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A preliminary randomized, controlled trial of executive function training for children with autism spectrum disorder

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Abstract

This randomized, controlled study examined the initial efficacy of an executive function training program for children with autism spectrum disorder. Seventy 7- to 11 year-olds with autism spectrum disorder and intelligence quotients $\geqslant$80 were randomly assigned to receive a web-based set of executive function training games combined with in-person metacognition coaching or to a waitlist. Primary outcomes were evaluated for neural responses related to executive function, lab-based executive function behavior, and generalization of executive function skills. Secondary outcomes included measures of social function. Post-testing and analyses were conducted by staff naïve to group assignment. Children exhibited a change in neural response following training relative to the waitlist group $(\eta_p^2 = 0.14)$. Training effects were not detected via lab-based tasks $(\eta_p^2\text{s} < 0.02)$ or generalized to caregiver-reported executive function skills outside the lab $(\eta_p^2 = 0.001)$. However, the training group demonstrated reduced symptoms of repetitive behavior $(\eta_p^2 < 0.15)$ following training. There were no adverse events or attrition from the training group. Findings suggest that brief, targeted computer-based training program accompanied by coaching is feasible and may improve neural responses and repetitive behaviors of school-aged children with autism spectrum disorder.

Lay abstract

Executive function, which is a set of thinking skills that includes stopping unwanted responses, being flexible, and remembering information needed to solve problems, is a challenge for many children on the autism spectrum. This study tested whether executive function could be improved with a computerized executive function training program under the guidance of a coach who reinforced the use of executive function skills. Seventy children with autism spectrum disorder from age 7 to 11 years of age participated in the study. They were randomly assigned to receive training or to a waiting group. The tests most likely to determine whether the training may be effective were chosen from a larger battery before the study started and included one task measuring brain responses, two measures of executive function in the lab, and a parent questionnaire. Changes in social functioning and repetitive behaviors were also explored. All children assigned to training completed the program and families generally reported the experience was positive. Brain responses of the training group changed following training, but not within the waiting group during a similar time period. Children who received training did not exhibit behavioral changes during the two the lab-based tasks. Parent report on questionnaires indicated that neither group showed a significant change in their broad use of executive function in other settings. Yet, children who received training were reported to have fewer restricted and repetitive behaviors following training. These initial findings suggest that short executive function training activities are feasible and may improve some functioning of school-aged children on the autism spectrum.

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autism spectrum disorder, clinical trial, event-related potential, executive function, inhibition

Autism spectrum disorder (ASD) is associated with lifelong impairments in executive function (EF) (Demetriou et al., 2017; Geurts, van den Bergh, & Ruzzano, 2014; Kenworthy et al., 2008). EF is the ability to manage complex or conflicting information in the service of attaining a goal and encompasses inhibition (i.e. the ability to deliberately suppress a dominant response or competing information), set-shifting (i.e. moving flexibly between tasks or mental representations), and working memory (i.e. holding information in mind and updating it while using it to solve a problem) (Lehto et al., 2003; McAuley & White, 2011; Miyake et al., 2000; Miyake & Friedman, 2012). EF ability relates to the severity of social and repetitive symptoms of ASD (Faja & Nelson Darling, 2019; Geurts, de Vries, & van den Bergh, 2014).

EF training programs that engage typically developing (TD) children in practice just beyond their current level of competency result in behavioral and neural changes (Diamond, 2013). Many EF training programs are delivered electronically (Jaeggi et al., 2011; Karbach & Kray, 2009; Karbach & Unger, 2014; Rueda et al., 2005, 2012; Thorell et al., 2009) and have small to moderate effect sizes for school-aged children (Takacs & Kassai, 2019), whereas more comprehensive and longer EF training programs typically result in greater transfer of skills and larger improvements (Diamond, 2013). Adding in-person metacognitive scaffolding during computerized EF training also enhances efficacy (Pozuelos et al., 2019). Finally, some EF training effects appear to generalize to theory-of-mind (ToM) (Kloo & Perner, 2003) and social competence (Greenberg, 2006; Riggs et al., 2006).

For children with ASD, EF training has received relatively little research attention. A randomized trial of a curriculum-based EF training program, *Unstuck and On Target*, compared children in classrooms who received either EF or social skills training. Better problem-solving, flexibility, planning, and EF behavior in the classroom were observed in the EF training group compared to the social skills group (Kenworthy et al., 2014). Although *Unstuck and On Target* has research support, individual intervention may be more feasible to implement outside educational settings and computer-based approaches are engaging and highly motivating (Bolte et al., 2010; Chen & Bernard-Opitz, 1993; Dichter et al., 2012), less socially demanding for children with ASD, and allow for individualized difficulty and pacing. A randomized trial of self-guided computer-based EF training (i.e. Braingame Brian) for 24 × 45 min sessions over 6 weeks included active engagement in one of three conditions: working memory, flexibility, or mock training activities. This program found comparable improvements for groups assigned to training and to an active control condition (de Vries et al., 2015). A pilot investigation with semi-random assignment to a self-guided app-based Neuroracer intervention (Project EVO) involved multitasking between a perceptual discrimination attention task and a continuous visuomotor driving task for 100 × 5 min sessions over 4 weeks. Project EVO reported moderate-to-large within group effect sizes on measures of Attention-Deficit/Hyperactivity Disorder (ADHD) symptoms, EF challenges, and social skills among a group of children with ASD + ADHD (Yerys et al., 2019). These studies suggest EF training may be useful in improving EF and social functioning in ASD and raise the possibility that face-to-face EF training *combined* with computer-based practice may be beneficial, particularly to support strategies that children with ASD may not spontaneously employ.

The combined approach has yet to be examined in ASD. To address this need, we selected computer games that emphasized set-shifting, inhibition, and spatial working memory with levels of difficulty that incrementally increased. Set-shifting and planning are impaired in ASD, with moderate to large effect sizes reported in meta-analyses (Demetriou et al., 2017; Willcutt et al., 2008). Inhibition is also affected in children with ASD, with comparable performance to groups with ADHD (Craig et al., 2016; Geurts, van den Bergh, & Ruzzano, 2014; Schmitt et al., 2018; Sergeant et al., 2002; Tye et al., 2014). Finally, working memory, particularly in the context of visuospatial tasks, is reduced in ASD (Habib et al., 2019; Kenworthy et al., 2008). We also developed a companion coaching manual to teach metacognition skills.

Outcomes in EF training studies include lab-based behavioral measures, parent report measures, and electrophysiological responses. Neural measures such as electroencephalography complement lab-based behavioral tasks by probing aspects of EF not directly captured by overt behavioral responses, such as response preparation and inhibition (Banaschewski & Brandeis, 2007), and may precede behavioral changes. Lab-based tasks allow for sensitive measurement of initial changes and differences in specific aspects of EF whereas broad surveys capture more global changes in behavior.

The N2 event-related potential (ERP) has been used as a measure of improved EF in several prior training studies (Liu et al., 2017; Millner et al., 2012; Rueda et al., 2012) as it is thought to reflect detection and monitoring of conflicting information (Abundis-Gutiérrez et al., 2014; Heil et al., 2000) or inhibition of competing information (Folstein & Van Petten, 2008; Van't Ent, 2002). These abilities are closely related to EF (Buss et al., 2011; Miyake et al., 2000; Rueda et al., 2004). N2 amplitude is generally larger (i.e. more negative) for trials with greater conflict (Brydges et al., 2014; Espinet et al., 2012, 2013) and for younger children who also do not exhibit clear condition effects under age 6 at typical N2 time windows (Buss et al., 2011; Rueda et al., 2004). For children with ASD, N2 amplitudes are more negative than controls overall and N2 amplitude relates to EF behavior (Faja et al., 2016; Jodo & Kayama, 1992; Pfefferbaum et al., 1985). The extent to which the N2 ERP component changes as a result of EF intervention in children with ASD is unknown.

The current study

The objective of the current project is a test of the initial efficacy of a brief computer-based EF training combined with in-person coaching for young children with ASD at the behavioral and neural level. Because of the preliminary nature of the study, children were not selected on the basis of an EF impairment and multiple outcomes were examined. We focused on young, verbal school-aged children because the training games were originally developed for preschoolers and young school-aged children without ASD. EF impairments are detected by this age in ASD (Kenworthy et al., 2008), and successful intervention could impact subsequent academic and social function. Neural and behavioral outcome measures were selected because they were used in investigations of similar training with TD children (Pozuelos et al., 2019; Rueda et al., 2012) or other EF interventions for children with ASD (Kenworthy et al., 2014; Yerys et al., 2019).

We report the findings for primary outcomes selected to examine three levels of analysis: (1) neural changes associated with EF (N2 ERP during the flanker task), (2) lab-based cognitive changes in EF subdomains emphasized in training (inhibition and flexibility), and (3) generalization of EF skills via a broadband measure of real-world EF. Secondary outcomes explored (1) performance on EF domains not addressed by intervention (verbal working memory, decision-making), (2) social functioning, and (3) a neural measure associated with EF that had lower acquisition rates in piloting (N2 ERP during the Go/Nogo Task). Finally, given the relation between EF and repetitive behaviors, we also explored repetitive symptoms.

We hypothesized that children with ASD who received training would exhibit changes in electrophysiological responses relative to children with ASD randomly assigned to a waitlist control group. Although outcome measures differed from training, we predicted that lab-based behavioral measures that were most closely related to training activities would be most sensitive to initial changes. Given the clinical importance of generalizing newly acquired EF, we also measured parent report of improved EF skills at home. Yet, we predicted that neural changes are likely to precede behavioral changes and generalization beyond the lab; thus, behavioral changes would only be detected if neural changes were observed. Finally, we explored untrained domains of EF, social function, and repetitive behaviors with the expectation that generalization would only be observed if changes were detected in primary outcomes. In sum, the battery is designed to detect the presence of a signal from a brief intervention via neural and lab-based measurement and, if detected, begin to explore the potential generalization of skills to other tasks and settings.

Method

Participants

Seventy children (seven girls), aged 7–11 years old, diagnosed with ASD participated. Inclusion criteria included age (7–11 years at enrollment), full-scale intelligence quotient (IQ) $\geqslant 80$, and a diagnosis of ASD (described below). Figure 1 presents the number of eligible participants at each stage of the study. Sample size was determined for this preliminary efficacy study based on generic effect sizes for planned analyses. Participants were recruited from 2015 to 2017 until the planned sample size was enrolled. Exclusionary criteria included colorblindness, inability to complete procedures in English or due to sensory or motor impairments, medical disorders that impact the central nervous system, prolonged prenatal substance exposure, and a history of seizures or use of seizure medication. Other medications were non-exclusionary and use did not differ by group (Table 1). The study was conducted at Boston Children's Hospital in the United States and approved by its Human Subjects Division; all parents provided consent and all children provided written assent to participate. The study, including selection of outcome measures and analyses, was pre-registered at ClinicalTrials.gov (NCT02361762).

Procedure

Parents of potential participants completed phone screening to establish initial eligibility. Diagnostic and cognitive eligibility were assessed at the first visit under the supervision of a licensed psychologist. During two additional baseline visits, neural and behavioral responses to a battery of EF and social cognition tasks were collected while parents completed questionnaires. Then, children were randomized equally to either active EF training or waitlist control (i.e. parallel design, 1:1 allocation ratio). Randomization order (simple) was computer generated by a staff member not involved with visits and assignments were concealed in sequential, sealed envelopes. Children returned for two post-testing visits conducted by staff who were unaware of group status. Post-testing followed the same procedures as baseline. Groups did not differ in the duration between randomization and the first post-testing visit, $t(66) = 0.54$, $p = 0.59$; $M_{\text{Training}} = 11.37$ weeks (standard

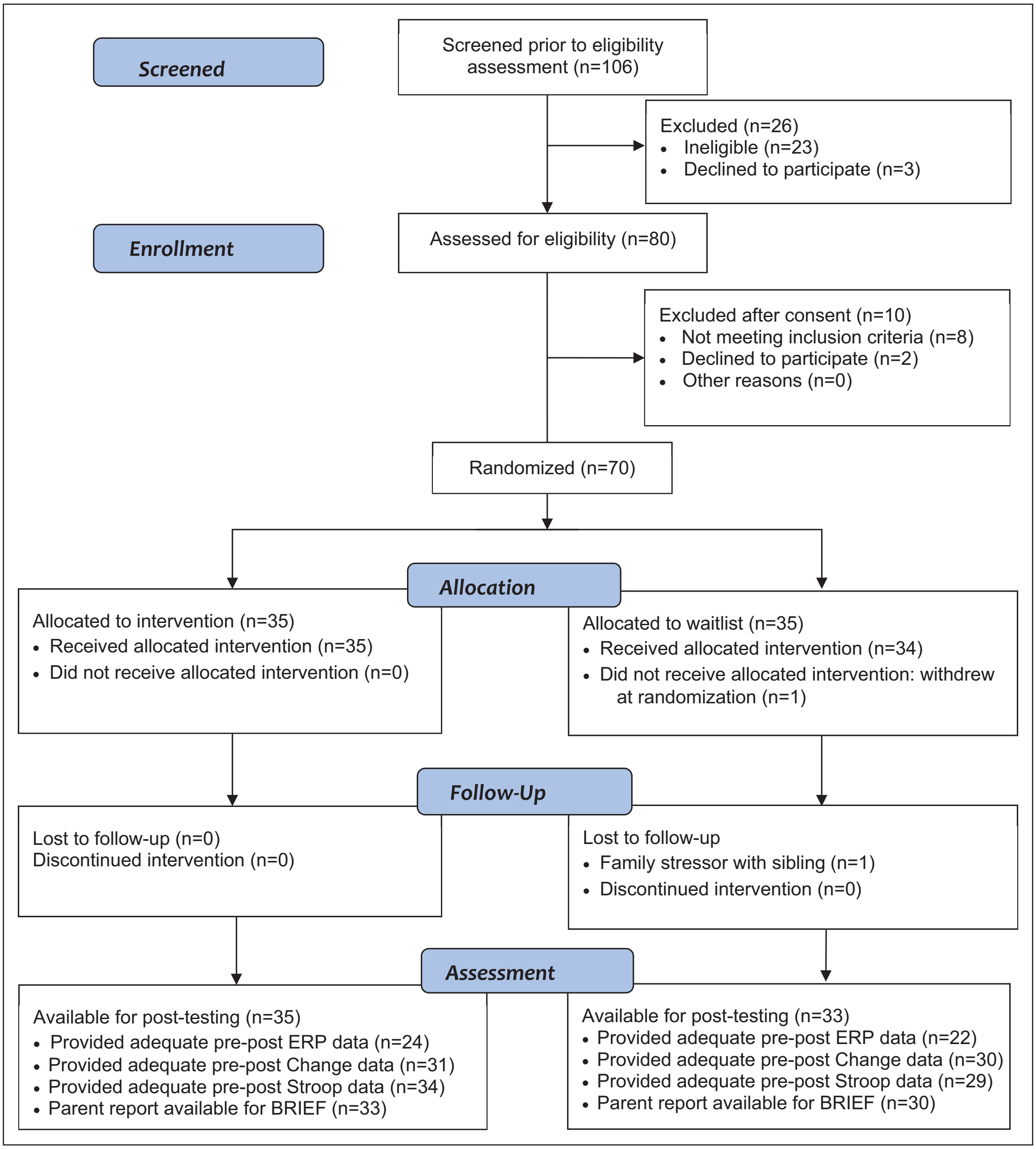

Figure 1. CONSORT diagram.

deviation (SD) = 2.50), $M_{Waitlist}$ = 11.07 weeks (SD = 1.95). All training participants returned for post-testing. In the Waitlist group, one family withdrew at randomization and one family was lost to contact. Training was offered to the waitlist group at the conclusion of the trial. No adverse events were reported.

Symptom assessment. Existing diagnosis of ASD was confirmed according to the *Diagnostic and Statistical Manual of Mental Disorders* (5th ed.; DSM-5; American Psychiatric Association, 2013) criteria based on expert clinical judgment, the Autism Diagnostic Interview–Revised (Rutter et al., 2003 scored according to Sung et al., 2005), and the Autism Diagnostic Observation Schedule–Second Edition (Lord et al., 2012). Symptoms of ADHD were assessed via the Child Behavior Checklist (Achenbach & Rescorla, 2001).

Cognitive assessment. Overall, cognitive ability was determined via the Wechsler Abbreviated Scale of Intelligence-2 (Wechsler, 2013).

Intervention

Training involved up to 10-h long visits with children approximately once a week led by a research assistant or

Table 1. Participant characteristics ($N=70$).

	Training group	Waitlist group	Statistical test
Age (in years)	M = 9.15 (1.38)	M = 9.10 (1.34)	$t(68)=0.18$, $p=0.86$
Reported gender	91% boys	89% boys	$\chi^2(1)=0.16$, $p=0.69$
Race	0% Asian	3% Asian	
	3% Black	9% Black	
	88% White	77% White	
	9% Biracial	11% Biracial	
Ethnicity	11% Hispanic	3% Hispanic	$\chi^2(1)=1.94$, $p=0.16$
Household income	15% <35 K	13% <35 K	$\chi^2(4)=2.11$, $p=0.72$
	6% 36–65 K	16% 36–65 K	
	27% 66–100 K	29% 66–100 K	
	26% 101–160 K	19% 101–160 K	
	26% >161 K	23% >161 K	
Primary caregiver education	9% high school	6% high school	$\chi^2(3)=1.60$, $p=0.66$
	26% associate	15% associate	
	28% some college	30% some college	
	37% bachelor	49% bachelor	
Stimulant medication use	23%	21%	$\chi^2(1)=0.05$, $p=0.82$
Non-stimulant ADHD medication	14%	26%	$\chi^2(1)=1.58$, $p=0.21$
Other medication use	34%	32%	$\chi^2(1)=0.02$, $p=0.87$
ADOS-2 comparison score	8.89 (1.6)	8.89 (1.2)	$t(68)=0.00$, $p=1.00$
Social affect CS	8.20 (1.6)	8.40 (1.2)	$t(68)=-0.59$, $p=0.56$
Restricted repetitive CS	9.09 (1.0)	9.06 (1.3)	$t(68)=0.11$, $p=0.92$
ADI-R social raw score	17.29 (4.8)	18.26 (5.2)	$t(68)=-0.82$, $p=0.42$
ADI-R verbal communication	15.51 (4.0)	16.63 (4.5)	$t(68)=-1.09$, $p=0.28$
ADI-R restricted and repetitive behavior	7.86 (3.1)	8.43 (2.3)	$t(68)=-0.87$, $p=0.39$
CBCL ADHD scale *T*-score	60.83 (6.7)	63.74 (8.4)	$t(67)=-1.60$, $p=0.12$
WASI-2 full-scale IQ	108.43 (13.6)	102.83 (12.2)	$t(68)=1.81$, $p=0.07$
Verbal comprehension index	106.60 (15.2)	102.40 (12.4)	$t(68)=1.27$, $p=0.21$
Perceptual reasoning Index	108.54 (15.0)	102.74 (13.1)	$t(68)=1.72$, $p=0.09$
BRIEF global executive composite	66.31 (12.0)	68.18 (10.2)	$t(67)=-0.69$, $p=0.49$
Metacognition index	65.03 (12.2)	67.59 (9.8)	$t(67)=-0.96$, $p=0.34$
Behavioral regulation index	65.46 (13.2)	67.06 (11.4)	$t(67)=-0.54$, $p=0.59$

ADHD: Attention-Deficit/Hyperactivity Disorder; ADOS-2: Autism Diagnostic Observation Schedule–Second Edition, CS: comparison score; ADI-R: Autism Diagnostic Interview–Revised; CBCL: Child Behavior Checklist; WASI-2: Wechsler Abbreviated Scale of Intelligence–Second Edition; IQ: intelligence quotient; BRIEF: Behavior Rating Inventory of Executive Function.

graduate student under the supervision of a clinical psychologist. A 5-min parent check-in at the end of each session provided the child and coach with an opportunity to share progress and key concepts. Each session aimed to include approximately 10 min of play for each of four training games that differed in their task demands from the assessment battery, as well as time for coaching EF strategies. The games (Pozuelos et al., 2019; Rueda et al., 2005, 2012) were developed for preschoolers and young school-aged children and emphasized EF skills related to visual working memory, set-shifting, and inhibition. Children advanced at their own pace and criteria for progress between levels included the number of consecutive correct responses and overall accuracy. A coaching manual was developed to increase metacognitive awareness, provide psychoeducation about EF to children and their families, support emotion regulation during challenging tasks, and foster generalization. It included procedures for introducing the games and the timing and content of each session (see Supplemental Materials for additional details).

Fidelity. Data confirmed that children played all four training games during each session unless they had already completed the highest level of a game. During each session, children spent 30–40 min playing the training games (M = 36.12 min, SD = 2.92). All children completed EF and emotion regulation psychoeducation at the first and second training session, respectively, and completed an exercise to consolidate their learning at a final training session. All trainers received formal instruction on how to deliver the manualized content and direct supervision for their initial sessions. Ongoing fidelity to key session elements was reviewed and trainers who did not adhere were retrained. Trainers also received ongoing supervision from a licensed psychologist to consult about optimal strategies for responding to challenging behaviors and obstacles to delivering intervention.

Electrophysiologic methods

Electroencephalogram (EEG) data recording, editing, and abstraction followed Faja et al. (2016) and are detailed in Supplemental Materials.

Stimuli and experimental procedure

Primary neural outcome: flanker. The flanker portion of the Child Attention Network Task (Rueda et al., 2004) was selected as a primary outcome given its sensitivity to EF training effects among children without ASD (Pozuelos et al., 2019; Rueda et al., 2005, 2012) and discrimination of children with ASD from children without (Faja et al., 2016). It included 12 practice and 108 test trials. Each trial began with a 150-ms beep paired with a 450-ms fixation cross at the center of the screen. Then, a target and flankers were presented for 2000 ms. Congruent trials (50%) consisted of a central target animal flanked by two animals on each side with the same orientation and size as the target. Incongruent trials (50%) were identical except that the target and flankers faced opposite directions. Children pressed a button indicating the direction the target animal faced (50% left, 50% right) and received feedback upon responding. The dependent variable was N2 mean amplitude.

Secondary neural outcome: Go/Nogo. The N2 was also examined with a cued Go/Nogo task. After reaching 80% accuracy on at least 20 practice trials, 200 test trials were presented in four blocks. Each trial was preceded by a 500-ms fixation cross followed by a 700-ms stimulus presentation. Go trials (70%) consisted of pressing a button each time a letter appeared on the screen. For Nogo trials (30%), responses were withheld when a specific letter appeared on the screen. To equate frequency across conditions, one Go letter appeared for 30% of trials and responses were analyzed only for that Go stimulus. To control for motor responses on the previous trial, only trials following correct Go responses were analyzed.

Included ERP data. Subjects with fewer than 10 trials per condition were excluded from analyses to optimize inclusion while maintaining an adequate signal-to-noise ratio (Lamm et al., 2006; Rueda et al., 2004; Todd et al., 2008). For children with adequate data at both timepoints (i.e. ⩾10 accurate trials per condition without movement artifacts), groups did not differ in the number of trials included, $F(1, 44)=3.33$, $p=0.08$, $\eta_p^2=0.07$, $M_{\text{Training}}=61.8\%$ (SD = 11.3), $M_{\text{Waitlist}}=54.4\%$ (SD = 16.2). Fewer children provided Go–Nogo data because it was always presented after the flanker task and groups did not differ in the number of trials included, $F(1, 29)=0.32$, $p=0.58$, $\eta_p^2=0.01$, $M_{\text{Training}}=49.0\%$ (SD = 10.4), $M_{\text{Waitlist}}=46.4\%$ (SD = 15.2).

Behavioral measures

Primary behavioral outcomes. Before and after training, two lab-based computer tasks and a broadband parent questionnaire were administered to evaluate changes in EF behavior. Higher scores for all primary outcomes indicate lower EF.

Change task. Following practice, four test blocks included Go trials (75%) and Change trials (25%) (De Jong et al., 1995; Oosterlaan & Sergeant, 1998). Change trials consisted of a visual signal to stop the dominant task (i.e. left/right button press) and change to the spacebar. To adjust for individual differences in reaction time (RT), each test block used the mean correct RT from the previous block, so stop signals occurred equally at 50, 200, 350, and 500 ms before each child's RT. The dependent variable was the stop signal reaction time (SSRT), which estimates the latency required to inhibit a dominant response when a stop signal was presented (Band et al., 2003; Crone & van der Molen, 2004). Higher scores indicated slower inhibition and shifting to the change response.

Stroop task. Following practice, test trials were presented in pseudorandom order for three conditions: (1) congruent (25%) with a color word written in the same color (e.g. *blue* written in blue); (2) incongruent (25%) with a color word written in a different color (e.g. *blue* written in red); and (3) neutral (50%) with a non-color word written in one of the four colors (e.g. *bear* written in blue) (Perlstein et al., 1998; Stroop, 1935). Button presses indicated the color of the text. The dependent variable was the difference between percent correct for congruent and incongruent trials. Higher scores indicated lower ability to suppress interfering information.

Behavior Rating Inventory of Executive Function. Caregiver-report of real-world EF was obtained as a measure of generalization (Gioia et al., 2000). The dependent variable was the Global Executive Composite.

Secondary behavioral outcomes. Five additional lab-based computer tasks and one parent questionnaire were administered to explore potential transfer of EF skills and changes in social ability. Higher scores for all secondary outcomes indicate better EF and social functioning.

Digit span. The numbers subtest of the Children's Memory Scale (CMS; Cohen, 1997) measured verbal working memory—an untrained EF subdomain. The dependent variable was the backward-scaled score.

Hungry Donkey. Hungry Donkey (Crone & van der Molen, 2004) measures decision-making in response to feedback—another untrained EF subdomain. Children fed a cartoon donkey by opening one of four doors with varying rewards and losses for 100 selections with feedback. Two doors were advantageous and resulted in net gains, and two were disadvantageous and resulted in net losses. Doors also varied on the frequency of loss (two high, two low). The dependent variable was the ratio of advantageous to disadvantageous selections for the final 40 trials.

TOM test. The TOM test measures social cognition via affective TOM, first-order false-belief, and second-order false-belief questions about drawings and vignettes. Reliability among raters was excellent ($r=0.93$). The dependent variable was percent correct.

ToM video composite. Two social cognition videos measured first-order false-belief about a location change (Saxe, 2009; Wimmer & Perner, 1983) and unexpected contents (Perner et al., 1987). The dependent variable was percent correct.

Social Attribution Task. Animated geometric figures (Heider & Simmel, 1944) were presented following the instructions and coding scheme used by Klin (2000). The animation is frequently understood as a social interaction and the task measures the degree to which the information is interpreted as social. The dependent variable was the problem-solving index (inter-rater reliability, $r=0.98$), which measured the number of correct responses to explicit questions.

Exploratory behavioral outcome

Repetitive Behavior Scale–Revised. Caregiver-report was collected to explore generalization to restricted and repetitive symptoms (Lam & Aman, 2007). The dependent variable was the total score.

Data analysis

Feasibility and acceptability were evaluated by examining the number of completed training visits and parent feedback. Efficacy data analyses were conducted without knowledge of group assignment and confirmed by an independent statistician. As specified in the a priori analysis plan, neural responses were examined via repeated measures analysis of variance (ANOVAs) because the group by condition by timepoint interaction was of primary interest. Planned behavioral analyses included examination of differences in baseline behavior via ANOVA and examination of treatment responses via analysis of covariance (ANCOVA)-of-change analyses controlling for baseline. Missing cases were excluded in a pairwise fashion so that for each dependent variable, all available participants who contributed data were included. Given the preliminary nature of this investigation, sample size, and measures of multiple levels of analysis, we did not correct for multiple comparisons.

Community involvement

ASD community members were not directly involved in the development of the research question and outcome measures, design of the study, its implementation, or the interpretation and dissemination of the findings.

Results

Feasibility and acceptability

All families assigned to the training group completed training and returned for follow-up; 89% completed all 10 planned training sessions and all families completed at least 7 sessions. Twenty-three families returned the feedback questionnaire of whom 74% ($n=17$) reported at least some improvement for their children and 83% ($n=19$) felt it improved their knowledge of EF or their ability to help their children develop EF. Additional qualitative responses are included in Supplemental Materials.

Neural responses

Primary neural outcome. Across both timepoints including baseline, the groups had significant differences in overall flanker N2 amplitude, $F(1, 44)=8.45$, $p=0.006$, $\eta_p^2=0.16$ (Training: M=−0.56, SD=3.22; Waitlist: M=−3.32, SD=3.22). Critically, the group (treatment/waitlist) by time (baseline/follow-up) by condition (congruent/incongruent) interaction was significant, $F(1, 44)=7.37$, $p=0.009$, $\eta_p^2=0.14$ (Figure 2).[1] No other main effects (condition) or interactions (condition × time, group × time) were significant (Fs < 2.70, ps > 0.10, $\eta_p^2<0.06$).

In order to interpret the interaction between group × time × condition, groups were examined separately. The training group exhibited a significant effect of time ($F(1, 23)=9.32$, $p=0.006$, $\eta_p^2=0.29$), and the change in amplitude over time differed by condition (time× condition) ($F(1, 23)=5.09$, $p=0.034$, $\eta_p^2=0.18$). Contrasts to compare changes for each condition indicated a significant increase in incongruent amplitude (i.e. more negative) ($F(1, 23)=14.58$, $p=0.001$, $\eta_p^2=0.39$), but not congruent amplitude ($p=0.23$), indicative of normalized differentiation between conditions. The waitlist group did not exhibit changes overall or by condition (Fs < 2.77, ps > 0.11).

Secondary neural outcome. The group × time × condition (Go/Nogo) interaction was non-significant despite a medium effect size ($F(1, 29)=2.92$, $p=0.098$, $\eta_p^2=0.09$).

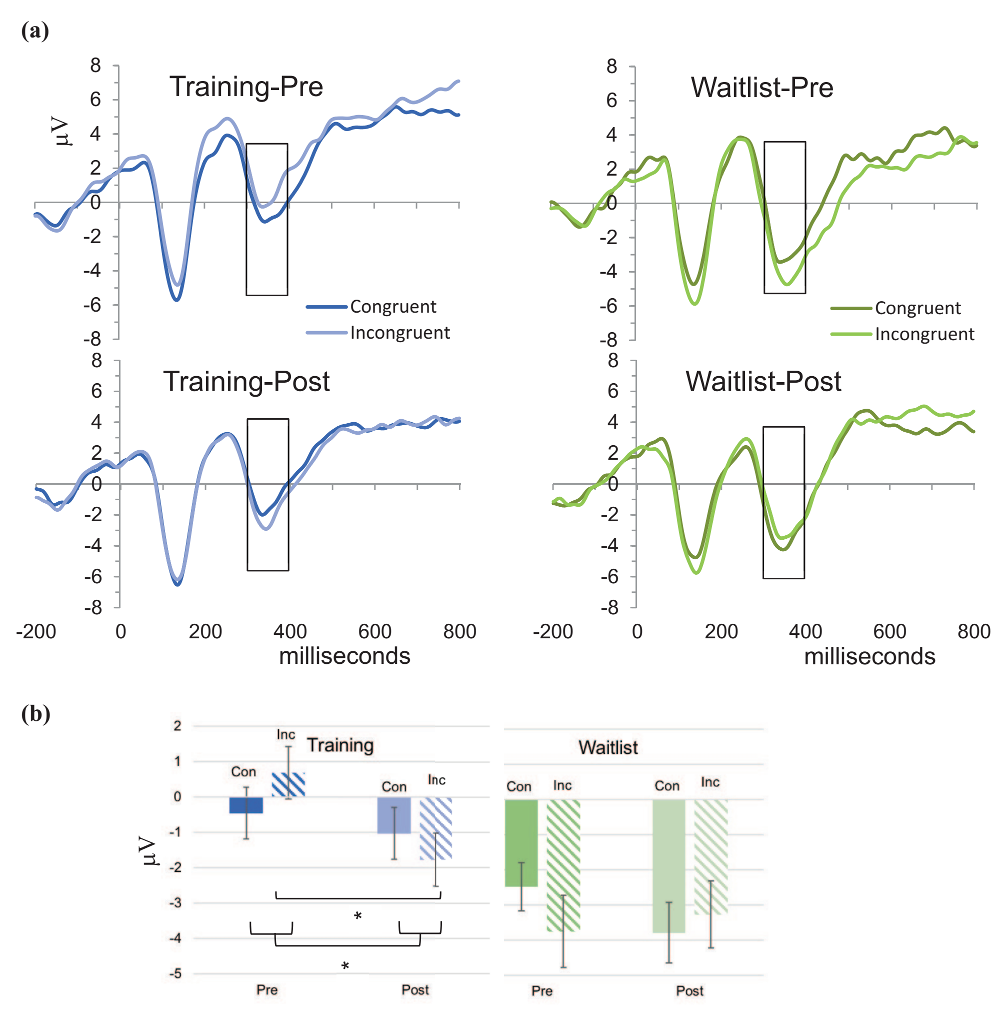

Figure 2. (a) ERP waveforms for the frontal electrode cluster (Fz) by timepoint and the flanker task condition and (b) time × flanker condition interaction for N2 mean amplitude.

Primary behavioral outcomes

At baseline, on average, both groups had EF challenges in the clinical range (Behavior Rating Inventory of Executive Function (BRIEF); Table 1). No group differences were detected in lab-based tasks or parent report of EF (see Table 2 and Figure 3 for all results).

Following training, no differences were detected between groups for the lab-based tasks (Change, Stroop) or generalization of EF skills beyond the lab by parent report on the BRIEF Global Executive Composite.

Secondary behavioral outcomes

At baseline, no group differences were detected for secondary outcome measures. After training, no changes were detected for verbal working memory, decision-making, social cognition, or social function.

Exploratory behavioral outcome

At baseline, groups differed in the severity of repetitive behaviors ($F(1, 58) = 5.47$, $p = 0.02$, $\eta_p^2 = 0.09$). Critically, when controlling for baseline, the training group exhibited lower levels of repetitive behavior following training ($F(1, 57) = 10.24$, $p = 0.002$, $\eta_p^2 = 0.15$).

Discussion

This study examined the initial efficacy of a computer-based EF training augmented by in-person metacognition coaching for children with ASD. We hypothesized that a signal would be most likely detected via neural measures of EF and challenging lab-based tasks that most directly related to training (Diamond, 2013). The training group demonstrated significantly increased neural differentiation of incongruent flankers at post-testing, whereas the

Table 2. Scores before and after training ($N = 68$).

Primary outcomes	Baseline			Post-testing			
	Sample size	Training	Waitlist	Training	Waitlist	Baseline	Post-testing
	N_T, N_{WL}	M (SD)	M (SD)	M (SD)	M (SD)	ANOVA, η_p^2 / d	ANCOVA, η_p^2 / d
Change SSRT	31, 30	233.8 (87.8)	238.3 (94.3)	213.6 (78.5)	234.7 (98.1)	$F(1, 59) = 0.04$, 0.001/−0.05	$F(1, 58) = 0.86$, 0.02/−0.24
Stroop task con-inc	34, 29	0.038 (0.08)	0.060 (0.12)	0.029 (0.13)	0.038 (0.09)	$F(1, 61) = 0.79$, 0.013/−0.22	$F(1, 60) = 0.07$, 0.001/−0.08
BRIEF GEC	33, 30	66.55 (11.51)	68.40 (10.19)	65.85 (9.96)	67.76 (10.42)	$F(1, 61) = 0.52$, 0.008/−0.17	$F(1, 60) = 0.07$, 0.001/−0.19
Flanker N2 con mean amp	24, 22	−0.198 (3.22)	−2.495 (3.26)	−1.050 (3.62)	−3.737 (4.09)		
Flanker N2 inc mean amp		0.825 (3.32)	−3.771 (4.84)	−1.798 (3.68)	−3.285 (4.49)		
Secondary outcomes							
Digit span	33, 30	10.42 (3.45)	9.83 (3.55)	10.15 (3.17)	9.55 (3.55)	$F(1, 61) = 0.45$, 0.007/0.17	$F(1, 60) = 0.27$, 0.004/0.18
Hungry Donkey	33, 31	1.39 (10.85)	0.16 (10.28)	0.33 (11.67)	1.74 (11.91)	$F(1, 62) = 0.22$, 0.003/0.12	$F(1, 61) = 0.25$, 0.004/−0.12
SSIS	32, 30	81.63 (12.48)	80.47 (15.66)	81.69 (10.55)	79.33 (14.17)	$F(1, 60) = 0.10$, 0.002/0.08	$F(1, 59) = 0.80$, 0.01/0.19
TOM task	34, 33	66.33 (14.34)	62.52 (12.72)	70.98 (12.32)	65.07 (10.49)	$F(1, 65) = 1.32$, 0.02/0.28	$F(1, 64) = 3.13$, 0.05/0.52*
Theory of mind composite	31, 29	74.93 (25.49)	70.94 (28.94)	89.52 (20.18)	84.48 (26.23)	$F(1, 58) = 0.33$, 0.006/0.15	$F(1, 57) = 0.38$, 0.007/0.22
Social attribution task	24, 21	34.58 (16.41)	33.81 (16.88)	32.92 (16.28)	30.95 (15.13)	$F(1, 43) = 0.02$, 0.001/0.05	$F(1, 42) = 0.17$, 0.004/0.13
Go N2 mean amp	16, 15	−2.409 (2.82)	−2.897 (4.06)	−1.090 (2.14)	−2.309 (2.99)		
Nogo N2 mean amp		−1.572 (3.44)	−3.028 (4.29)	−2.780 (3.57)	−2.525 (4.51)		
Exploratory outcome							
RBS-R total score	31, 29	16.61 (10.75)	24.14 (14.06)	13.61 (9.04)	27.03 (17.90)	$F(1, 58) = 5.47$, 0.09/−0.60*	$F(1, 57) = 10.24$, 0.15/−0.96**

SD: standard deviation; ANOVA: analysis of variance; ANCOVA: analysis of covariance; η_p^2: partial eta squared effect size estimate; *d*: Cohen's d effect size estimate; SSRT: stop signal reaction time; BRIEF GEC: Behavior Rating Inventory of Executive Function Global Executive Composite; con: congruent; inc: incongruent; amp: amplitude; SSIS: Social Skills Improvement System rating scales; TOM: theory of mind; RBS-R: Repetitive Behavior Scale–Revised.

$^*p < 0.1$; $^{**}p < 0.01$.

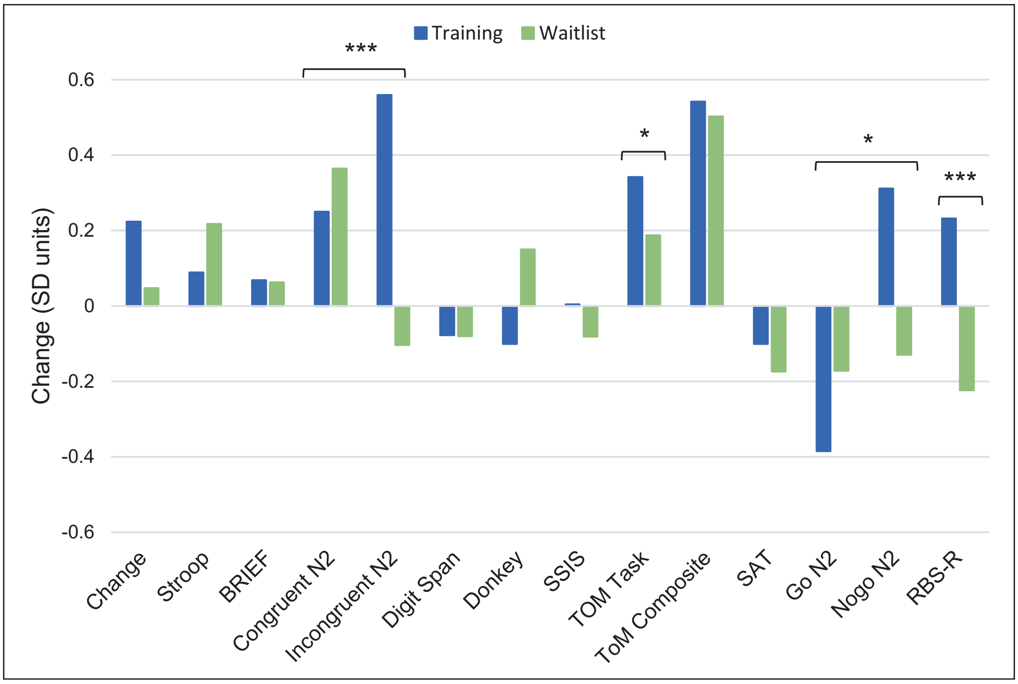

Figure 3. Differences between baseline and post-training. Scores were computed by calculating the z-scores relative to the combined group means at baseline and are presented so that positive values reflect better functioning following training.

*$p < 0.01$, **$p < 0.05$, ***$p < 0.01$.

waitlist group did not. Neural differentiation develops by age 6 among children without ASD (Buss et al., 2011), suggesting training may lead to more age-appropriate neural responses and enhanced monitoring of conflicting information to support effective EF. Although non-significant, a similar pattern was observed for the Go–Nogo task (i.e. more negative N2 amplitude for Nogo relative to Go trials after training compared to the waitlist group).

Given these findings, we then examined behavioral outcomes for lab-based measures of related EF subdomains, generalization, and transfer of skills. Lab-based tasks examining response inhibition combined with shifting ability and interference suppression were not sensitive to training. Even with more comprehensive and intensive training, results on lab-based tasks have been mixed for children with ASD. Specifically, Yerys et al. (2019) reported a non-significant within group change on a related lab-based task with a medium–large effect size. de Vries et al. (2015) reported a non-significant trend for working memory training on one of two working memory tasks and no effects related to flexibility for either EF training group. Kenworthy et al. (2014) found significant, medium effects on their challenge task for the flexibility domain but not for the planning portion. Unsurprisingly, we found no evidence of significant transfer to social cognition or function or to untrained EF subdomains (verbal working memory, decision-making), which was consistent with other studies that reported non-significant transfer in lab-based social (Kenworthy et al., 2014) or untrained EF tasks (de Vries et al., 2015). Generalization to affect regulation was observed among children without ASD who completed a similar EF training program (Pozuelos et al., 2019; Rueda et al., 2005, 2012) suggesting that this type of training may confer a greater benefit to children without neurodevelopmental disorders. Nonetheless, our findings are consistent with a meta-analysis of EF training programs that indicates most have limited transfer (Kassai et al., 2019).

Following the suggestion that EF training may be helpful in ameliorating restricted and repetitive behavioral symptoms for children with ASD (Kenworthy et al., 2014), we explored this domain and found the training group had reduced parent-reported symptoms when controlling for baseline levels. In contrast, parent report of general real-world EF skills did not change following training, although some parents reported specific training-related changes. Generalization and the overall lack of behavioral EF changes are a concern for children with ASD (Ramdoss et al., 2012).

It is possible that children with ASD may require more than 10 h of intervention in order to demonstrate the improvements made by children without ASD in response to a similar EF training program, which included both N2 changes and behavioral improvements in inhibitory control (Pozuelos et al., 2019; Rueda et al., 2005, 2012). Yet, the computer training with greatest intensity for children with ASD (18.75 h) yielded no significant treatment-related effects on real-world EFs, social behavior, or quality of life, despite a trend for slightly improved ADHD behavior in the working memory training group (de Vries et al., 2015). It may also be the case that subject selection limited our ability to detect more generalized changes. Project EVO selected children with ASD and co-occurring ADHD and reported significant reductions in ADHD symptoms, EF challenges, and social difficulties with large effect sizes after only 8.3 h of training. Computer-based EF training is generally more limited in its benefits for TD children than comprehensive, curriculum-based training (Diamond, 2013; Kassai et al., 2019) such that greater intensity of computer-based training may not provide the same benefit of curriculum-based training. Indeed, curriculum-based training resulted in changes on parent and teacher report of set-shifting and planning (Kenworthy et al., 2014) for children with ASD; however, the scalability of such comprehensive interventions is difficult. Computer-based EF training is appealing for service delivery across settings and to individual children. Thus, given an initial "signal" on the primary neural outcome measure, it will be critical to determine whether a larger dose of computer-based EF training or selection of a more impaired group leads to more robust behavioral changes.

Our training differed from previously published computer-delivered EF training for ASD (de Vries et al., 2015; Yerys et al., 2019) because it included coaching, the content was broader (inhibition, set-shifting working, memory, and metacognition), it was relatively less intense, and participant selection differed, although our program was similar to these programs in that the games were adaptive and adjusted difficulty according to child performance. Given that EF training is thought to have its greatest impact when task demands exceed a child's current abilities (Holmes et al., 2009; Karbach et al., 2015), coaches encouraged children with ASD to continue to play and provided emotional regulation and EF strategies. Thus, computer-based training combined with coaching may confer some of the benefits of a more comprehensive EF curriculum in the context of an inexpensive, individualized format. Prior to the implementation of such programs, it will be critical to determine which aspects of EF training promote generalization from initial neural changes to clinically significant effects such as the reduction of restricted and repetitive behaviors and improved EF behavior.

Limitations and future directions

The current investigation demonstrated the initial neural effects of computer-based EF training for ASD but raises additional questions for future research. First, although a variety of computer-based interventions have been used to enhance the EF of TD children (Jaeggi et al., 2011; Karbach & Kray, 2009; Karbach & Unger, 2014; Rueda et al., 2005, 2012; Thorell et al., 2009), children with larger initial EF impairments tend to have the largest gains (Diamond, 2013). Likewise, Project EVO reported moderate–large effect sizes within a training group comprised of children with ASD + ADHD (Yerys et al., 2019). The current investigation did not specifically select children with ASD who had initial EF impairments. If targeted interventions such as EF training are to have their greatest benefit, it will be critical to determine which children with ASD are most likely to benefit and respond to training including samples with more diverse backgrounds.

Second, a *brief* 10 session duration was selected for the initial examination of efficacy based on prior reports of similar training with children without ASD (Pozuelos et al., 2019) while also balancing the demand on child and family time. The intensity of training—either more regular training sessions (Yerys et al., 2019) or more hours of intervention (Kenworthy et al., 2014)—may be especially critical for children with ASD. Embedding comprehensive interventions like *Unstuck and On Target* in the classroom likely increases the opportunities to practice new EF skills—further increasing the intensity. Future systematic studies are needed to determine the optimal intensity.

Third, it will be important to determine whether training generalizes to more clinically significant changes. It is possible that, as predicted, changes in brain responses may precede or lay the foundation for additional behavioral changes (e.g. Chen et al., 2016; McDermott et al., 2018; Tremblay et al., 1998) that could be detected via longer-term follow-up. Indeed, conflict monitoring, detected via the N2, may underlie successful inhibitory control, particularly earlier in development (Richardson et al., 2018). However, this study did not include follow-up beyond immediate post-testing. In addition, given our sample size, power estimates indicate that only large behavioral effects could be detected. Replication of initial findings with a larger sample combined with long-term follow-up will allow for examination of these possibilities and more rigorous analyses.

Finally, although initial data demonstrate that our training program may be feasibly conducted with fidelity to the delivery of computer games and basic elements of the manualized intervention and that training is acceptable to families, it will be useful to elicit input from other key stakeholders to inform the implementation and dissemination of programs like ours. Future work that elicits formal acceptability data from children with ASD who receive the training and the input of other stakeholders including community providers and autistic self-advocates will be valuable in refining EF training to best meet the needs of children on the spectrum.

In summary, this study demonstrated that 10 h of targeted EF training delivered to 7- to 11-year-old children on the autism spectrum via computer combined with coaching led to changes in neural response and parent report of restricted and repetitive behaviors. This work adds to a previous clinical trial of curriculum-based EF intervention and an app for children with ASD + ADHD to show that the significant EF difficulties experienced by many children with ASD may be reduced via intervention. For the substantial subgroup of children with ASD who experience EF difficulties, this represents an important development in identifying more individualized intervention because EF is related to the development of social competence and the expression of ASD symptoms (Faja & Nelson Darling, 2019; Geurts, de Vries, & van den Bergh, 2014; Pellicano, 2013).

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Supplemental material

Supplemental material for this article is available online.

Note

1. Results remained the same without two children with extreme N2 amplitudes: group × time × condition remained significant ($F=5.96$, $p=0.02$, $\eta_p^2 = 0.12$), and groups differed ($F=5.65$, $p=0.02$, $\eta_p^2 = 0.12$).

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