Prepotent response inhibition and interference control in autism spectrum disorders: two meta-analyses
Geurts, H.M.; van den Bergh, S.F.W.M.; Ruzzano, L.

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Two meta-analyses

Hilde M. Geurts 1,2,3,4*, Sanne F. W. M. van den Bergh 2,3, & Laura Ruzzano 2,3

1 Department of Psychology, Brain & Cognition, University of Amsterdam, Amsterdam, the Netherlands
2 Research & Development, Dr Leo Kannerhuis, Center for Autism, Amsterdam, the Netherlands
3 Dutch Autism and ADHD Research Center (d’Arc), Amsterdam, the Netherlands
4 Cognitive Science Center Amsterdam, University of Amsterdam, the Netherlands

*Corresponding author: Hilde Geurts, University of Amsterdam, Department of Psychology, Dutch Autism & ADHD research center (d’ARC), Weesperplein 4, 1018 XA Amsterdam, The Netherlands. Telephone: +31 20 525 6843. Email: H.M.Geurts@uva.nl
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Lay Abstract

Inhibition - the ability to suppress an action which is irrelevant, no longer needed, and/or inappropriate - is an ability which contributes to many aspects of everyday functioning.

Individuals with an autism spectrum disorder (ASD) are thought to have a disability in inhibitory control. However, studies that have examined inhibition in ASD have provided inconsistent and even opposing conclusions. Therefore, this study aimed to clarify the nature of inhibitory control among individuals with ASD. To do so, we conducted two meta-analyses: one for cancelling an initiated response (i.e., prepotent response inhibition) and one for the ability to ignore irrelevant information (i.e., interference control). In addition, we explored whether age and IQ may influence performance on inhibitory control tasks. In contrast to the general belief, we found that both prepotent response inhibition and interference control problems are observable in individuals with ASD. We also found large differences between studies (e.g., heterogeneity), which could not be explained by age or IQ. Thus, while people with ASD do appear to experience some difficulties with inhibitory control, this study suggests that there are additional factors that still need to be discovered, in order to fully understand their performance on inhibitory tasks.
Abstract

There is a substantial amount of data providing evidence for, but also against the hypothesis that individuals with autism spectrum disorders (ASD) encounter inhibitory control deficits. ASD is often associated with interference control deficits, rather than prepotent response inhibition. Moreover, the developmental trajectory for these inhibitory control processes is hypothesized to differ in ASD as compared to typical development. In efforts to gain a more comprehensive perspective of inhibition in ASD, separate quantitative analysis for prepotent response inhibition studies and interference control studies were conducted. Together, these two meta-analyses included 41 studies with a combined sample size of 1091 people with ASD (M age 14.8 years), and 1306 typically developing (TD) controls (M age 13.8 years). The meta-analyses indicated that individuals with ASD show increased difficulties in prepotent response inhibition (effect size 0.55) and in interference control (effect size 0.31). In addition, age was a relevant moderator for prepotent response inhibition, but not for interference control. Exploratory analyses revealed that when IQ was taken into account, heterogeneity considerably decreased among interference control studies, but not among prepotent response inhibition. In contrast to the general belief, both prepotent response inhibition and interference control problems were observed in individuals with ASD. However, a large variation between studies was also found. Therefore, there remains factors beyond inhibition type, age, or IQ that significantly influence inhibitory control performance among individuals with ASD.

KEY WORDS: ASD, autism, inhibition, interference, cognitive control, meta-analysis
The fact that you are able to read this article while ignoring e-mail alerts, text messages, and a phone ringing nearby, is related to your ability to exert cognitive control. Cognitive control refers to the ability to maintain task relevant information in order to suppress inappropriate behaviors, and to flexibly adjust behavior according to environmental contingencies (Carter, 2005). A disability in suppressing inappropriate behavior is thought to be an important characteristic of individuals with an autism spectrum disorder (ASD), and these so called inhibition problems are often observed in their communication and social interactions. For example, to not answer a phone when it rings can be a difficult task for individuals with ASD, if they have learned that answering a ringing phone is a polite thing to do. Interpreting language in the most literal form is another behavioral characteristic of ASD, illustrating their inability to inhibit frequently used meanings of words. In addition, repetitive behaviors characteristic of ASD are often associated with a lack of inhibitory control, due to the difficulties seen among individuals with ASD to suppress behaviors despite negative consequences (Langen et al., 2011). Thus, there is a general notion that inhibitory abilities underlie many of the atypical behaviors seen in people with ASD.

Since the first series of studies by Ozonoff, Russell, and colleagues in the nineties (Hughes et al., 1994; Hughes & Russell, 1993; Ozonoff et al., 1994) various research groups have focused on inhibition in individuals with ASD. Consequently, there is a substantial amount of data providing evidence for and against the hypothesis that individuals with ASD encounter inhibition deficits. While these findings have made valuable contributions, the inconsistencies between results have complicated our understanding of inhibitory abilities in ASD. In efforts to better understand these abilities in ASD, we will review the recent literature by presenting a quantitative analysis. However, first we will discuss the concept of inhibition in more detail.
Inhibition

Inhibition is the ability to cancel or suppress an action which is irrelevant, no longer needed, and/or inappropriate. While inhibition is often discussed as a unitary construct, from a behavioral and cognitive neuroscience perspective, it is considered to be multifaceted (Aron, 2011; Friedman & Miyake, 2004; Nigg, 2000). Therefore, inhibition is commonly divided into prepotent response inhibition and resistance to distractor interference. Some add a third component of inhibition coined resistance to proactive interference (Friedman & Miyake, 2004; Miyake & Friedman, 2012). A broad range of measures have been used to measure these three inhibitory control constructs. We focus on prepotent response inhibition and resistance to distractor interference, as these types of inhibition are the most frequently studied in the ASD literature.

Prepotent response inhibition refers to the ability to suppress a dominant motor response (Casey et al., 2001; Nigg, 2000), which requires completely cancelling the initiated response (reactive stopping; Aron, 2011). This is typically measured with tasks that require participants to respond as fast as possible to a majority of stimuli, while withholding a response (inhibit) to a minority of stimuli, which are signaled by the presence of a specific stimuli (e.g., a specific letter or tone). Hence, participants must completely countermand an initiated response to perform well. There are two main dependent measures on prepotent response tasks: (1) an estimation of the time it took the participant to inhibit the response, (2) the percentage of incorrect inhibitory responses made on those trials which participants were told not to respond. Independent of the inhibition taxonomy used, Stop tasks and Go/No-Go tasks (Logan et al., 1984) are consistently classified as tasks which measure prepotent response inhibition. However, Stroop like tasks
(Stroop, 1935), where one must focus on a specific aspect of a stimulus and ignore another aspect of the same stimulus, have been classified by some as a prepotent inhibition task (Friedman & Miyake, 2004) and by others as an interference control task (Nigg, 2000). Resistance to distractor interference (i.e., interference control) refers to the efficiency with which one is able to ignore irrelevant information while processing target stimuli. The Flanker (Eriksen & Eriksen, 1974) and Simon paradigms (Simon & Wolf, 1963) are the most commonly used measures to assess resistance to distractor interference. Typically in these tasks, participants must respond to a stimulus as quickly as possible (e.g., correct response). Simultaneously, information is presented that evokes an opposite response (incongruent information) or a similar response to the correct response. Hence, this differs from prepotent response tasks, because inhibition is reflected by slower responses due to the conflicting information (i.e., irrelevant; Friedman & Miyake, 2004; Miyake & Friedman, 2012; Nigg, 2000). The main dependent measure is the difference in accuracy and/or speed between these conditions, although accuracy or speed on the incongruent condition may also be used.

**Inhibition and ASD**

As previously mentioned, various studies show that individuals with an ASD encounter problems in prepotent response inhibition (Bishop & Norbury, 2005; Christ et al., 2007; Corbett & Constantine, 2006; Corbett et al., 2009; Geurts et al., 2004; Geurts & Vissers, 2011; Johnson et al., 2007; Kilincaslan et al., 2010; Langen et al., 2011; Ozonoff & Strayer, 1997; Xiao et al., 2012) as well as in interference control (Ames & Jarrold, 2007; Christ et al., 2007; Christ et al., 2011; Corbett & Constantine, 2006; Corbett et al., 2009; Yoran-Hegesh et al., 2009). However, there are also studies that have found no difference between typically developing and ASD
individuals in either of these two inhibition domains (prepotent response inhibition: Chan et al., 2009; Happé et al., 2006; Lee et al., 2009; Ozonoff et al., 1994; Schmitz et al., 2006; Sinzig et al., 2008); interference control: Goldberg et al., 2005; Johnston et al., 2011; Kilincaslan et al., 2010; Larson et al., 2012; Schmitz et al., 2006; Solomon et al., 2008; Solomon et al., 2009; Xiao et al., 2012). Given that inhibition is a multifaceted construct, several researchers have tested multiple measures of inhibitory control on a single cohort of participants (Adams & Jarrold, 2012; Adams & Jarrold, 2009; Christ et al., 2011; Christ et al., 2007; Geurts et al., 2004; Kilincaslan et al., 2010; Sanderson & Allen, 2012; Xiao et al., 2012). Based on multiple measures, Christ and colleagues (Christ et al., 2011; Christ et al., 2007) concluded that children with autism do encounter interference control deficits (as measured with the Flanker paradigm), but have no problems with inhibiting prepotent responses (as measured with Stroop [like] tasks and the Go/No-Go task; for contrasting findings see (Geurts et al., 2004). Moreover, their cross-sectional data suggested that the observed interference control deficits might resolve with increasing age (from childhood to adolescence). This idea is in line with ASD being a developmental disorder, where interference control may be delayed in development, rather than continuously deviant throughout development. However, this conclusion is tentative, as some studies do show that adults with ASD perform worse than typically developing individuals on both classes of inhibition (Agam et al., 2010; Geurts & Vissers, 2011; Langen et al., 2011). In addition, those studies utilizing multiple inhibition measures produce rather inconsistent findings, independent of the inhibition taxonomy used. Therefore, in the current paper we present two meta-analyses of inhibitory control.
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Based on the study by Christ and colleagues (Christ et al., 2007; Christ et al., 2011) we predict that the meta-analysis for prepotent response inhibition studies will yield a small effect size, and that age will not moderate this effect. For the meta-analysis of interference control studies, we predict that the effect size will be medium and that age will moderate the effect size, which is in line with the delayed development of interference control hypothesis.
Methods

A systematic literature review was conducted in two electronic databases (PubMed/Medline and PsycINFO) using search terms related to autism (autism, autistic disorder, pervasive developmental disorder, asperger, PDD-NOS, ASD), combined with terms associated with inhibition (inhibition, inhibitory control, interference, cognitive control, emotion, Stop task, Go/NoGo task, Stroop task, Simon task, Flanker task). Only those studies adhering to the following eligibility criteria were included: (1) ASD participants were the population being studied and they met diagnostic criteria according to the DSM-III-R, DSM-IV, or ICD-10 (defined by clinical diagnoses, autism questionnaires, interviews or observation schedules: please see Table 1 for details); (2) a typically developing (TD) control group was included; (3) widely known experimental or neuropsychological inhibition tasks were used; (4) studies were published in a peer-reviewed journal before June 2013 and were written in English.

This review yielded 47 studies that met eligibility criteria (see Table 1 for details). Six studies reported insufficient information to calculate the effect size (Dichter & Belger, 2007; Eskes et al., 1990; Henderson et al., 2006; Kana et al., 2007; Raymaekers et al., 2006; Raymaekers et al., 2007). Please note that some studies included more than one inhibition task, resulting in 51 effect sizes. This resulted in a combined sample size of 1091 people with ASD (M age 14.8 years) and 1306 TD controls (M age 13.8 years). All the study information listed in Table 1 was first recorded by SvB and then checked by LR. When LR discovered mistakes, HMG made the final decision as to which information to include before effect sizes were inspected.
First, tasks were divided into the two categories of inhibitory control according to Nigg’s inhibition taxonomy (2000): Prepotent response inhibition (e.g., Go/No-Go and Stop signal tasks) and Interference control (e.g., Stroop, Flanker, and Simon). As some might argue that the Stroop is a measure of prepotent response inhibition (Friedman & Miyake, 2004) we also explored whether the findings altered when the Stroop was included as a measure of prepotent response inhibition, rather than as a measure of interference control. Second, we recorded the dependent measure for each task. However it is important to note, that despite the use of similar tasks, the studies differed considerably in the reported dependent measure. In addition, the majority of studies reported more than one dependent measure for the task of interest. Therefore, we selected the measure that best reflected inhibitory control (for example, the stop signal reaction time [SSRT] in a Stop task), and was most commonly reported among the included studies. If this measure was not reported, we selected the next measure most demonstrative of inhibitory control (for example, a failure to inhibit when a stop signal was presented). The selection of dependent measures was made before effect sizes were calculated to minimize experimenter bias. See Table 1 for the dependent measure that was selected per task.

To conduct the meta-analyses, Hedges’ g (Hedges & Olkin, 1985)- the difference between the mean score of the ASD group and control group divided by the pooled standard deviation—was calculated per inhibition task in each study (see Table 1). Two studies did not report the mean and standard deviation, therefore Hedges’g was computed from the t statistic (Langen et al., 2011) and F statistic (Dichter & Belger, 2008). Effect sizes were interpreted accordingly: g=0.20 is small; g=0.50 is medium; g=0.80 is large. Therefore, a smaller Hedges’g indicates a
smaller distinction between the ASD and control group. A positive effect size indicates poorer performance by the ASD group as compared to the TD group, whereas a negative effect size indicates that the ASD group outperformed the control group. Second, variability among the true effect was expected due to differences in methods and sample characteristics between studies. Therefore, a random effects meta-regression model was chosen in order to account for within as well as between study variation (QE statistic). A significant degree of between-study variation would imply heterogeneity between studies, driven by additional factors other than prepotent response inhibition or interference control (Huizenga et al., 2011). Third, meta-regression techniques were applied using R package, metaphor (Viechtbauer, 2010), to investigate age as a potentially influential study characteristic. Age was indexed as the mean age of the ASD participants. Using this same technique IQ and mode of dependent measure [reaction time vs. accuracy] were explored.

-Please insert Table 1 around here-
Results

Forest plots (Figure 2, panel a & b) were used to visually inspect the presence of potential outliers. In addition, Cook’s distance was below one for all studies, indicating that no study was overly influential on the observed outcome. Publication bias was considered using Funnel plots (Figure 3, panel a & b), which did not appear to show a publication bias. Regression tests and Trim and Fill methods were used to confirm funnel plot asymmetry. For the sample of prepotent response studies (panel a), the regression test suggested potential asymmetry \( (p = .05) \), however the Trim and Fill method indicated no missing studies on either extreme side of the funnel plot. For the sample of interference studies (panel b), the regression test did not suggest publication bias. Results from the Trim and Fill method did suggest potential asymmetry on the right side of the funnel plot \( (p = .06) \), indicating that the true effect for interference studies may be larger than the effect yielded by the included studies. Hence, there seems to be some evidence for a publication bias in either form of inhibitory control, however there is no evidently strong publication bias.

Inhibition types

We first conducted separate meta-analyses for each inhibition type according to Nigg’s taxonomy (2000): prepotent response and interference control. Studies assessing prepotent response inhibition \( (N=23) \) showed a significant and positive deviation from zero \( (b = .55, SE=0.12, p < .0001) \). Heterogeneity between studies was significant \( (QE = 70.6, df=22, p < .0001) \). Studies assessing interference control \( (N=28) \) also yielded a significant effect \( (b = .31, SE=0.13, p < .0001) \).
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$SE = 0.13, p = .02$), and heterogeneity between studies was again significant ($QE = 113.1, df = 27, p < .0001$). However, when we explored inhibition type as a moderator ($N = 51$), inhibition type was not found to moderate the effect sizes ($QM = 1.9, df = 1, p = .17$).

When categorizing tasks according to the Friedman and Miyake taxonomy (2004), the effect size for prepotent response inhibition slightly decreased ($b = .48, p < .0001$), while the heterogeneity increased ($QE = 149.2$). For interference control (i.e., excluding the Stroop task), the effect size decreased ($b = .19$) and was no longer significant ($p = .36$). Moreover, the heterogeneity decreased ($QE = 43.9$), yet was still significant ($p < .0001$). Taken together, these findings suggest that a substantial amount of heterogeneity exists between inhibition studies, and in particular, among studies that utilize the Stroop task.

*Age effects*

Age was entered as a centered continuous moderator (Fairchild & McQuillin, 2010). Please note that 35 studies focused on children and/or adolescents, while only 6 studies focused on adults with ASD (see Table 1). Age effects were assessed within each inhibition type (following Nigg, 2000).

For prepotent response inhibition, age did not seem to significantly moderate effect sizes ($QM = 0.01, df = 1, p = .92$), and heterogeneity between studies remained significant ($QE = 70.3, df = 21, p < .0001$). However, in three studies the mean age of the ASD participants was three standard errors above the mean age across all studies. Therefore, these studies were identified as outliers (Geurts & Vissers, 2011; Langen et al., 2011; Schmitz et al., 2006). Excluding these three studies did alter the findings considerably as age was now a significant moderator ($QM = 4.5, df = 1, p = .033$) and accounted for 25% of the heterogeneity. Nonetheless heterogeneity
between studies remained significant ($QE = 50.6, df=18, p<.0001$). The negative estimate of age (-.15) suggests that an increase in age is related to a decrease in the observed effect size for prepotent response inhibition.

For interference inhibition, age did not significantly moderate effects sizes ($QM = 1.4, df=1, p = .24$), and heterogeneity between studies remained significant ($QE = 107.9, df=26, p<.0001$). Two studies were identified as outliers (Johnston et al., 2011; Schmitz et al., 2006), however, excluding these studies did not alter the findings ($QM = 2.4, df=1, p = .12; QE = 103.9, df=24, p<.0001$). In contrast with the hypothesis, age did not seem to influence the effect sizes.

**Exploratory moderator analyses**

There was still a significant amount of heterogeneity among the studies, after accounting for inhibition type and age. Therefore, we explored whether additional factors may help to explain this heterogeneity.

First, IQ is known to influence inhibitory control performance (Ogilvie et al., 2011; Polderman et al., 2009; Salthouse, 2010). As studies differed considerably in the inclusion criteria with respect to IQ, we first tested whether IQ was a significant moderator. Please note that not all studies ($N = 7$) reported Wechsler scaled IQ (Adams & Jarrold, 2012; Adams & Jarrold, 2009; Ames & Jarrold, 2007; Jahromi et al., 2013; Robinson et al., 2009; Sanderson & Allen, 2012; Yoran-Hegesh et al., 2009), therefore these exploratory analyses are based on a subset of the studies included in the planned analyses.

For prepotent response inhibition, IQ was not a significant moderator ($QM = 0.84, df =1, p = .36$) and the heterogeneity was still significant ($QE = 48.1, df=19, p<.0001$). Among the
interference inhibition studies, IQ was a significant moderator ($Q_M = 18.4, df = 1, p < .0001$), and reduced the heterogeneity tremendously (62% of the heterogeneity was accounted for) although the heterogeneity remained significant ($QE = 47.6, df = 20, p < .001$). The negative estimate of IQ (-.07) suggests that an increase in IQ is related to a decrease in the observed effect size for interference control.

Secondly, the modality of reported dependent measures varied between reaction time and accuracy measures. There is some evidence to suggest that this may be a relevant factor to observed inhibitory performance (Adams & Jarrold, 2012; Prinzmetal et al., 2005; Sanderson & Allen, 2012). Hence we also explored modality of the dependent measures as a potential influence on the effect sizes (see Table 1). For prepotent response inhibition, the modality of the dependent measure was a significant moderator ($Q_M = 3.95, df = 1, p = .05; QE = 60.7, df = 21, p < .0001$). Both modes yielded significant effects: accuracy measures (.42) and reaction time measures (.57). For interference inhibition, ($Q_M = 0.04, df = 1, p = .84; QE = 113.0, df = 26, p < .0001$) the mode of the dependent measure did not influence the observed effect sizes or observed heterogeneity.
Discussion

The aim of this study was to determine whether people with ASD encounter difficulties in two forms of inhibitory control: prepotent response inhibition and interference control. Following the taxonomy of Nigg (2000), the meta-analyses revealed an overall difference in performance between people with ASD and without ASD in both forms of inhibition. The latter result supports previous studies which have observed interference control deficits in ASD. However, our findings indicated a slightly larger effect for prepotent response inhibition. Hence our findings also contrast previous studies (Christ et al., 2007; Christ et al., 2011), and suggests that prepotent response inhibition is more difficult for individuals with ASD as compared to TD.

Besides type of inhibitory control, we also focused on age. Across studies, the age range was rather broad (4 to 83 years of age), and it is known that behavioral improvements are seen up to adulthood in both inhibition types (Huizinga et al., 2006). In addition, a cross sectional study has shown that problems with interference control seem to resolve with an increase in age (Christ et al., 2011). However, our results showed the opposite effect of age and inhibition type. That is, age moderated performance on prepotent response inhibition tasks, but not interference control tasks. Thus, our meta-analyses did not support the idea of a delayed development of interference control in individuals with ASD.

While our sample did include adults, the majority of the studies focused on children who were between 8 and 15 years, therefore we could not test aging effects into late adulthood. Moreover, for several studies (Adams & Jarrold, 2009; Ames & Jarrold, 2007; Brian et al., 2003; Sanderson & Allen, 2012) the mean age between the ASD and TD group differed substantially.
In some studies this was due to the choice to match on IQ (Adams & Jarrold, 2009; Ames & Jarrold, 2007; Sanderson & Allen, 2012), therefore we explored IQ as a potential moderator. Our findings revealed that IQ was in fact a relevant moderator for interference inhibition, but not for prepotent response inhibition. That is, IQ showed the opposite effect as compared to age.

The different role of age and IQ for interference control abilities might explain some of the discrepant findings between ASD studies that utilize similar interference tasks. For example, in a study by Christ and colleagues (2011), an interference problem was observed in individuals with ASD. These ASD individuals had a slightly lower IQ than the TD group. In order to statistically control for this, IQ was always entered as a covariate in the analyses. However, covarying IQ might not be a sufficient technique to control for the observed differences (Dennis et al., 2009), and therefore, these differences in IQ may confound the observed effects on the Flanker task. The study by Sanderson and Allen (2012) corresponds with this interpretation. In this study, participants were matched on IQ (i.e., mental age) resulting in an age difference between the ASD and TD group and they observed no difference in Flanker task performance. This is what one would predict if indeed for interference control, IQ is the relevant moderator influencing performance in people with ASD.

However, it is important to consider that we focused on the effects of age and IQ in the context of the Nigg taxonomy (2000). In contrast, previous studies, such as Christ and colleagues (2011), interpret findings according to the Friedman and Miyake taxonomy (2004) in which the Stroop is a measure of prepotent response inhibition. It is likely that this difference may contribute to the discrepancies between inhibition studies and the conclusions that have been drawn. Therefore we also assessed inhibition effects with the Stroop classified as a prepotent
response measure (e.g., Friedman & Miyake, 2004). For prepotent response inhibition, the effect remained significant, whereas the effect for interference control became insignificant. Hence, using the Friedman and Miyake taxonomy (2004) actually seems to strengthen the conclusion that people with ASD predominantly experience problems with prepotent response inhibition.

However, upon further inspection, it seems that the effects for age and IQ might be highly dependent on the taxonomy used. When tested according to the Friedman and Miyake taxonomy (2004), the moderating effects were altered with respect to prepotent response inhibition (i.e, now including the Stroop findings). IQ, rather than age, approached significance as a moderating variable (results can be obtained from the first author). This minor change in moderator effects is telling, as it suggests that the associations between age, IQ, and inhibition type on inhibitory control are limited to how tasks are categorized. The differential effect of moderators, together with different taxonomies used across studies, seems to largely account for the discrepant findings between studies assessing inhibition among ASD individuals.

Consistently across all analyses, there remained considerable variability between study effects. Hence, it is important to explore additional factors that may influence the performance of inhibitory control among ASD individuals. One possible explanation may be that alternative taxonomies would be better at determining which task (construct or dependent measure) has the most discriminative power. For example, the included tasks might differ in sensitivity to performance differences; a function of a task’s difficulty and reliability (MacDonald & Carter, 2002). With respect to task difficulty, there are likely differences among tasks in the strength of the goal (i.e., how important is the information one needs to keep online) and in the strength of the prepotent response tendency. The latter might be related to whether or not participants had to
inhibit recently trained associations (Go/NoGo task) or have to inhibit intrinsically learned associations (Simon task). With respect to task reliability, a recent study with healthy adults (N=23; (Wöstmann et al., 2013), which focused on test-retest reliability of several inhibition tasks (e.g., Stroop, Simon, Flanker, Stop task, Go/NoGo, CPT) showed that most of the measures displayed good test-retest reliability and internal consistency. However, results showed poor reliability for the stop task (SSRT; see also Kuntsi et al., 2001), but see (Soreni et al., 2009) for contrasting findings in ADHD), and a reduction in variability of reaction time and of the reaction time for the incongruent trials in the Stroop, Simon, and Flanker task. Therefore, it seems that performance is closely intertwined with detailed task characteristics.

ASD severity may be another explanation for the variability in effect sizes. No distinction has been made between the different subtypes within ASD. Individuals with autism, Asperger syndrome, and pervasive developmental disorders not otherwise specified (PDD-NOS) were all treated as one category in line with the DSM-5 (Tanguay, 2011). To our knowledge there is one study (Verté et al., 2006), which compared children of different ASD subtypes on prepotent response inhibition and interference control. Results indicated no difference in performance among subtypes (see also Christ et al., 2011). However, instead of focusing on subtypes, it might be more relevant to study the role of ASD symptom severity on inhibition performance.

Unfortunately studies differed largely in how the ASD diagnoses were verified and which measures (if any) were used to determine ASD severity. Hence this could not be tested in the current study. If inhibitory control were to be related to ASD severity, this would strengthen the hypothesis that inhibition deficits are not due to comorbid diagnoses in the ASD population, such
as with ADHD (e.g., Geurts et al., 2004; Sanderson & Allen, 2012; Sinzig et al., 2008) or schizophrenia spectrum disorders (Barneveld et al., 2013), but to ASD itself.

Lastly, large variability and modifications exist between task procedures and dependent measures in the included studies. This was the case even when similar tasks (studies utilizing the Stroop task actually showed the largest variability) were used. Tasks differed on a wide variety of factors such as the inter stimulus interval, stimulus presentation duration, type of stimulus (arrows, colors, figures/shapes, letters/numbers, faces), number of trials, percentage of conflict/NoGo/Stop trials. Each of these task manipulations are known to influence task performance (see Adams & Jarrold, 2012) for a qualitative discussion of inhibition paradigms used in ASD studies). Hence, it is not surprising that we observed large heterogeneity. Based on our exploratory results, modality of the dependent measure was one influential variable. That is, while differences between ASD and TD on inhibition tasks can be observed when recording both RT and accuracy, the degree of this difference may be higher when RT serves as the dependent measure. However, if we focus solely on RT we still observe heterogeneity as, for example, some studies reported the preferred actual interference scores (i.e., difference score) with which one rules out more global deficits like a generally slower processing speed, while most studies reported the performance on the interference (i.e., incongruent) condition which incorporates much more processes than solely conflict resolution. The large variation between studies highlights a major complication to the study of inhibitory control, and illustrates the need for further investigation into which specific factors influence inhibitory performance in ASD. Factors that are potentially important are motivation (Geurts et al., 2008; Kohls et al., 2009), attention (Sanderson & Allen, 2012; Tye et al., 2013), and working memory (Kana et al., 2007;
Luna et al., 2007). Thus, this study shows that there are likely to be many factors involved in inhibitory control, and further, that these factors may differ given the type of inhibition.

Despite these limitations, our study suggests that people with ASD do in fact show poorer performance on prepotent response inhibition and interference control tasks in comparison to TD individuals. Poor performance seems to be most apparent in prepotent response inhibition.

However, we do not conclude that prepotent response inhibition is the most promising indicator of inhibitory control, nor that ASD is characterized by an inhibition impairment, as this seems to be premature. Rather, our findings emphasize the multi-faceted nature of inhibition, and illustrate the contribution of factors, such as age, and IQ and their differential effects between each type of inhibition.

**Future directions**

Future studies should focus on unraveling these facets of inhibition, by focusing on the different abilities used, and the elements that influence performance in each type of inhibition. For this reason, the focus of many of studies that examine inhibition among ASD may not render the most fruitful insight. We, like others, have posed the question of whether or not people with ASD encounter prepotent response inhibition and/or interference control deficits. However, our findings suggest that this question does not fully reflect the specific challenges that people with ASD encounter. While much discussion has been focused on whether we should use the Nigg taxonomy (2000) or the Friedman and Miyake taxonomy (2004), from the perspective of cognitive modeling both are probably an oversimplification of the cognitive processes involved in the included inhibition tasks. Our findings indicate that ASD research into inhibition would greatly benefit from a well-organized framework, explicating the mechanisms of inhibitory
control and the potential role of age and IQ. For example, in both taxonomies applied in the present study (Friedman & Miyake, 2004; Nigg, 2000) the Stop tasks and Go/NoGo tasks are considered to be prepotent response inhibition tasks. However, it is possible that performance on these tasks differ when we consider action *cancellation* (Stop) and action *constraint* (Go/NoGo; Eagle et al., 2008)) abilities in people with ASD. It has recently been shown that the Stop task and Go/NoGo task are associated with partially overlapping, but also distinct neural networks which stems from the different cognitive processes needed to perform well on these tasks (Swick et al., 2011). With respect to interference control, a distinction can be made based on the difficulty in *suppressing* the effect of task *irrelevant* information (Simon) and the difficulty with *enhancing* the effect of task *relevant* information (Stroop; Egner, 2008; Fan et al., 2003). A deficit in either of these processes will result in less optimal conflict resolution. Moreover, do people with ASD mainly have conflict resolution problems when these conflicts arise at a perceptual level or when they arise at the response selection stage? To disentangle which deficient processes actually lead to an overall performance decrease, we need to apply more elaborate models of cognitive control (for a good example, see (Solomon et al., 2008; Solomon et al., 2009). Together as the ASD field, we need to: (1) be transparent regarding the specific cognitive processes we refer to when we use the term inhibition; (2) report at least those dependent measures that actually reflect inhibition (for example SSRT on the stop task, commission errors on the Go/NoGo task, and inference as difference score between congruent and incongruent trials on the Flanker and Simon task); (3) incorporate the knowledge from cognitive science when designing inhibitory control studies so we can actually determine which cognitive control processes are challenging for people with ASD.
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Neuropsychological mechanisms of digit symbol substitution test impairment in asperger disorder. Psychiatry Research, 166, 35-45.
Footnotes

1 A study conducted by Ashwin, Wheelwright, and Baron-Cohen (2013) was not included as we determined that the task used did not meet inclusion criteria 3. Unlike standard interference tasks (e.g., Stroop & Flanker), the interference component did not elicit an alternative response.
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Table & Figure Legend

Table 1. Characteristics of the included studies, which assessed inhibition in individuals with ASD

Figure 1. Flow diagram showing the literature search and study selection process.

Figure 2. Forest plot indicating effect sizes (Hedges g) and confidence intervals for each study effect included in the two meta-analyses (panel a: prepotent response inhibition; panel b: interference control). Positive effect sizes indicate worse performance in the ASD group as compared to controls while negative effect sizes indicate that the ASD group outperforms the control group.

Figure 3. Funnel plots (panel a: prepotent response inhibition; panel b: interference control); used to explore publication bias.
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A Random Effects for Prepotent Response Studies (N=23)

B Random Effects for Interference Inhibition (N=28)

A Prepotent Response Inhibition (N=23)

B Interference Control (N=28)
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<th>IQ M (SD)</th>
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**Notes:**
- ADOS: Autism Diagnostic Observation Schedule
- ADI-R: Autism Diagnostic Interview-Revised
- CLAS: Clinical Assessment System
- DSM-IV-TR: *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision*
- Go/NoGo: Go/NoGo Task
- Stroop: Stroop Test
- Flanker: Flanker Task
- Stop signal: Stop Signal Task
- CPT: Continuous Performance Test
- CARS: Conners’ Adult ADHD Rating Scale
- Opposite Worlds: Opposite Worlds Task
- Walk don’t walk: Walk Don’t Walk Task
- Standardized incongruent Nr correct trials: Standardized incongruent % correct trials
- Commission errors: Commission errors
- RT incongruent: Reaction Time Incongruent
- ES: Effect Size
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# Prepotent response inhibition and interference control in autism spectrum disorders: Two meta-analyses

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<td></td>
<td>TD 29/3</td>
<td>8-17.2/12.2 (2.5)</td>
<td>115 (12)</td>
<td>Si:</td>
<td>ADOS-G</td>
<td>RT incongruent</td>
<td></td>
</tr>
<tr>
<td>Solomon et al., 2009</td>
<td>ASD 17/5</td>
<td>12-18/15.2 (1.7)</td>
<td>107 (14)</td>
<td>Q:</td>
<td>P</td>
<td>POP task (color/arrow)</td>
<td>.01</td>
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<tr>
<td></td>
<td>TD 18/5</td>
<td>12-19/16 (2)</td>
<td>113 (11)</td>
<td>Si:</td>
<td>ADOS-G</td>
<td>RT incongruent</td>
<td></td>
</tr>
<tr>
<td>South et al., 2010</td>
<td>ASD 22/2</td>
<td>9-21/14 (2.4)</td>
<td>109.7 (13.2)</td>
<td>Q:</td>
<td>P</td>
<td>Flanker (arrows)</td>
<td>-.50</td>
</tr>
<tr>
<td></td>
<td>TD 20/1</td>
<td>8-18/14.2 (2.8)</td>
<td>112.1 (14.4)</td>
<td>Si:</td>
<td>ADOS-G</td>
<td>RT incongruent</td>
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<tr>
<td>Vaidya et al., 2011</td>
<td>ASD 11/4</td>
<td>10.8 (1.3)</td>
<td>113.9 (15.4)</td>
<td>Q:</td>
<td>P</td>
<td>Simon/Flanker (arrow/word)</td>
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<td></td>
<td>TD 14/4</td>
<td>11.0 (1.3)</td>
<td>119.2 (14.2)</td>
<td>Si:</td>
<td>ADI-R, ADOS-G</td>
<td>RT incongruent</td>
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</table>
Running head: Inhibition in ASD: Meta-analyses

<table>
<thead>
<tr>
<th>Study</th>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
<th>Measure 1</th>
<th>Measure 2</th>
<th>Measure 3</th>
<th>Effect Size</th>
</tr>
</thead>
<tbody>
<tr>
<td>Xiao et al., 2012</td>
<td>ASD 19/0</td>
<td>ADHD 16/0</td>
<td>TD 16/0</td>
<td>8-14/10.1</td>
<td>8-14/9.8</td>
<td>8-14/9.7</td>
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<td>99.3 (9)</td>
<td>103.6 (8.1)</td>
<td>105.6 (13.1)</td>
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<td>Q: - SI: ADI-R NSCA: clinical diagnosis</td>
<td>Stroop (Chinese characters)</td>
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<td>CLAS: DSM-IV</td>
<td>Go/NoGo (letters)</td>
<td>Commission errors</td>
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<td>Yoran-Hegesh et al., 2009</td>
<td>ASD 23/0</td>
<td>TD 43/0</td>
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<td>11-17/15.1</td>
<td>14-16/15.5</td>
<td>IQ &gt; 70</td>
<td>1.4</td>
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</tbody>
</table>

Please note that a positive effect size indicates better performance by the TD group, whereas a negative effect size indicates better performance by the ASD group. For each of the studies we chose one dependent measure. The selection was based on the following criteria: 1) Which reported measure best reflects inhibitory control? 2) What dependent measure has been most often reported across studies? 3) If specific experimental manipulations were added the reported measure was chosen on which the largest effect was reported.

1 These studies included additional inhibition tasks, which could not be included in the meta-analysis. 2 IQ was assessed using other instruments than the Wechsler Intelligence Scales (WISC, WAIS). 3 The number of participants selected differed from the number of participants included in the analysis (e.g., excluded participants). The calculated effect size is based on the number of participants who were included in the analysis in order to ensure the most accurate effect size. The number of selected participants is shown in the above table. In Christ et al. (2007), the number of participants in the table was different from the text. We used the numbers from the text because they appeared to be correct. 4 In this study, analyses were conducted on subgroups of participants matched on IQ. The effect size is based on the whole group. 5 Six studies did not provide enough information to calculate an effect size, therefore they were excluded from further analyses. 6 The M(SD) were not reported for the selected dependent measure, therefore the effect size was calculated from the t statistic. 7 The dependent variable has been interpreted as an accuracy score, however this is not explicitly stated in the article.

ADHD=Attention Deficit Hyperactivity Disorder; ADHDc=ADHD-combined type; ADHDI=ADHD—inattentive type; ADI-R=Autism Diagnostic Interview Revised; ADOS-G=Autism Diagnostic Observation Schedule—Generic; ASD=Autism spectrum disorders (could include autism, Asperger syndrome or PDD-NOS); CARS = Childhood Autism Rating Scale; CLAS=Classification system used; CPT= Continuous Performance Test; D-KEFS=Dellis-Kaplan Executive Function System; DSM-IV=Diagnostic and Statistical Manual of Mental Disorders, fourth edition; F=Female; Incongruent= raw score on incongruent trial; IQ=Intelligence Quotient; Interference= difference score between baseline and incongruent trial. LD=Learning Disability group; M=male; NSCA=Nonstructural clinical assessment; P=Parent; POP= Preparing to Overcome Prepotency; Q= Questionnaire; RT=Reaction Time; SART=Sustained Attention to Response Test; S = self; SI=Structured instrument such as specially developed standardized interviews and observation schedules; SSRT= Stop-Signal Reaction Time; T=Teacher; TD=Typically developing group; TEA-Ch= Test of Everyday Attention for Children.