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Effects of Response Preparation on Developmental Improvements in Inhibitory Control

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Abstract

Studies in adults indicate that response preparation is crucial to inhibitory control, but it remains unclear whether preparation contributes to improvements in inhibitory control over the course of childhood and adolescence. In order to assess the role of response preparation in developmental improvements in inhibitory control, we parametrically manipulated the duration of the instruction period in an antisaccade (AS) task given to participants ages 8 to 31 years. Regressions showing a protracted development of AS performance were consistent with existing research, and two novel findings emerged. First, all participants showed improved performance with increased preparation time, indicating that response preparation is crucial to inhibitory control at all stages of development. Preparatory processes did not deteriorate at even the longest preparatory period, indicating that the youngest participants were able to sustain preparation at even the longest interval. Second, developmental trajectories did not differ for different preparatory period lengths, highlighting that the processes supporting response preparation continue to mature in tandem with improvements in AS performance. Our findings suggest that developmental improvements are not simply due to an inhibitory system that is faster to engage but may also reflect qualitative changes in the processes engaged during the preparatory period.

Keywords

response preparation; cognitive control; antisaccade; inhibitory control; development

1. Introduction

Inhibitory control is the ability to direct behavior through internally-represented goals and it is crucial for exerting top-down control of behavior. Various studies using different measures of inhibitory control have shown that performance improves through childhood into adolescence (Davidson, Amso, Anderson, & Diamond, 2006; Dempster, 1992; Diamond & Taylor, 1996; Fuster, 2002; Luciana & Nelson, 1998; Ridderinkhof, Band, & Logan, 1999; Ridderinkhof, van den Wildenberg, Segalowitz, & Carter, 2004; Ridderinkhof & van der Molen, 1997; Williams, Ponesse, Schachar, Logan, & Tannock, 1999), and its improvement

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enhances information-processing abilities that facilitate overall cognitive development (Dempster, 1992). However, what underlies developmental improvements in inhibitory control remains unclear. Single-cell monkey studies and human neuroimaging studies have shown that essential to inhibitory control is response preparation (Connolly, Goodale, Menon, & Munoz, 2002; Curtis & D'Esposito, 2003; DeSouza, Menon, & Everling, 2003; Ford, Goltz, Brown, & Everling, 2005), the ability to engage inhibitory processes during the time of instruction prior to the period when a response is required. Response preparation, or engaging preparatory set, is a prospective function that involves choosing, planning, and readying a response prior to target appearance (Connolly et al., 2002; Fuster, 2002; LaBerge, Auclair, & Sieroff, 2000). In the present study, we aimed to characterize the role of response preparation in age-related improvements in inhibitory control from childhood into adulthood by parametrically varying the length of the preparatory interval (also referred to as the instruction period). We chose a range of intervals that included prolonged time intervals so as to allow exploration of upper limits in the ability to sustain a preparatory state over development.

The antisaccade (AS) task (Hallett, 1978), which requires the suppression of a reflexive visually elicited eye movement and the generation of a voluntary response guided by an internal representation, is particularly well-suited for exploring the role of response preparation on developmental improvements of inhibitory control. Single-cell non-human primate studies and human neuroimaging studies of this task have carefully delineated the role of response preparation on the ability to inhibit a response (Amador, Schlag-Rey, & Schlag, 2004; Connolly et al., 2002; Curtis & Connolly, 2008; Curtis & D'Esposito, 2003; DeSouza et al., 2003; Everling, Dorris, Klein, & Munoz, 1999; Everling & Fischer, 1998; Everling & Munoz, 2000; Ford et al., 2005; Funahashi, Chafee, & Goldman-Rakic, 1993; Schlag-Rey, Amador, Sanchez, & Schlag, 1997). Given that the AS task is not easily amenable to strategy use and responses do not require transferring information across modalities (stimulus input and response output both occur in the visual domain), it is particularly well-suited to studies of developmental change.

Developmental improvements in AS performance have been well-characterized in healthy children and adolescents and consistently indicate a protracted pattern of maturation into adolescence (Fischer, Biscaldi, & Gezeck, 1997; Fukushima, Hatta, & Fukushima, 2000; Klein, 2001; Klein & Feige, 2005; Klein & Foerster, 2001; Klein, Foerster, Hartnegg, & Fischer, 2005; Luna, Garver, Urban, Lazar, & Sweeney, 2004; Munoz, Broughton, Goldring, & Armstrong, 1998; Nieuwenhuis, Ridderinkhof, van der Molen, & Kok, 1999; Romine & Reynolds, 2005). Specifically, from childhood to mid-adolescence, there is a significant decrease in rates of inhibitory errors, indicating improvements in the ability to consistently exert inhibitory control. Latencies to initiate correct antisaccades also show a significant decline over childhood and into adolescence, with adult levels being reached at approximately fifteen years of age. For both inhibitory parameters, developmental trajectories are characterized by a curve fit (Klein & Foerster, 2001; Luna et al., 2004), indicating that improvements in inhibitory abilities occur more rapidly in childhood and rates of change slow in the adolescent years.

Behavioral studies have manipulated the length of the preparatory period to examine the role of preparation in performance of adults. These studies indicate advantages of prolonged preparatory periods in supporting inhibitory control (Cepeda, Kramer, & Gonzalez de Sather, 2001; Kramer, Hahn, & Gopher, 1999; Meiran, 1996, 2000; Rogers & Monsell, 1995) and AS performance in particular (Barton, Greenzang, Hefter, Edelman, & Manoach, 2006; Connolly et al., 2002). In the AS task, the preparatory period is well-defined by the period of instruction when subjects see a cue instructing them to prepare to inhibit a response but are awaiting the unpredictable location where the visual target they must suppress will appear. During this period, participants must prepare by fixating on the instruction cue, maintaining the task

instruction to inhibit a response, and pre-setting the oculomotor system to decrease the probability of making a reflexive saccade upon seeing the target in order to successfully execute an AS. Adult studies have established that longer preparatory times lead to fewer errors and shorter latencies to initiate a correct AS response (Barton et al., 2006; Connolly et al., 2002), and that preparation in adults can be sustained for long instruction periods spanning more than 7000 ms (Curtis & Connolly, 2008).

Successful inhibition on the AS task requires recruitment of a widely distributed brain circuitry that includes the frontal eye fields (FEF), supplementary eye fields (SEF), dorsolateral prefrontal cortex (DLPFC), posterior parietal cortex, anterior cingulate cortex, basal ganglia, dorsomedial thalamus, and superior colliculus (Burman & Bruce, 1997; Doricchi et al., 1997; Everling et al., 1999; Funahashi et al., 1993; Gottlieb & Goldberg, 1999; Luna et al., 2001; O'Driscoll et al., 1995; Schlag-Rey et al., 1997; Sweeney et al., 1996). Single-cell studies have shown that successful generation of antisaccades requires enhanced activity in cortical and subcortical regions that support oculomotor control including the DLPFC (Funahashi et al., 1993), lateral intraparietal area (Gottlieb & Goldberg, 1999), SEF (Amador et al., 2004; Schlag-Rey et al., 1997), FEF (Everling & Munoz, 2000), and superior colliculus (Everling et al., 1999; Everling & Fischer, 1998) during the instruction phase, prior to target appearance. Findings from neuroimaging studies suggest similar processes occur in humans, with studies indicating that frontal and parietal areas show greater activity during the instruction period but not the response generation period for correct trials (Brown, Vilis, & Everling, 2007; Connolly et al., 2002; Curtis & D'Esposito, 2003; DeSouza et al., 2003; Ford et al., 2005). These preparatory modulations of the oculomotor control circuitry are also correlated with performance (Curtis & D'Esposito, 2003; Ford et al., 2005). Importantly, regions identified to support response preparation and AS performance in general are recruited by children, teens, and adults, but are activated at different magnitudes across development (Luna et al., 2001; Velanova, Wheeler, & Luna, 2008). Limitations in AS performance in children and adolescents may be underlied by immaturities in the ability to rapidly process information in task-relevant regional circuitry that would undermine the ability to engage areas crucial to AS performance during the preparatory period. This suggests that, in light of their immaturities, children and adolescents may benefit from additional time to prepare an inhibitory response. This study sought to examine the role of preparation on AS performance over the course of development using a behavioral approach.

While this has not yet been investigated using the AS task, three studies have examined the role of preparation on inhibitory control over development. These studies found improved performance with increased preparation times in children using the stop-signal task (Carver, Livesey, & Charles, 2001a, 2001b) and the continuous performance task-AX (CPT-AX) (Okazaki et al., 2004), suggesting that increased preparation time does benefit performance in younger age groups. However, results regarding interactions of age group and preparation time were mixed. Two studies using short preparatory intervals (none longer than 900 ms) reported a synergistic interactions in samples of five to nine year old children (Carver et al., 2001a, 2001b), suggesting that increases in preparation time actually *enhance* age-related differences in inhibitory control performance rather than allow younger participants to compensate for slow preparatory processes. Another study by (Okazaki et al., 2004) that included older children (ages nine to thirteen) and used longer time intervals (800 to 3000 ms) did not find an interaction of preparation time and age, suggesting that increased preparation does *not* affect age-related differences. Given the non-overlapping age ranges and preparatory periods across studies using two different tasks, it is not clear if these results are discrepant due to methodological variations or if they actually represent different effects of preparation at different periods in development.

We extend this research by considering age as a continuous variable as well as in defined age groups and by including a wider age range. This approach allowed us to characterize the shape

of development and more precisely identify when adult levels of performance are reached. In addition, we also apply group comparisons when probing the nature of simple effects in order to compare our results with the existing literature and to maximize statistical power. The age range used is wider than in previously reported studies, making this the first study of the effects of preparation over development to include adolescents in addition to children and adults. Adolescents are relevant to this study because during this period inhibitory abilities continue to improve (Fischer et al., 1997; Fukushima et al., 2000; Klein, 2001; Klein & Foerster, 2001; Luna et al., 2004; Luna & Sweeney, 2004; Munoz et al., 1998; Nieuwenhuis et al., 1999; Romine & Reynolds, 2005) and psychopathologies characterized by impairments in inhibitory control typically emerge (Ettinger et al., 2004; Everling & Fischer, 1998; Hutton & Ettinger, 2006). Importantly, we were able to examine patterns of developmental improvement and their interactions with response preparation using a continuous age variable, which allowed us to use a regression framework to examine and model the nature of developmental change. As noted by Klein and colleagues (Klein & Feige, 2005; Klein, Foerster, & Hartnegg, 2007), this is an important departure from previous developmental studies that have relied on group-based comparisons that require imposing artificial boundaries between age groups that may alter the nature of results or undermine our ability to understand when developmental changes occur. Still, to facilitate interpretation of our data in the context of the existing literature, we supplemented our analyses by also examining the effects of preparation time on performance at discrete stages of development (childhood, adolescence, and adulthood).

The AS task was chosen over other inhibitory control tasks because the role of response preparation has been well-delineated at multiple levels of analysis and has not yet been studied over development. To accommodate our study question, task parameters were chosen to enhance the role of advance preparation for performance and minimize developmental confounds by presenting the cue throughout the instruction period, which minimizes working memory demands (Curtis & Connolly, 2008). Importantly, instruction periods were chosen to span a wide interval, from as short as 500 ms to as long as 6000 ms, all of which provide sufficient time to prepare a response. Both 4000 and 6000 ms preparatory intervals are longer than have been used in previous developmental studies and provide a manner to probe upper limits. Providing ample time allowed us to explore the ability to sustain preparation over extended periods, and therefore characterize optimal preparation times for different age groups.

In accordance with previous AS research, we expected that the percentage of errors and response latencies would decrease with age in a nonlinear fashion (Luna et al., 2004) and that adults would demonstrate parametric improvements in performance with increased preparation time across the full range of preparatory intervals (500 ms to 6000 ms) (Barton et al., 2006; Connolly et al., 2002; Curtis & D'Esposito, 2003). Given the finding of significant effects of preparation in adults performing the AS task and children performing other inhibitory control measures, we predicted that all age groups would evidence parametric improvements in AS performance with increases in preparation time, though children would be less able to sustain a preparatory state at the longest time intervals. In light of the existing literature, we anticipated one of three potential results in regard to the interaction of age and preparation. The first would be a significant buffering interaction, in which the effect of preparation on AS performance (errors and latency) would be stronger for younger participants than for older participants. This finding would indicate that increased time to prepare a response differentially aids the performance of children over teens and adults. A second potential finding, which is suggested by the literature using younger children and shorter preparation times (Carver et al., 2001a, 2001b), would be a significant synergistic interaction of age and preparation, in which the effect of preparation on AS performance would be stronger at older ages. Such a finding would imply that preparation enhances existing developmental differences. The third possibility, suggested by the Okazaki et al. (2004) study using older children and longer preparation times, would be a non-significant interaction with preparation benefitting all three age groups equally;

this would suggest that developmental improvements in AS performance are not driven by more efficient core preparatory processes.

2. Methods

2.1. Participants

Participants were 160 individuals (85 male) age 8 to 31 years (mean=14.3 years). Mean age did not differ by sex ($t(158) = .039, p = .969$). For the purposes of analyzing the effects of preparation within age groups, the sample was separated into three groups: children ages 8-12 (mean age = 10.4; $n = 67$; 31 male), adolescents ages 13-17 (mean age = 15.0; $n = 62$; 31 male), and adults ages 18-31 (mean age = 21.7; $n = 31$; 14 male), of whom the majority (80%) of the adults were between the ages of 18 and 25. The sample reflected the racial demographics of the Allegheny County, Pennsylvania area, with the racial distribution being: 77% White, non-Hispanic, 14% Black, non-Hispanic, 2% Asian/Pacific Islander, 2% Hispanic, and 5% more than one race. Forty-four of the 160 participants were siblings of other participants in the sample, and relatedness was accounted for within the statistical analyses. Participants were recruited through advertisements in the local newspapers and flyers. Based on interview it was determined that participants were medically healthy, free of medications known to affect eye movements, negative for history of psychiatric disorders, and had no first-degree relatives with psychiatric disorders. Experimental procedures complied with the Code of Ethics of the World Medical Association (1964 Declaration of Helsinki) and the standards of the University of Pittsburgh Internal Review Board. Participants and/or their legal guardians provided informed consent after the nature of the studies was explained. Individuals under the age of 18 also provided assent indicating that they understood the nature of the study and agreed to participate. Participants were compensated for their time.

To estimate IQ, all four subsets of the Wechsler Abbreviated Scale of Intelligence (Wechsler, 1999) were administered to participants. Mean full-scale IQ scores were in the Average range (mean = 108.2, $s.d. = 11.4$). Age was not correlated with full-scale IQ score in the full sample ($r = .060, p = .452$). Additionally, age did not correlate with IQ score within the child ($r = -.184, p = .136$), adolescent ($r = -.055, p = .671$), or adult ($r = .306, p = .100$) age groups.

2.2. Antisaccade (AS) Task

The AS task was run using a PC running E-Prime software (version 1.0, Psychology Software Tools, Pittsburgh, PA, USA). Participants were instructed to fixate on a central red cross subtending approximately 1.5 degrees visual angle which was present for either 500, 2000, 4000, or 6000 ms (instruction period). The red fixation indicated that they were to prepare not to look at the peripheral cue but instead to its mirror location. The peripheral stimulus was a yellow circle, subtending approximately 1.5 degrees visual angle that appeared unpredictably for 1000 ms at one of four locations: 4 and 8 degrees of visual angle to the left or right of center fixation. Following this, the screen remained black for 200 ms before the instruction cue of the subsequent trial appeared. There were a total of 16 different types of AS trials, representing all combinations of the four instruction period lengths and four stimulus locations. Each of the trial types were presented three times each for a total of 48 AS trials and twelve trials per preparatory interval. All 48 trials were administered in a random order in a blocked format.

Eye movement measurements were obtained using an Applied Science Laboratories (ASL, Bedford, MA) Model 504 table-mounted near-infrared eye tracker with a sampling rate of 60 Hz. Participants were seated and positioned 54 cm from a 15" computer screen with a table-mounted chinrest and Velcro head restraint to minimize head motion and position the eyes at a fixed distance from the screen. They were tested in a darkened room and provided instructions by an experimenter in the same room. Monitoring in real time permitted immediate

identification of head movement or gross inattention to the task. If a subject did not appear to be attentive to the task, he/she was redirected by the experimenter and reminded of the instructions.

The AS task was administered as part of a larger study of neurocognitive development that included neuropsychological assessments and IQ testing. The oculomotor portion of the testing session started with nine-point eye tracker calibration for each potential target location. The AS task was administered after participants had completed blocks of an oculomotor delayed response task and a visually guided response task, which are part of other studies. Prior to administering each task-block, an experimenter explained the upcoming task to the participant, and this was immediately followed by practice trials to ensure that the participant understood the task directions. Participants' performance was monitored, and testing did not begin until they were able to perform three correct trials in a row. No participants required more than 10 trials before testing commenced. Participants completed additional oculomotor tasks and computerized cognitive tasks following AS task administration.

2.3. Data Processing

Eye movement recordings were analyzed offline using a combination of ILAB (Gitelman et al., 1999) and in-house programs written in MATLAB (MathWorks, Inc.). Results of algorithm-based measurements were presented graphically and numerically to the operator for inspection of measurements for each saccade of each trial. Saccades were identified using a velocity algorithm employing a 30 deg/sec criterion. Off-line, a technician reviewed the results generated by the computer algorithms to identify blink artifacts and occasional failures of the software to identify primary saccades, and to make modifications, if necessary, using the editing features available in ILAB.

Each eye movement trial was scored for accuracy and latency. Correct AS trials were defined as those in which the participant did not look at the peripheral target and instead generated a saccade towards the opposite visual field. Eye movements toward the peripheral target were defined as error trials. Most errors were followed by a saccade to the correct location indicating that participants understood the instruction but were unable to inhibit the automatic response towards the cue. Trials which begun with express saccades, characterized by an initial saccadic latency of less than 100 ms and generated towards the peripheral cue (Fischer & Ramsperger, 1984; Fischer & Weber, 1993), were dropped from analyses. For these analyses, we compiled two metrics of AS performance: the percentage of trials in which the participant looked toward the peripheral target (error rates or response suppression errors) and the latency to initiate the AS on correct trials, which were compiled for further analysis.

Response latencies were calculated based on correct trials. This resulted in fewer trials for younger subjects, but this was unlikely to undermine power to find differences since we report significant age-related differences in percentage of error trials. Furthermore, previous findings in our laboratory using an equivalent AS task has indicated that despite fewer trials in the younger groups, the fMRI timecourse of younger groups was equivalent to that of adults (Velanova et al., 2008)

2.4. Data Analysis

Performance at all four cue locations was averaged to provide a single value for each of the four preparation times. Data were inspected for outliers using visual inspection and statistical indices of discrepancy and global influence. Based on this, none of the participants were excluded from the analyses.

We characterized the effect of preparation time, age, and their interactions on the percentage of error trials and mean latency to initiate a response on correct trials using a regression framework. Regressions allowed us to utilize a continuous measure of age while still using a categorical measure of preparation. Analyses utilized the inverse function with age, consistent with prior studies indicating that a this function provides the best model of AS performance over development (Luna et al., 2004). were used for the analyses because they explained the largest percentage of variance for all preparation times. Importantly, this is consistent with past studies indicating that a regression utilizing the inverse function with age is the best model of AS performance over development (Luna et al., 2004).

Regression models were run using hierarchical linear modeling (HLM) (Bryk & Raudenbush, 1987, 2002), which uses multi-level fixed effects and random effects analyses to account for nesting of data within individuals or groups. This approach allowed us to extend multiple regression for use with repeated-measured data. As HLM can account for nesting of individuals within families, this enabled us to include 44 participants who were siblings of other 116 individuals in the sample. Intraclass correlations indicated that performance clustered by family, so the 44 siblings would have to be removed from the sample in a regression analysis that could not account for familial nesting. Instead, inclusion of these individuals allowed us to enhance statistical power.

The current analysis controls for (partials out) the differences in mean performance per family when the impact of age on AS performance is estimated for each preparation time function. Our design included three levels: the level 1 model was nested within individuals at level 2, and the level 2 model was nested within families at level 3. The level 1 unit of analysis was preparation time, the within-subjects variable, and the level 2 unit of analysis was inverse age (centered), the between-subjects variable. Preparation time was coded using three dummy variables to account for the four different preparatory periods. The shortest (500 ms) preparation time was used as the reference group, though models were run using each of the other preparation times as reference groups in order to obtain contrast scores. The coefficient of the intercept term in the level 1 equation was estimated as a random effect at level 2, while coefficients of the three dummy coded preparation time variables were fixed at level 2. Coefficients of the age variables ($1/\text{age}$) in the level 2 equations were fixed effects at level 3. The coefficients of the intercept terms at level 2 were estimated as random effects at level 3. This was necessary for model specification and to reliably estimate coefficients.

HLM analyses were run in the eponymous program, HLM version 6 (Scientific Software International, Inc.). To test for main effects of age and preparation time, chi-square difference tests were used to compare a model with dummy codes of preparation time and inverse of age to models without the inverse of age or without preparation time variables. To test for an omnibus interaction of age across all preparation times, a chi-square difference test was used to compare a model with preparation time, inverse of age, and their interaction to a model without the interaction terms.

To examine simple effects of preparation using HLM, the sample was separated into three age groups: children ages 8-12, adolescents ages 13-17, and adults ages 18-31 (see description of participants in Methods section for further details). Aforementioned HLM regressions were run separately for each group. Bonferroni corrections were used to correct for multiple comparisons for contrasts.

3. Results

The proportion of variance in AS error rates and response latencies for correct trials for the following analyses are shown in Table 1. The proportion of variance explained by each variable

is reflected by the Pseudo- R^2 statistic typically used in the HLM framework (Snijders & Bosker, 1999).

3.1. Main Effect of Age

AS error rates decreased significantly as a function of the inverse of age ($X^2(3) = 58.576, p < .001$) when controlling for the effect of preparation time on performance. Response latencies on correct AS trials also decreased significantly as a function of the inverse of age when controlling for the effect of preparation time on performance, ($X^2(3) = 26.886, p < .001$).

3.2. Simple Effects of Age at Each Preparatory Period

To test whether there were developmental improvements in performance at each preparatory period length, the significance of the coefficient reflecting simple effects of the inverse of age at each preparatory interval was tested.

Regressions of the percentage of error trials on the inverse of age were significant at 500 ms ($t(158) = 8.584, p < .001$), 2000 ms ($t(158) = 6.415, p < .001$), 4000 ms ($t(158) = 6.812, p < .001$), and 6000 ms ($t(158) = 6.977, p < .001$) trials (See Figure 1).

Regressions for response latencies were significant for 500 ms ($t(158) = 3.671, p < .001$), 2000 ms ($t(158) = 3.639, p < .001$), 4000 ms ($t(158) = 3.585, p < .001$), and 6000 ms ($t(158) = 35.037, p < .001$) trials (See Figure 2).

3.3. Main Effect of Preparation Time

The effect of preparation time on error rates was significant when accounting for the effect of age ($X^2(5) = 45.083, p < .001$) (see Figure 3a). Age explained 4.8% of the variance in preparation time. After Bonferroni correction, error rates were higher on trials with 500 ms preparation time than 2000 ($t(635) = -3.722, p < .001$), 4000 ($t(635) = -4.598, p < .001$), and 6000 ($t(635) = -5.024, p < .001$) ms trials.

Similarly, there were significant effects of preparation time on response latencies after accounting for the effect of age ($X^2(5) = 91.483, p < .001$) (see Figure 3b). After Bonferroni correction, response latencies were higher on trials with 500 ms preparation time than 2000 ($t(614) = -7.977, p < 0.000$), 4000 ($t(614) = -8.012, p < .000$), and 6000 ($t(614) = -7.856, p < .000$) ms trials.

3.4. Interaction of Age and Preparation Time

The omnibus interaction was not significant ($X^2(3) = 0.484, p > .500$). None of the slopes for the four preparatory period regression lines were significantly different from any of the other slopes ($df = 632$, all $ps \geq .510$) prior to Bonferroni corrections, indicating no interaction contrasts.

For response latencies, a comparable chi-square difference test indicated that the interactions as a set were not significant ($X^2(3) = 0.525, p > .500$). Contrasts revealed no significant interactions between any of the four different preparation times and age ($df = 611$; all $ps \geq .550$).

Possible interactions at the youngest ages in the sample were explored due to the visual appearance of potential interactions (See Figures 3a and 3b). Regression lines were estimated based only on data from children ages 8-12 for both variables. Analyses for error rates revealed no interaction between preparation time and age within this range ($X^2(3) = 0.227, p > .500$). Similarly, there was no interaction between age within this range and the preparation time condition for response latencies ($X^2(3) = 1.675, p > .500$).

3.5. Simple Effects of Preparation Time Within Age Groups

To test whether the effects of preparation time on performance differed across children, adolescents, and adults, the sample was subdivided into three age groups (as described earlier) and main effects of response preparation were tested. Means for each age group at each preparation time are plotted in Figure 4a for error rates and Figure 4b for latencies on correct trials.

Within the child age group, the main effect of preparation time on error rates was significant ($X^2(3) = 12.227, p < .01$), though there were no significant contrasts between the four preparatory periods; this was because Bonferroni correction was applied to contrasts but not to main effects significance testing; as a result, contrasts trended after Bonferroni correction, but were no longer significant. Adolescents demonstrated a significant main effect of preparation time ($X^2(3) = 18.997, p < .001$) on error rate, with contrasts indicating significantly higher error rates for 500 ms trials than 2000 ($t(243) = -3.037, p < .01$), 4000 ($t(243) = -2.970, p < .01$), and 6000 ($t(243) = -3.973, p < .001$) ms trials. Main effects of preparation were also significant for adults ($X^2(3) = 19.607, p < .001$), who demonstrated higher error rates for 500 ms trials than 4000 ($t(119) = -3.426, p < .001$), and 6000 ($t(119) = -3.101, p < .01$) ms trials. Unlike children and adolescents, error rates did not differ between 500 and 2000 ms trials ($t(119) = -1.953, p = .053$).

For response latencies on correct trials, the main effect of preparation time on latencies for correct trials was significant ($X^2(3) = 26.682, p < .001$) within the child group. Children's response latencies were longer for 500 ms trials than 2000 ($t(245) = -3.841, p < 0.001$), 4000 ($t(245) = -4.324, p < .001$), and 6000 ($t(245) = -4.337, p < .001$) ms trials. Adolescents also evidenced a significant main effect of preparation time ($X^2(3) = 36.984, p < .001$), with significantly longer latencies for 500 ms trials than 2000 ($t(240) = -4.796, p < .001$), 4000 ($t(240) = -5.033, p < .001$), and 6000 ($t(240) = -4.968, p < .001$) ms trials. The main effect of preparation time was also significant for adults ($X^2(3) = 60.631, p < .001$), who had longer latencies for 500 ms trials than 2000 ($t(119) = -4.880, p < .001$), 4000 ($t(119) = -6.375, p < .001$), and 6000 ($t(119) = -7.414, p < .001$) ms trials.

4. Discussion

The aim of this study was to examine whether response preparation contributes to developmental changes in inhibitory control abilities. We examined this by parametrically varying the lengths of the instruction period on a task that is relevant to this question because prior research has demonstrated that preparatory processes are crucial for successful performance. While a few studies using other measures of inhibitory control have compared the effects of preparation in children and adults (Carver et al., 2001a, 2001b; Okazaki et al., 2004), this study included participants who covered a range of ages from 8 to 31 years. Two main findings emerged. First, across all ages, AS performance improved with increasing preparation time and performance did not worsen at the longest preparatory periods. This indicates that response preparation can be sustained over extended periods and can benefit performance across development. Second, gradual age-related improvements in performance were evident, but preparation time did not moderate developmental trajectories. The lack of a preparation time by age interaction paired with the existence of age-related differences at even the longest preparatory intervals suggest that developmental improvements in rates of inhibitory successes and latencies to inhibit a response are not supported by limitations in the time needed to prepare a response. Rather, persistent age-related differences in inhibitory control may instead reflect qualitative differences in control aspects of preparatory processing.

4.1. Effects of Preparation Time on Inhibitory Control

Significant main effects of preparation time indicating that AS performance improves with increases in preparatory period length are consistent with existing behavioral studies using the AS task in adults (Barton et al., 2006; Connolly et al., 2002; Curtis & D'Esposito, 2003) and with behavioral studies using other inhibitory and motor tasks in children (Carver et al., 2001a, 2001b; Okazaki et al., 2004) (Olivier, 2002). For both error rates and response latencies, main effects of preparation were driven by better performance in trials with longer intervals to prepare (2000, 4000, and 6000 ms) over trials with only 500 ms to prepare. However, after 2000 ms there were no significant improvements in performance across all subjects, suggesting a time window when preparation can affect performance.

To probe developmental differences in the effects of preparation time on performance, simple effects of preparation time were examined within child, adolescent, and adult age groups. The relationship between preparation time and error rates varied across age groups, but the relationship between preparation and response latencies was the same for children, adolescents, and adults. Specifically, error rates for children did not change over varied preparatory period lengths, but adolescents and adults had lower error rates with increasing preparation time. Adolescents showed an improvement from 500 to 2000 ms trials but no improvements thereafter whereas adults demonstrated improvement from 500 to 4000 ms trials but no further improvements at 6000 ms. That adults' error rates did not differ between 500 and 2000 ms trials indicates more gradual decreases in error rates with parametric increases in preparation time. This may reflect adults' relatively high levels performance at all preparation times (mean error rates of 26.9% at the shortest preparatory interval as compared to error rates of 41.5% for teens and 60.1% for children), which does not allow for steep gains in performance among the adult group as it would for adolescents. Childrens' performance did not differ across any of the preparation times and was generally poor, suggesting limitations in the ability to enhance performance with additional preparation and planning and in overall abilities to inhibit responses.

All age groups demonstrated longer latencies in 500 ms trials as compared to 2000, 4000, and 6000 ms trials, where speeds of response were equivalent. These results showing no decreases in response latencies after 2000 ms are consistent with prior studies of adults using the AS task. A study of adults by Connolly et al. (2002) reported significant shortening of AS latencies from 0 to 2000 ms to prepare, but not from 2000 to 4000 ms. Another AS study of adults by Connolly and Curtis (2008) reported no improvements in response latencies with lengthened periods of preparation using long intervals ranging from 7500 ms to 13.5 seconds. Our data extend the prior adult research to show that the relationship between preparation time and speed of initiating a voluntary response is consistent across development. These results suggest that basic aspects of response preparation are present early in development.

The difference in the pattern of results across developmental age groups for error rates and latencies highlights that the effects of response preparation over the range of preparatory period lengths used in this study is less modulated by age for response latencies than for error rates. This may reflect the different nature of the underlying processes assessed by error rates and latencies on correct trials. Though error rates and response latencies are both broad measures of inhibitory control, error rates specifically measure the ability to voluntarily suppress a response while latencies reflect the speed of generating a voluntary, goal-directed response, reflecting the speed of information-processing (Fry & Hale, 2000). Importantly, latencies only assess performance on correct trials, thus reflecting a disproportionate number of trials for older participants but only a minority of trials for the youngest participants. Thus latencies do not reflect consistencies in performance as much as they represent optimal capabilities. In this light, it is not surprising that we see that children, adolescents, and adults show the same relationship between preparatory interval length and response latencies despite overall age-

related decreases in latencies, which have been well characterized in the literature for AS (Fischer et al., 1997; Fukushima et al., 2000; Klein, 2001; Klein & Foerster, 2001; Luna et al., 2004; Munoz et al., 1998; Nieuwenhuis et al., 1999; Romine & Reynolds, 2005) as well as other cognitive tasks (Kail, 1988; Kail & Ferrer, 2007).

A consistent finding across all ages modeled was a dramatic improvement in the response latencies from 500 ms trials to 2000 ms trials. Latencies shortened negligibly with increases in preparation beyond 2000 ms. The consistency of the results for response latencies across development is notable and suggests that a comparable mechanism reduces response latencies from 500 to 2000 ms in children, teens, and adults. One possibility is that, across development, an amount of time between 500 to 2000 ms prior to cue appearance is needed to modulate saccadic neuron activity. This follows from a “race” to threshold model (Massen, 2004; Munoz & Everling, 2004) that posits that upon target appearance, there is an elevation in neuronal activity in the saccade-generating neurons of the frontal eye fields (FEF) and superior colliculus (SC) that occurs when the cue appears. This sums with existing levels of neuronal activity, and determines the nature and speed of the response. If activity levels are too high in saccade-generating neurons, there will be a prosaccade error, but if activity levels are too low, then the latency for AS generation will be slower. Modulation of saccadic neuron activity prior to AS generation may be an iterative process in which (1) saccadic neuron activity must first be reach a threshold to ensure that there are no errors and then (2) activity levels in saccadic neurons are fine-tuned to be just under threshold so as to facilitate a fast saccadic response upon cue appearance. Provided the first step occurs (a motor response can be generated in less than 500 ms), our results suggest that the second step takes between 500 and 2000 ms for all age groups. Results could also reflect that an instruction period length between 500 and 2000 ms is needed to overcome task-set inertia from the previous trial in order to produce a speedy response. These results suggest that these mechanisms are online by childhood and do not directly affect age-related differences in inhibitory control.

The use of preparatory intervals spanning from relatively short (500 ms) to very long (6000 ms) allowed for exploration of whether there are optimal preparatory period lengths that would be indicated by an inverted U-shaped relationship between preparation and performance. A consistent finding across both measures and all age groups was that performance maintained level or continued to improve with longer preparation, indicating that children, adolescents, and adults can sustain an active preparatory state for the longest interval used in this study. While these results are consistent with the adult AS literature (Connolly et al., 2002; Curtis & Connolly, 2008), this is a departure from previous developmental studies of inhibitory control that did not use the AS task indicating that children may not be able to sustain preparatory states for extended periods of time. A study by Okazaki et al. (2004) reported an inverted U-shaped relationship between preparation time and inhibitory control performance in 13 year olds and a worsening of performance with increases in preparation time in 9 and 11 year olds. The Okazaki et al. (2004) study used a set of shorter preparation times (the longest was 3000 ms). Importantly, the preparation for the CPT-AX task used in Okazaki et al.’s (2004) study is stimulus driven (a specific number triggers preparation to a specific subsequent digit), which has been termed exogenous preparation (Cepeda et al., 2001; Rogers & Monsell, 1995). By contrast, preparation in the AS task is considered to be endogenous, as the nature of the response to be prepared (a saccade) is known in advance, and it is simply the direction of the response which must be cued by the target (Curtis & Connolly, 2008; Rogers & Monsell, 1995). A developmental study examining both endogenous and exogenous preparation found (Olivier & Rival, 2002) improvements with age similar to our results in the endogenous condition and an inverted - U shaped relationship with age for exogenous preparation, which is comparable to the results reported by Okazaki et al. (2004). Taken together, these results suggest that endogenously driven preparation shows a different relationship to preparation than exogenously driven preparation and continues to improve into adulthood, when it stabilizes.

Our results indicate that for a task requiring endogenous preparation, there is not one optimal preparatory period length within the range of intervals studied here. Related to that, there was no decline in performance at the longest preparatory intervals, suggesting that even children were able to sustain preparation in spite of the factors that come into play at longer intervals, such as elevated demands on working memory, which have been shown to affect AS performance in childhood, adolescence, and adulthood (Eenshuistra, Ridderinkhof, & van der Molen, 2004; Eenshuistra, Ridderinkhof, Weidema, & van der Molen, 2007). We suggest that our use of a limited number of preparatory intervals produced a state of persistent preparation that enabled performance to stay at high levels at all age groups. That is, it is possible that participants may have been able to sustain attention for as long as 6000 ms in our task because the use of varied preparatory period lengths in relatively evenly-spaced intervals of 500, 2000, and 4000 ms may have enabled participants to engage in a state of *persistent* preparation. Participants may have quickly learned that preparatory periods would be only one of four possible lengths – so for all trials regardless of the preparatory period length, participants may have first prepared for a 500 ms wait period. Then if the cue did not appear, the participant prepared in case the cue appeared at the 2000 ms intervals, and so on. Thus, the 6000 ms may not have been a period of passive waiting, but was rather a period of persistent readiness.

4.2. Preparation Time and Developmental Improvements in Inhibitory Control

Overall, results confirm previous findings, including our past studies, indicating age- related improvements in the rate of correct inhibitory responses and in the speed to prepare a correct response, which appear to stabilize by mid adolescence (Fischer et al., 1997; Fukushima et al., 2000; Klein, 2001; Klein & Foerster, 2001; Luna et al., 2004; Munoz et al., 1998; Nieuwenhuis et al., 1999; Romine & Reynolds, 2005). We add to this literature with results showing a lack of interaction between age and preparation time for either error rates or latencies and a similar shape of developmental trajectory (inverse function) modeled at all four preparation times for both accuracy and latency measures. Increased preparation time does not seem to alter the basic nature of developmental trajectories of inhibitory control. Rather, lengthened preparatory periods simply elevate performance levels uniformly across development. These results suggest that limitations in preparing to inhibit a response are not related to time limitations in engaging appropriate mechanisms but instead may be due to qualitative differences in the control processes invoked to prepare a response.

Furthermore, it is important to note that even at the longest preparatory times, younger groups were not able to reach adult levels of performance. Thus, while preparatory systems are available early in development (as evidenced by children and adolescents' demonstration of the capacity to voluntarily inhibit their responses), cognitive processes that may enhance the effectiveness of preparatory processes may not yet be mature. This may reflect developmental changes in the circuits that support AS performance. Electrophysiological developmental studies have characterized preparatory attention for inhibitory tasks by examining the contingent negative variation (CNV) signal. These studies indicate that children utilize parietal regions to engage in motor preparatory processes, while adolescents and adults rely on more anterior-frontal regions (Bender, Weisbrod, Bornfleth, Resch, & Oelkers-Ax, 2005; Jonkman, Lansbergen, & Stauder, 2003; Klein & Feige, 2005). Data from a developmental functional imaging study of AS performance by Luna et al. (2001) converge with these findings, with neural correlates of overall AS performance (including both correct and incorrect responses) showing that while children rely primarily on parietal regions, adolescents showed an increased activity of prefrontal regions. By adulthood, activity was more evenly distributed across a wide network, showing the incorporation of prefrontal, premotor, and parietal regions to support optimal AS performance. Importantly, children and adolescents engaged canonical eye-movement regions known to support preparation for an inhibitory response, such as the frontal eye field, but they showed less recruitment of these regions than adults (Luna et al., 2001).

When another study examined only neural activity associated with correct trials, activation of oculomotor control regions used to prepare a response was equivalent across children, adolescents, and adults, providing further support that the primary circuitry supporting preparation to inhibit a saccade is available by childhood (Velanova et al., 2008). Taken together, behavioral, electrophysiology, and neuroimaging evidence indicate that preparatory processes for inhibitory control are available in childhood but are not yet reliable as in adults.

Neuroimaging studies indicate important immaturities at this time. From childhood to adulthood, there is evidence for a shift with age to reliance on a widely-distributed circuitry that integrates executive frontal regions that may underlie continued developmental improvements in inhibitory control (Luna, Velanova, & Geier, 2008). Recent imaging studies examining the neural correlates of correct and erroneous AS performance have highlighted that developmental changes in circuitries may support behavioral improvements by facilitating the ability to use errors to inform future performance and to use a distributed network to sustain a task-set that enables correct performance (Velanova et al., 2008; Velanova, Wheeler, & Luna, 2009). An analysis of activity associated with error AS trials found that adults but not children or adolescents show increased recruitment of areas of the anterior cingulate implicated in error monitoring, suggesting that performance monitoring systems continue to mature into adulthood (Velanova et al., 2008). The ability to integrate error information may inform preparatory systems, enhancing their effectiveness. Additionally, a developmental neuroimaging study that examined transient versus sustained activation associated with AS performance indicated that adults compared to children and adolescents recruit a circuitry including posterior parietal and prefrontal regions that enhance the ability to *sustain* correct performance (Velanova et al., 2009). This indicates that primary to the development of inhibitory control is the ability to engage a circuitry that supports the maintenance of a state of inhibitory control. How these changes relate to preparatory activities remains unclear. It is possible that as the cortical areas (prefrontal, premotor, and parietal regions) used to regulate activity in saccade-generating oculomotor regions become better integrated with age, there is enhanced regulation of levels of activity in oculomotor regions during the preparatory period in accordance with the aforementioned “race to threshold” models of saccadic preparation (Massen, 2004; Munoz & Everling, 2004).

In the context of this literature, these results suggest that improvements in the ability to voluntarily inhibit a saccade may not be due to directly to enhancements in basic aspects of response preparation, which appear to be online early in development, but to age-related changes in cognitive control mechanisms that enhance response preparation to improve inhibitory control.

4.3 Implications to General Aspects of Inhibitory Control

The AS task is believed to assess a specific aspect of inhibitory control, that of suppression of a reflexive motor responses in the context of uncertainty in the direction of the response. This is distinct from interference control measured in the Stroop task, incompatibility measures in the continuous performance task and go-no-go tasks, or inhibition of a planned, ongoing action in the stop-signal task (Kok, 1999; Michel & Anderson, 2009). Past developmental studies looking at response preparation to inhibit a response have used the CPT-AX task (Okazaki et al., 2004) and the stop-signal task (Carver et al., 2001a, 2001b). Results from studies using the stop-signal task (Carver et al., 2001a, 2001b) differed from our results in that they found that increases in preparation time actually enhanced developmental differences in performance. By contrast, the study using the CPT-AX (Okazaki et al., 2004) reported similar results to our own, as developmental improvements did not vary as a function of preparation time. While the AS task has more inhibitory demand similarities with the CPT-AX task than the stop-signal task, the CPT-AX task has different preparatory demands than the AS task, as noted earlier in the

discussion. In light of these differences, our results indicate that regarding the ability to stop a prepotent motor response in which inhibition is cued in advance although the directions of the response is unknown, basic preparatory processes are on line by childhood but control processes that enhance the ability to optimize preparation and inhibitory control, continue to mature into adulthood.

As indicated by single cell studies, response preparation is integral to inhibitory control in general. That is, in the AS task, activity in the superior colliculus and frontal eye fields must show activity in the preparatory period in order for there to be a successful inhibitory response (Everling et al., 1999; Everling & Munoz, 2000). Our particular manipulation of response preparation time, however, allowed us to assess processes that support aspects of response preparation that reflect basic aspects of the ability to initiate a voluntary response from processes that allow this preparation to result in a correct inhibitory response. We propose that our results indicate that basic aspects of response preparation are available by childhood, as is the ability to voluntarily inhibit a response. What continues to improve into adulthood is the ability to produce a high rate of correct responses. This particular ability may reflect higher order control processes that enhance the effectiveness of basic preparatory processes and which have a protracted development into adulthood.

4.4. Future Studies

We have noted dramatic improvements in response latencies from trials with 500 ms of preparation time to those with 2000 ms, and speculated upon mechanisms for such improvements based on the neurophysiological literature. This study was designed to examine the nature of sustained preparatory processes, and therefore we were not able to examine the nature of changes from 500 to 2000 ms of preparation. While our results (see Figure 3b) suggest a qualitative shift in performance from one preparatory condition to another, future studies are needed to explore whether there is actually a parametric improvement in latencies between 500 and 2000 ms in accordance with increases in preparation at intervals on the order of 100 or 200 ms. Given a neurophysiological model of preparation in saccade-generating neurons of the FEF and superior colliculus, studies using small increments of preparation time could provide important insight into the nature and duration of preparatory processing for this inhibitory task. Findings showing the consistent nature of improvements in response latencies with small increases in preparation time across development would indicate that the speed of producing an inhibitory response may reflect age-invariant processes and could reveal a specific preparatory interval between 500 and 2000 ms that represents the threshold time needed to generate a speedy AS response. Alternatively, findings could reveal more subtle differences in the trajectory of developmental change within this interval.

Follow-up investigations focusing on response latency variables would also benefit from administering a greater number of AS trials. The number of AS trials in this study was limited due to time and attentional constraints because participants completed other cognitive tasks during the study. This limited the number of trials means that the range of estimates for trials for some individuals the range of trials included

Inhibitory errors in the AS task encompass both self-corrected and uncorrected errors, which may not reflect a unitary concept. These different errors may reflect impairments in different processes reflecting different preparatory mechanisms- self-corrected errors may reflect insufficient preparation of activity levels in fixation neurons relative to saccadic neurons whereas uncorrected errors may reflect poor working memory abilities or error monitoring abilities, which show improvements over development in the oculomotor domain (Luna et al., 2008; Velanova et al., 2008). Additionally, recent evidence suggests that age-related change may differ for different types of inhibitory errors (Michel & Anderson, 2009), which highlights the need to understand more fully the nature of developmental change for these different errors

as well as to explore the effects of different response preparation parameters over development. This analysis did not have the power to examine this question because the majority of errors were self-corrected, but future research using AS paradigms designed to generate sufficient numbers of uncorrected error trials may shed light on important developmental changes which are differentially influenced by different response preparation parameters.

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Figure 1. Scatterplots of percentage of errors by age separated by preparation time, with superimposed developmental function specific to each preparation time. Linear regression functions are equivalent to those shown in Figure 3b.

Trials with 2000 ms Preparation Time **Trials with 4000 ms Preparation Time**

Figure 2. Scatterplots of response latency on correct trials by age separated by preparation time, with superimposed developmental function specific to each preparation time. Linear regression functions are equivalent to those shown in Figure 3b.

Figure 3.

- Regression of percentage of errors by preparation time and age.
- Regression of latency on correct trials by preparation time and age.

Figure 4.

a. Mean percentage of errors by age group and preparation time. Asterisks indicate significant preparation time contrasts within each age group after Bonferroni correction. As there were no significant contrasts between 2000, 4000, and 6000 ms trials, asterisks are used to represent significant differences in performance from 500 ms trials.

b. Mean response latencies on correct trials by age group and preparation time. Asterisks indicate significant preparation time contrasts within each age group after Bonferroni correction. As there were no significant contrasts between 2000, 4000, and 6000 ms trials, asterisks are used to represent significant differences in performance from 500 ms trials.

Table 1

Proportion of variance explained by age, preparation time, and their interaction

Effect	R ²
<i>Proportion of Error Trials</i>	
Age	0.282
Preparation time	0.047
Age X preparation time	0.000
Preparation time - children	0.017
Preparation time- adolescents	0.026
Preparation time - adults	0.067
Age X preparation time - children	0.000
Full model	0.295
<i>Latency on Correct Trials</i>	
Age	0.081
Preparation time	0.055
Age X preparation time	0.000
Preparation time - children	0.064
Preparation time- adolescents	0.075
Preparation time - adults	0.100
Age X preparation time - children	0.003
Full model	0.148