. (2018) may have arisen due to the additional attentional demands of the AX-CPT. Alternatively, because the Stroop Task was quite long and demanding, many potential participants with high levels of AD/H problems were unable to attempt or complete the task. Thus, it is unknown whether this relationship would have been replicated in a sample with higher rates of AD/H problems. Future work with larger ASD samples and samples with greater incidence of psychopathology is necessary.

Regarding RBS-R, it is important to note that the current sample had very low scores on all subscales. Hogeveen et al. (2018) reported higher compulsive behavior scores (M=3.65 vs. M=2.02). This is not surprising, given the mean ages of ASD participants (10.44 years in Hogeveen et al.; 17.56 years in the current study). Total repetitive behaviors, as well as each subtype of repetitive behavior measured by RBS-R subscales, decreases with age, even when controlling for intellectual disability, gender, and psychotropic medication use (Esbensen, Seltzer, Lam, & Bodfish, 2009). Relationships between repetitive behaviors and cognition may be of less significance in older, more able populations.

In conclusion, adolescents and young adults with ASD are not impaired on proactive control in comparison to individuals with TD. However, for individuals with ASD, symptoms of depression were associated with reduced implementation of proactive control. Future

research on interventions targeting comorbid psychopathology as well as proactive control processes specifically will be of utmost importance, both in reducing distressing symptoms and in improving essential cognitive processes which are required for adult life.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements:

This work was supported by the National Institute of Mental Health (R01 MH106518-01A1 held by Marjorie Solomon) as well as recruitment and statistical support from the MIND Institute Intellectual and Developmental Disabilities Research Center (IDDRC) awarded by the National Institute of Child Health and Human Development (U54 HD079125).

We would like to thank Todd Braver, Julie Bugg, and Corentin Gonthier for helpful comments, advice, and task materials, Ana-Maria Iosif for statistical advice, Cory Coleman, Andria Farrens, and Dennis Thompson for technical support, and Seoyoung Gam, Raphael Geddert, Garrett Gower, Jennifer Farren, Andria Farrens, Sarah Mahdavi, and Ashley Tay for help with data collection and/or scoring.

This work was funded by the National Institute of Mental Health, R01 MH106518-01A1, awarded to Marjorie Solomon.

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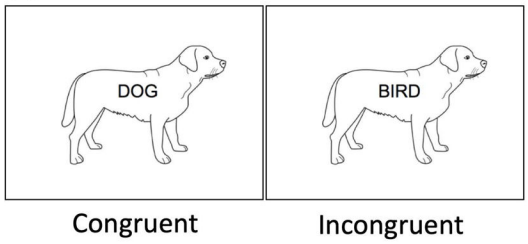
A.

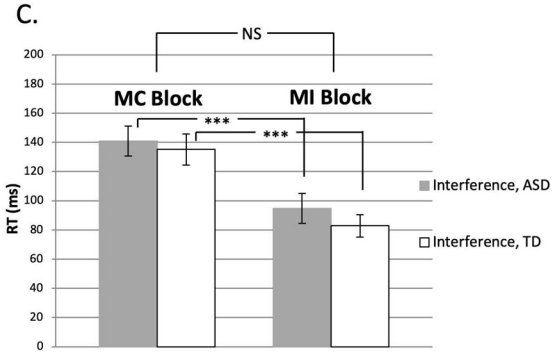


B.

	MC Block		MI Block	
Trial Types	MC Items	PC-50 Items	MI Items	PC-50 Items
Congruent	216	48	72	48
Incongruent	72	48	216	48

Proactive Benefit = [MC Block(PC-50, incongruent-congruent)] – MI Block(PC-50, incongruent-congruent)]

C.



D.

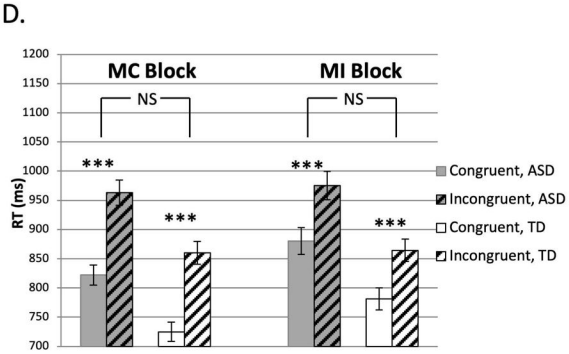


Figure 1.

ASD and TD show evidence of proactive control in the Stroop Task. **(A)** Example of congruent and incongruent stimuli. Participants were instructed to verbally name the animal pictured. **(B)** Trials counts are shown for the MC and MI blocks. In both blocks, there were biased items and PC-50 items. **(C)** Interference effects (incongruent– congruent RT) are displayed. There were no group differences in reduction in interference for the MI block compared to the MC block (proactive control). However, both ASD and TD had a significant proactive control effect. **(D).** There were no between group differences when interference effects for the MC and MI blocks were analyzed separately. Both ASD and TD showed significant interference effects (incongruent trials slower than congruent trials) in both blocks.

Note: For C and D, data is displayed for PC-50 items.

ASD=Autism Spectrum Disorder; TD=Typical Development; MC=Mostly Congruent; MI=Mostly Incongruent; PC-50 = Proportion Congruent-50; RT=reaction time

***p<.001

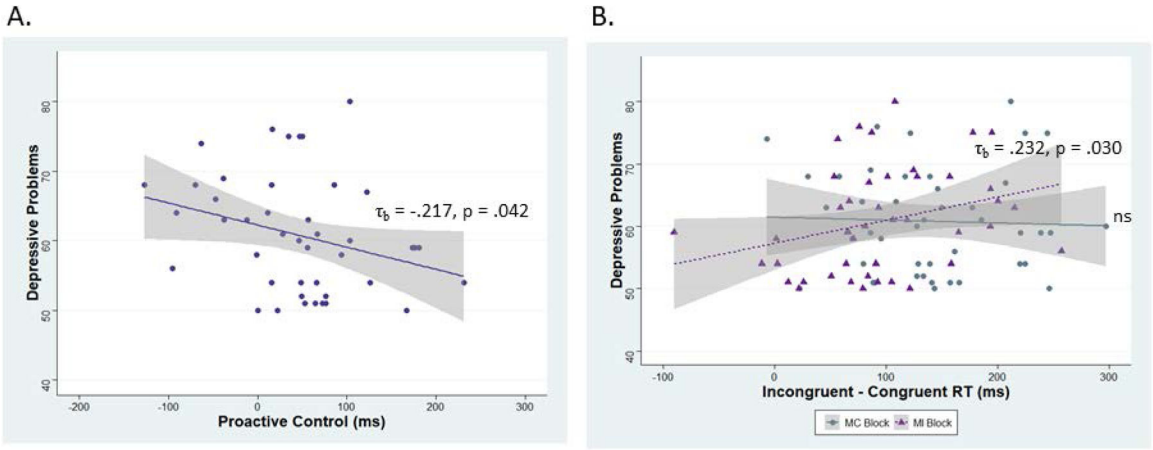


Figure 2.

Relationship between Stroop Task Performance and ASEBA Depressive Problems. **(A)** For the ASD group, proactive control was lower in individuals with greater Depressive Problems. **(B)** Depressive Problems were associated with higher interference in the MI block, but not the MC block.

Note: For ASEBA data, analyses were conducted on age-adjusted T-scores.

ASEBA=Achenbach System of Empirically Based Assessment; ASD=Autism Spectrum Disorder; MC=Mostly Congruent; MI=Mostly Incongruent

Table 1.

Participant characteristics.

	ASD (N=44)	TD (N=44)	Group Comparison
Age (years)	17.56*(2.91)*	17.24*(3.24)*	U=916.500, p=.661, r_{pb}=.053
Sex (F, M)	9, 35	11, 33	X^2=0.259, p=.611, φ=.054
WASI-II Full-Scale IQ	104.23*(12.67)*	107.55*(11.86)*	t(86)=1.269, p=.208, d=.214
WASI-II Verbal Comprehension	98.66*(13.21)*	102.84*(11.33)*	t(86)=1.594, p=.115, d=.344
WASI-II Perceptual Reasoning	109.48*(14.91)*	110.86*(15.37)*	t(86)=0.429, p=.669, d=.093
Social Communication Questionnaire	21.51*(5.75)*	2.11*(2.69)*	U=4.000, p<.001***, r_{pb}=.996
ADOS (calibrated severity score)	7.52*(1.56)*	NA	NA
ASEBA			
Depressive Problems	60.80*(8.385)*	53.25*(5.444)*	U=384.500, p<.001***, r_{pb}=.603
Anxiety Problems	51.23*(7.606)*	52.45*(3.903)*	U=540.000, p<.001***, r_{pb}=.442
Attention Deficit/Hyperactivity Problems	58.45*(6.866)*	51.45*(2.645)*	U=314.500, p<.001***, r_{pb}=.615
RBS-R			
	ASD (N = 43)	**TD (N = 42)**	**Group Comparison**
Stereotypic Behavior	3.88*(4.130)*	0.31*(0.780)*	U=290.000, p<.001***, r_{pb}=.619
Self-Injurious Behavior	1.63*(2.526)*	0.40*(0.912)*	U=593.500, p=.002**, r_{pb}=.343
Compulsive Behavior	2.02*(2.395)*	0.33*(0.928)*	U=511.000, p<.001***, r_{pb}=.434
Ritualistic/Sameness Behavior	1.53*(7.232)*	0.11*(2.288)*	U=203.500, p<.001***, r_{pb}=.115
Restricted Interests	3.09*(2.515)*	0.19*(0.833)*	U=216.500, p<.001***, r_{pb}=.160

Note: Mean displayed with standard deviation in parentheses. If data were normally distributed, a Student's t-test *was* performed. If data were not normally distributed, *a* Mann-Whitney U test *was* performed. *All* statistical tests were two-tailed.

** p<.01;

*** p<.001

ASD=Autism Spectrum Disorder; TD=Typical Development; WASI=Weschler Abbreviated Scale of Intelligence; ADOS=Autism Diagnostic Observation Schedule; ASEBA=Achenbach System of Empirically Based Assessment; RBS-R=Repetitive Behavior Scale-Revised

Table 2.

Behavioral data for the Stroop Task.

	ASD (N=44)	TD (N=44)
C, MC Block	822.095*(113.314)*	124.949*(109.862)*
I, MC Block	962.945*(142.375)*	860.043*(130.470)*
Interference (I-C), MC Block	140.850*(68.703)*	135.094*(70.787)*
C, MI Block	880.352*(150.945)*	781.438*(124.781)*
I, MI Block	975.112*(161.759)*	864.303*(128.066)*
Interference (I-C), MI Block	94.820*(67.635)*	82.865*(51.120)*
Proactive Control: [(Interference (I-C), MC Block)-(Interference (I-C), MI Block)]	46.030*(77.438)*	52.228*(66.248)*

Note: Mean reaction time (RT) is given in milliseconds, with standard deviation in parentheses. All data displayed is for Proportion Congruent-50 (PC-50) items.

ASD=Autism Spectrum Disorder; TD=Typical Development; C=Congruent; I=Incongruent; MC=Mostly Congruent; MI=Mostly Incongruent