BRIEF REPORT

The Early Start Denver Model Intervention and Mu Rhythm Attenuation in Autism Spectrum Disorders

Benjamin Aaronson1 [·](http://orcid.org/0000-0002-4180-377X) Annette Estes2 · Sally J. Rogers3 · Geraldine Dawson4 · Raphael Bernier5

Accepted: 6 July 2021 / Published online: 26 July 2021

© The Author(s), under exclusive licence to Springer Science+Business Media, LLC, part of Springer Nature 2021

Abstract

We examined the relationship between the Early start Denver model (ESDM) intervention and mu rhythm attenuation, an EEG paradigm refecting neural processes associated with action perception and social information processing. Children were assigned to either receive comprehensive ESDM intervention for two years, or were encouraged to pursue resources in the community. Two years after intervention, EEG was collected during the execution and observation of grasping actions performed by familiar and unfamiliar agents. The ESDM group showed signifcantly greater attenuation when viewing a parent or caregiver executing a grasping action, compared with an unfamiliar individual executing the same action. Our fndings suggest that the ESDM may have a unique impact on neural circuitry underlying social cognition and familiarity.

Keywords Mu rhythm · Autism spectrum disorders · Early start denver model · EEG

Introduction

The attenuation of the mu rhythm in the human brain has been demonstrated during the observation and execution of motor actions, and has been characterized as an observationexecution matching system (Muthukumaraswamy & Johnson, [2004](#page-8-0)) Mu attenuation is theorized to play an integral role in action interpretation along with more advanced elements of social cognition (for review, see Kilner & Lemon, [2013;](#page-8-1) Rizzolatti & Craighero, [2004\)](#page-8-2). There has been signifcant interest spanning over two decades in this neural system, including multi-modal experimental investigations and complex theoretical models (Heyes & Catmur, [2020](#page-7-0)). While there has been some concerns expressed regarding

 \boxtimes Benjamin Aaronson ba1@uw.edu

- Department of Pediatrics, University of Washington, Box 357920, Seattle, WA 98195, USA
- Department of Speech and Hearing Sciences, University of Washington, Seattle, WA, USA
- ³ Department of Psychiatry and Behavioral Sciences, UC Davis Mind Institute, Sacramento, CA, USA
- ⁴ Department of Psychiatry and Behavioral Sciences, Duke University, Durham, NC, USA
- ⁵ Department of Psychiatry and Behavioral Sciences, University of Washington, Seattle, WA, USA

the interpretation of the EEG mu rhythm in particular (Coll et al., [2017](#page-7-1); Hobson & Bishop, [2016](#page-7-2), [2017\)](#page-7-3), others have continued to defend it as useful index of neural activity (Bowman et al., [2017;](#page-7-4) Vanderwert et al., [2013](#page-9-0)).

Oberman and colleagues ([2005](#page-8-3)) investigated mu attenuation in a sample of individuals ages 6–47 (mean $age = 16.6$) with a clinical diagnosis of ASD and corresponding sample of age and gender-matched controls. They found that although the ASD group displayed mu attenuation during the execution of motor actions, mu attenuation was not exhibited during the observation of motor actions (Oberman et al., [2005\)](#page-8-3). Later studies replicated this fnding (Bernier et al., [2007](#page-7-5); Martineau et al., [2008\)](#page-8-4) and demonstrated a correlation between mu attenuation and imitation ability in a sample of adults (mean age = 25.15) with ASD (Bernier et al., 2007). Further studies failed to show diferences between diagnostic groups (Fan et al., [2010](#page-7-6); Raymaekers et al., [2009](#page-8-5)), although a subsequent study in children (mean $age = 6.65$) demonstrated that mu attenuation correlated with imitation ability, independent of diagnosis (Bernier et al., [2013](#page-7-7)), noting that since imitation deficits are commonly associated with ASD but are not part of the diagnostic criteria, ASD groups may inconsistently demonstrate mu attenuation depending on imitation and social cognitive abilities. Other studies have not supported a correlation with imitation abilities (Fan et al., [2010](#page-7-6); Ruysschaert et al., [2014](#page-8-6)),

though imitation was assessed through various and potentially less rigorous methods (for a critical review, see Hobson & Bishop, [2017\)](#page-7-3). A review of 4 EEG studies found a signifcant relationship between mu attenuation and age, irrespective of diagnosis (Oberman et al., [2013](#page-8-7)).

Familiarity may be a signifcant factor in modulating neural functioning. For example, face processing diferences have been well documented in ASD (Dawson et al., [2005](#page-7-8); McPartland et al., [2004](#page-8-8); Pierce, [2001;](#page-8-9) Schultz et al., [2000](#page-8-10); for review see Campatelli et al., [2013\)](#page-7-9). However, familiarity with the face seems to alleviate the observed diferences (Pierce & Redcay, [2008](#page-8-11); Pierce et al., [2004\)](#page-8-12). Similar results were found using eye-tracking to observe diferential gaze patterns (Gillespie-Smith et al., [2014](#page-7-10)). Familiarity and attentional engagement have also been shown to modulate ERPs to faces (Dawson et al., [2002](#page-7-11)).

Oberman and colleagues ([2008](#page-8-13)) examined mu attenuation in children ages $8-12$ (mean age = 10.23) with ASD in response to the observation of familiar and unfamiliar actors. They found that the children with ASD showed greater activation in response to the observation of familiar actors compared with unfamiliar actors (Oberman et al., [2008\)](#page-8-13). However, in this paradigm, the unfamiliar condition contained only a video of a hand without a person visible in the screen, whereas the familiar condition contained both the familiar individual and hand. This requires an inference as to the presence of an unfamiliar person. Given documented defcits in holistic processing in ASD (Behrmann et al., [2006](#page-7-12); Dawson et al., [2005;](#page-7-8) Nakahachi et al., [2008\)](#page-8-14), this may have infuenced the lack of attenuation to the unfamiliar condition in the ASD group (Oberman et al., [2008\)](#page-8-13). It is also not clear whether the familiarity effect is evident in younger individuals with ASD or whether it may be enhanced through interventions that promote social learning and development.

The early start Denver model (ESDM; Dawson et al.,[2010,](#page-7-13) [2012\)](#page-7-14), a naturalistic developmental behavioral intervention (Schreibman et al., [2015\)](#page-8-15), focuses on building foundational cognitive, social, communication, motor, and adaptive skills, using evidence-based teaching practices. It incorporates principles of applied behavior analysis and developmental science to inform a developmental curriculum that targets goals across key domains. Caregivers receive training in basic ESDM strategies facilitating implementation across environments. There is a specifc emphasis on facilitating caregiver-child engagement and interaction, with a focus on foundational social affective processes. A randomized-control trial examining the efficacy of the ESDM demonstrated signifcant gains in IQ, language development, social, and adaptive skills (Dawson et al., [2010](#page-7-13)) and these gains were generally maintained 2 years after treatment ended (Estes et al., [2015\)](#page-7-15). There have since been further extensions (Rogers et al.,[2019a](#page-8-16)) and replications (Rogers et al., [2019b\)](#page-8-17) examining the clinical impact of ESDM.

In a follow-up study of this ESDM sample, changes in brain activity attributed to ESDM intervention were identifed (Dawson et al., [2012\)](#page-7-14). EEG activity (event-related potentials and spectral power) was measured during the presentation of faces versus objects. The ESDM group and chronological-age-matched typical children showed a shorter Nc latency and increased cortical activation (decreased alpha power and increased theta power) when viewing faces, whereas the community group showed the opposite pattern (shorter latency event-related potential and greater cortical activation when viewing objects). Greater cortical activation while viewing faces was associated with improved social behavior (Dawson et al., [2012](#page-7-14)). Additional studies have shown changes in brain activity in response to pivotal response treatment using fMRI. A study examining the effects of 4 months of pivotal response treatment indicated greater activation in the right posterior superior temporal sulcus, fusiform gyrus, dorsolateral and ventrolateral prefrontal cortex, key brain areas related to biological motion (Voos et al., [2013\)](#page-9-1). A further study of pivotal response treatment demonstrated reduced activation in thalamus, amygdala, and hippocampus post treatment in a group that displayed hyperactivation at baseline, and increased activation in the ventral striatum and putamen in a group that displayed hypoactivation at baseline (Ventola et al., [2015](#page-9-2)).

Given ESDM's presumptive impact on IQ, language development, and adaptive skills, with a focus on foundational social afective processes, mu attenuation may be an appropriate marker of treatment change given its role as an index of neural activity related social cognition.

Purpose and Hypotheses

Our primary aim was to investigate the relationship between ESDM intervention and neural activity underlying social cognitive abilities, as assessed by EEG mu attenuation. The current study capitalizes on the rigorous design of the ESDM intervention study (Dawson et al., [2010](#page-7-13)), and applies a carefully defned and established social neuroscience paradigm of mu rhythm attenuation. Given the evidence that ESDM impacts neural functioning (Dawson et al., [2012\)](#page-7-14), that the intervention targets social cognitive behaviors such as imitation (Dawson et al., [2010](#page-7-13); Rogers et al., [2012](#page-8-18)), and that mu attenuation is linked to imitation ability (Bernier et al., [2007,](#page-7-5) [2013](#page-7-7)), we hypothesized greater mu attenuation in response to the observation of motor actions would be found in the ESDM group as compared with the community group. A further aim was to examine the impact of familiarity on this neural index. We hypothesized that greater mu attenuation would be observed across both groups in response to viewing familiar actors compared with unfamiliar actors.

Methods

All procedures were reviewed and approved by our Institutional review board (IRB).

Participants

Participants were recruited from the original 48 participants in the ESDM randomized controlled trial (Dawson et al., [2010](#page-7-13)). As described in that trial, forty-eight children between 18 and 30 months with a documented diagnosis of an autism spectrum disorder were randomized into two groups using a stratifed randomization procedure based on gender and IQ. The intervention (ESDM) group received two years of comprehensive behavioral intervention by trained ESDM therapists in children's homes for 15.2 h per week. The community (COM) control group received regular assessment and monitoring and was encouraged to pursue services available in the community. Measures of IQ, ASD symptoms, adaptive behavior, and repetitive behavior were collected at one-year post-entry and two years post-entry into the study by clinicians who were blind to subject status. These fndings have been previously reported (Dawson et al., [2010\)](#page-7-13).

In the current study, participants were recruited to participate in a follow-up study when the children were 6 years of age, approximately 2 years post-experimental intervention. Of the original sample, 39 children participated in the follow-up study. Clinicians who were naive to intervention group status collected measures of IQ (Diferential Abilities Scales), adaptive behavior (Vineland Adaptive Behavior Scales), and ASD symptoms using the Autism diagnostic observation schedule (ADOS; Lord et al., [2000\)](#page-8-19). These

results have also been previously reported (Estes et al., [2015](#page-7-15)).

Of the 39 children who participated at the 6-year old time point, 27 participants agreed to participate in the EEG assessment within 4 weeks of their 6th birthday. Twenty participants (10 ESDM, 10 COM group) completed the EEG assessment successfully and produced usable EEG data. Seven participants did not produce usable data. In the ESDM group, 3 did not produce artifact free rest data, and 1 did not complete the paradigm. In the COM group, 1 did not produce artifact free rest data, and 2 did not complete the paradigm. The group of 20 that participated in the EEG demonstrated higher IQ than the 19 that did not participate in the EEG $t(37) = 3.60$, $p < 0.05$. This is consistent with other ASD imaging research, which often features children with higher IQ due to the constraints of participation. The intervention and community groups that participated in the EEG did not difer signifcantly in age, gender, verbal IQ, nonverbal IQ, adaptive behavior, or autism symptoms. Results of these comparisons are listed in Table [1.](#page-2-0) Thus the EEG assessment was conducted on well-matched groups.

EEG Assessment

Brain activity was recorded at rest and during the observation and execution of motor actions using a 128-electrode EEG system (Electrical Geodesics, Eugene OR). The electrical brain activity was analog fltered (01. Hz high-pass, 100 Hz elliptical low-pass), amplifed, and digitized at 500 samples per second. Impedances were below 50 k Ω with signals referenced to the vertex at acquisition. EEG and video were recorded simultaneously using NetStation 4.3. This allows for subsequent video inspection of the session to ensure the participant was attending to the presented stimuli,

GCA general conceptual ability, *ABC* adaptive behavior composite, *ADOS CSS* autism diagnostic observation schedule - calibrated severity score

**p*<.05 when adjusted for multiple comparisons using Bonferroni (controlling familywise by construct). Observed unadjusted *p*-values also given

Table 1 Comparison of measures collected at age six: ESDM and community subsamples with EEG data

and assists with identifying eye blink and other movement artifacts.

EEG Paradigm

The paradigm included an observe condition, an execute condition, and a rest condition to evaluate baseline activity, adapted from an established procedure designed to assess mu attenuation via EEG (Muthukumaraswamy & Johnson, [2004\)](#page-8-0). In the observe condition, participants watched a 6-s clip on a video monitor displaying a person grasping a block of wood. Within the observe condition, participants observed videos of their parent or guardian conducting a grasping motion, as well as an unfamiliar person executing the same grasping motion. This allowed for the examination of potential diferential brain responses to the observation of actions performed by familiar versus unfamiliar actors. A photocell installed on the video monitor allowed the EEG recording to be time-locked to the display of the grasping motion. In the execute condition, participants grasped a block of wood identical to the one displayed in the video clip. A sensor on the block of wood allowed the EEG recording to be time-locked to the participant's grasping motion. In the rest condition, participants sat with eyes opened and watched a plus sign on the monitor.

The blocks proceeded as follows: Unfamiliar Observe (10 trials), Familiar Observe (10 trials), Execute (10 trials), Rest (30 s), Unfamiliar Observe (10 trials), Familiar Observe (10 trials), Execute (10 trials), Rest (30 s). Block order was counterbalanced for familiarity to eliminate order efects.

EEG Analysis

While signals are referenced to the vertex at acquisition, signals were re-referenced to an average reference offline. Artifact detection was conducted using an automated algorithm in NetStation 4.3 to remove eye-blinks and movement artifacts, defned as and fast average amplitudes exceeding 200 μ Vs, differential average amplitudes exceeding 100 μVs, and zero variance across trials. Manual video inspection using NetStation 4.3 ensured subjects were attending to the stimuli, and further visual inspection of each trial to eliminate eye-blinks was conducted, identifying any large power changes across frontal electrodes in the 1–4 Hz band. Matlab was also used to identify trials with movement artifacts indicated by large power fuctuations within a trial to be excluded from analysis. The rejection rate did not differ across groups, with an average rejection rate of 53.38% (intervention 52.50%, community 54.25%).

Following procedures outlined by Muthukumaraswamy and colleagues ([2004](#page-8-0)), a group of eight electrodes in each hemisphere surrounding the standardized positions for C3 and C4 respectively were selected for analysis. A photocell

was used to identify the culmination of the grasping motion during the observe condition, and 1 s of data preceding and succeeding the grasp was selected for analysis. The output from each condition was divided into 2-s epochs and a fast Fourier transform (FFT) was performed. Similar to previously described methods focused on the mu (8–13 Hz) range (Babiloni et al., [1999;](#page-7-16) Muthukumaraswamy et al., [2004](#page-8-20); Muthukumaraswamy & Johnson, [2004;](#page-8-0) Pfurtscheller et al., [1997\)](#page-8-21), individual spectral plots were generated for each subject, and the Hz band yielding the maximum diference in power between the execute condition and rest condition was selected as the subject's specifc Hz band, instead of averaging across the entire range (Coll et al., [2017;](#page-7-1) Marshall & Meltzoff, 2011 ; Wang et al., 2012). The mean identified peak frequency was 8.55 (SD = 1.26) for the ESDM group and for the COM group was 8.00 (SD = 0.913). The mean did not differ across groups $t(18) = 1.21$, $p = 0.28$. Power was averaged across trials within conditions and across blocks, and these values were then exported to Matlab in order to provide a single numerical value representing the average power for a given condition.

This paradigm yields a score representing a scale-dependent variable of mu attenuation. This was calculated by computing the log of the ratio between the observe and rest condition. The dependent variables of interest are the log of the ratio of the observe-familiar over the rest condition, and the log of the ratio of the observe-unfamiliar over the rest condition. This yields a single numerical value representing mu attenuation for a given subject in a given condition, which can be compared across conditions and across subjects.

Results

An examination of studentized residuals revealed no outliers $(>=\pm 3)$. Shapiro–Wilk's test ($p>0.05$) and visual inspection of Q-Q Plot indicated the data was normally distributed. Levene's test showed homogeneity of variance $(p > 0.05)$ and Box's test of equality of covariance matrices showed homogeneity of covariances $(p=0.750)$. *t*-Tests revealed no signifcant diferences in overall power between groups during the observe familiar $t(18)=0.38$, $p>0.05$, observe unfamiliar *t*(18)=. 96, *p*>0.05, and rest *t*(18)=1.42, *p*>0.05 conditions, indicating consistent recording and analysis across groups. Values by individual subject are represented in Fig. [1](#page-4-0) and listed in Table [2](#page-5-0).

A two-way repeated measures ANOVA was computed to examine main efects of group and familiarity on mu attenuation, as well as the interaction between the two. As shown in Fig. [2,](#page-5-1) results indicated no main effect for group $(F(1,19)=1.23, p>0.05,$ partial $p^2=0.000$) and no signifcant diference between mu attenuation to familiar and unfamiliar actions within subjects, $F(1,18) = 2.35$, $p > 0.05$,

Fig. 1 Attenuation of mu rhythm in response the observation of a motor action, by individual subject, divided by familiar or unfamiliar actor over rest condition

partial η^2 =0.115. However, there was a significant familiarity by group interaction, $F(1,18) = 6.405$, $p < 0.05$, partial η^2 = 0.262, with the intervention group showing significantly greater mu attenuation during familiar observation (Fig. [2](#page-5-1)).

Correlational analyses of mu attenuation with measures of Global conceptual ability (GCA) as assessed by the Differential abilities scale II (DAS-II; Elliot, [2007](#page-7-17)), hand and face imitation as assessed by the Mature Imitation Task (Rogers et al., [2005](#page-8-23)), and autism symptoms based on the ADOS (Lord et al., [2000](#page-8-19)) calibrated severity score are displayed in Table [3.](#page-6-0) There was no signifcant correlation between mu attenuation and global conceptual ability, hand or face imitation, or autism symptom severity (Table [3](#page-6-0)).

Discussion

The primary aim of this study was to further examine neural functioning in young children with ASD who received intensive early comprehensive intervention based on the ESDM or services in the community. We found that mu attenuation during the observation of grasping actions did not difer between the intervention (ESDM) and community (COM) groups, as both groups displayed attenuation to the observation of motor actions. However, there was a signifcant group by treatment interaction in which mu attenuation was greater within the ESDM group when viewing a parent or caregiver versus an unfamiliar individual executing identical actions.

Table 2 Attenuation of mu rhythm values in response the observation of a motor action, by individual subject, the log transform of the familiar or unfamiliar condition over rest condition

	Fam/Rest	Unfam/Rest
ESDM 1	-0.545344	-0.267628
ESDM ₂	-0.595952	-0.706332
ESDM ₃	-0.25255	-0.1491
ESDM 4	-1.40263	-1.006261
ESDM 5	-0.41936	-0.056478
ESDM 6	-0.833425	-0.747447
ESDM 7	-0.325708	-0.492652
ESDM 8	-0.587256	-0.169914
ESDM 9	-0.550415	-0.356417
ESDM 10	-0.85611	-0.292363
COM ₁₁	-0.281792	-0.483899
COM ₁₂	-0.623051	-0.61536
COM ₁₃	-0.499026	-0.412485
COM ₁₄	-0.673415	-0.802769
COM ₁₅	-0.135408	-0.324267
COM 16	-0.576126	-0.394285
COM17	-0.402416	-0.221742
COM 18	-0.100604	-0.676819
COM ₁₉	-0.480141	-0.378821
COM ₂₀	-0.019974	-0.003919

The COM group showed no diference in mu attenuation when viewing familiar versus unfamiliar individuals. Our fndings suggest a potential relationship between the ESDM and neural development in a carefully designed paradigm. Our study provides evidence indicating a potential efect of the ESDM on neural activity underlying social-cognitive processes.

Overall, the presence of a familiarity efect is consistent with existing literature. Our fndings may indicate unique neural responsiveness to familiarity. Previous research has demonstrated sensitivity within neural circuitry associated with social cognition to context (Iacoboni, [1999\)](#page-7-18), intention (Iacoboni et al., [2005\)](#page-7-19), and even experience with the action being performed (Calvo-Merino et al., [2006\)](#page-7-20). However, the observed diference may also be the result of modulation from other brain regions sensitive to familiarity (Perkins et al., [2010](#page-8-24)). With connections to the limbic system (Carr et al., [2003](#page-7-21)), empathy and emotional valence may infuence neural activation, as well as attentional, perceptual, and motivational factors. For example, the anterior cingulate cortex has been implicated in both personal familiarity (Donix et al., [2010;](#page-7-22) Shah et al., [2001](#page-8-25)) and vicarious responses to pain (Morrison et al., [2004\)](#page-8-26), supporting the notion of multiple systems involved in human action perception (Filimon et al., [2007](#page-7-23)). The diferential response observed may be

Fig. 2 Attenuation of mu rhythm in response the observation of a motor action executed by a familiar actor, unfamiliar actor, and both combined. The ESDM group showed signifcantly greater attenuation in response to a familiar actor

specifc to the circuitry of the execution-observation matching system, or a system to connected to this network.

Our results are consistent with the possibility that specifc features of the ESDM intervention program may infuence the development of neural circuitry. The ESDM includes a strong focus on promoting social relationships, including joint attention and shared engagement, imitating and being imitated, positive social afect, adult responsiveness, and verbal and non-verbal communication. Caregivers are taught specifc strategies and asked to implement these strategies across many activities daily (Dawson et al., [2010\)](#page-7-13). These factors may increase the number of specifc types of social interactions that children with ASD have with parents and other caregivers. This may in turn modulate attention and motivation, and early training and experience may alter the child's neural responsiveness to familiar individuals. Future studies are needed to evaluate the active ingredients of efficacious early ASD interventions such as the ESDM.

Previous research using multiple modalities demonstrates diferential responses to familiarity across samples of children and adults with ASD and typical development (Key & Stone, [2012;](#page-8-27) Taylor et al., [2009](#page-9-4); Webb et al., [2010](#page-9-5)). Several regions have been implicated in this diferentiation, including the posterior cingulate, amygdala, and medial frontal lobes, the posterior cingulate cortex (Shah et al., [2001\)](#page-8-25), and the inferior parietal lobule (Liew et al., [2011\)](#page-8-28). Research has shown that individuals with ASD demonstrated an expected pattern of face processing to their mother or other children, but attenuated responses to unfamiliar adults (Pierce & Redcay, [2008\)](#page-8-11). Although simultaneous eye-tracking was not

Table 3 Correlational analyses of mu attenuation in the observe condition over rest with Global conceptual ability (GCA) as assessed by the Diferential abilities scale II, single hand, face, and complex hand imitation as assessed by the Mature imitation task, and autism symptom severity as assessed by the Autism diagnostic observation schedule (ADOS)

*Correlation is signifcant at the 0.05 level (2-tailed)

**Correlation is signifcant at the 0.01 level (2-tailed)

recorded in our study, we used behavioral coding and visual inspection via time-locked video to ensure participants were attending to the stimuli during included trials. However, differential responses to familiarity are likely due to diferences in neural activation and not attention or gaze patterns (Sterling et al., [2008\)](#page-9-6), diagnosis (Gillespie-Smith et al., [2014\)](#page-7-10), or fxation patterns (Key & Stone, [2012](#page-8-27)).

While Oberman and colleagues ([2008\)](#page-8-13) did find a familiarity effect, their study compared the observation of a familiar person executing a motor action with the observation of an unfamiliar hand with no person attached to it. Their results may thus not refect a diferential response to familiarity, but may rather refect diferences in holistic processing (Behrmann et al., [2006](#page-7-12); Dawson et al., [2005](#page-7-8); Nakahachi et al., [2008\)](#page-8-14) or context (Iacoboni, [2005](#page-7-24); Iacoboni & Dapretto, [2006](#page-7-25)).

Mu attenuation did not correlate with any of the evaluated behavioral measures, including face and hand imitation, IQ, or autism symptom severity. This stands in contrast to previous fndings using a similar paradigm indicating a correlation between imitation and mu attenuation (Bernier et al., [2007;](#page-7-5) Bernier et al., [2013\)](#page-7-7). These fndings are included for transparency, though further investigation is warranted, especially given the small sample size, as to whether there exists a relationship among these factors.

The implications of this study must be considered in the context of existing limitations. Attrition within the sample stands as the most signifcant limitation. Only a subset of the 48 children who participated in the original trial were included in this study. EEG as a modality presents some inherent limitations to acquiring usable data in children and clinical populations. This limits conclusions that can be drawn from our results. Secondly, there is a lack of baseline mu activity prior to the intervention. Ideally, mu rhythm attenuation would have been assessed pre and post intervention. In this instance, we were forced to rely on data from a single time point. Nonetheless, the careful randomization procedures prior to intervention, and the fact that the groups were similar across measures of IQ, adaptive behavior, and ASD symptoms at the EEG, make the comparison worthy of consideration. Another limitation concerns the nature of the control group. In many intervention studies, the control group receives no intervention or delayed intervention. However, the COM control group in this trial received a similar number of intervention hours to the ESDM intervention group. Without details of the individual interventions received, it is difficult to precisely characterize the COM group. Taken together, this study provides preliminary evidence of a connection between the efects of ESDM and mu attenuation, but replication in a larger prospective study is needed.

This study applied an established cognitive neuroscience paradigm to examine the association between ESDM intervention and neural activity associated with social information processing. Our fndings indicate a potential relationship between the ESDM and neural activity underlying responses to social cognition and familiarity.

Acknowledgments We are grateful for the many families that that gave of their time to participate in this study and the many faculty, staf, and students that supported this research at the University of Washington Autism Center.

Author Contributions All authors contributed to the study conception and design. Programming, data collection, and data analysis were performed by BA with supervision from RB. The frst draft of the manuscript was written by BA with supervision from RB, and all authors commented on previous versions of the manuscript. All authors read and approved the fnal manuscript.

Funding This work was supported by grants from the Simons Foundation (SFARI #89638), the National Institute of Child Health and Human Development (U19HD34565, P50HD066782, R01HD-55741), and the National Institute of Mental Health (U54MH066399).

Declarations

Conflict of interest Dr. Aaronson, Dr. Estes, and Dr. Bernier declare no competing interests. Dr. Dawson and Dr. Rogers are authors of *The Early Start Denver Model for Young Children with Autism* from which they receive royalties from Guilford Press. Dr. Dawson is on the Scientifc Advisory Boards of Janssen Research and Development, Akili, Inc., Roche Pharmaceutical Company, and LabCorp, and has received grant funding from Janssen Research and Development, LLC, and PerkinElmer, speaker fees from ViaCord, and receives royalties from Oxford University Press.

References

- Babiloni, C., Carducci, F., Cincotti, F., Rossini, P. M., Neuper, C., Pfurtscheller, G., & Babiloni, F. (1999). Human movement-related potentials vs desynchronization of EEG alpha rhythm: A highresolution EEG study. *NeuroImage, 10*(6), 658–665. [https://doi.](https://doi.org/10.1006/nimg.1999.0504) [org/10.1006/nimg.1999.0504](https://doi.org/10.1006/nimg.1999.0504)
- Behrmann, M., Thomas, C., & Humphreys, K. (2006). Seeing it diferently: Visual processing in autism. *Trends in Cognitive Sciences, 10*(6), 258–264.<https://doi.org/10.1016/j.tics.2006.05.001>
- Bernier, R., Aaronson, B., & McPartland, J. (2013). The role of imitation in the observed heterogeneity in EEG mu rhythm in autism and typical development. *Brain and Cognition, 82*(1), 69–75. <https://doi.org/10.1016/j.bandc.2013.02.008>
- Bernier, R., Dawson, G., Webb, S., & Murias, M. (2007). EEG mu rhythm and imitation impairments in individuals with autism spectrum disorder. *Brain and Cognition*, *64*(3), 228–237. [https://](https://doi.org/10.1016/j.bandc.2007.03.004) doi.org/10.1016/j.bandc.2007.03.004
- Bowman, L. C., Bakermans-Kranenburg, M. J., Yoo, K. H., Cannon, E. N., Vanderwert, R. E., Ferrari, P. F., & Fox, N. A. (2017). The mu-rhythm can mirror: Insights from experimental design, and looking past the controversy. *Cortex, 96*, 121–125. [https://doi.org/](https://doi.org/10.1016/j.cortex.2017.03.025) [10.1016/j.cortex.2017.03.025](https://doi.org/10.1016/j.cortex.2017.03.025)
- Calvo-Merino, B., Grèzes, J., Glaser, D. E., Passingham, R. E., & Haggard, P. (2006). Seeing or doing? Infuence of visual and motor familiarity in action observation. *Current Biology, 16*(19), 1905– 1910.<https://doi.org/10.1016/j.cub.2006.07.065>
- Campatelli, G., Federico, R. R., Apicella, F., Sicca, F., & Muratori, F. (2013). Face processing in children with ASD: Literature review. *Research in Autism Spectrum Disorders, 7*(3), 444–454. [https://](https://doi.org/10.1016/j.rasd.2012.10.003) doi.org/10.1016/j.rasd.2012.10.003
- Carr, L., Iacoboni, M., Dubeau, M. -C., Mazziotta, J. C., & Lenzi, G. L. (2003). Neural mechanisms of empathy in humans: A relay from neural systems for imitation to limbic areas. *Proceedings of the National Academy of Sciences*, *100*(9), 5497–5502. [https://doi.](https://doi.org/10.1073/pnas.0935845100) [org/10.1073/pnas.0935845100](https://doi.org/10.1073/pnas.0935845100)
- Coll, M. P., Press, C., Hobson, H., Catmur, C., & Bird, G. (2017). Crossmodal classifcation of mu rhythm activity during action observation and execution suggests specifcity to somatosensory features of actions. *Journal of Neuroscience, 37*(24), 5936–5947. <https://doi.org/10.1523/JNEUROSCI.3393-16.2017>
- Dawson, G., Carver, L., Meltzof, A. N., Panagiotides, H., McPartland, J., & Webb, S. J. (2002). Neural correlates of face and object recognition in young children with autism spectrum disorder, developmental delay, and typical development. *Child Development*, *73*(3), 700–717.
- Dawson, G., Jones, E. J. H., Merkle, K., Venema, K., Lowy, R., Faja, S., & Webb, S. J. (2012). Early behavioral intervention is associated with normalized brain activity in young children with autism. *Journal of the American Academy of Child and Adolescent Psychiatry, 51*(11), 1150–1159. [https://doi.org/10.1016/j.jaac.2012.](https://doi.org/10.1016/j.jaac.2012.08.018) [08.018](https://doi.org/10.1016/j.jaac.2012.08.018)
- Dawson, G., Rogers, S., Munson, J., Smith, M., Winter, J., Greenson, J., & Varley, J. (2010a). Randomized, controlled trial of an intervention for toddlers with autism: The early start Denver model. *Pediatrics, 125*(1), e17–e23. [https://doi.org/10.1542/peds.](https://doi.org/10.1542/peds.2009-0958) [2009-0958](https://doi.org/10.1542/peds.2009-0958)
- Dawson, G., Webb, S. J., & Mcpartland, J. (2005). Understanding the nature of face processing impairment in autism: Insights from behavioral and electrophysiological studies. *Developmental Neuropsychology, 27*(3), 403–424.
- Donix, M., Petrowski, K., Jurjanz, L., Huebner, T., Herold, U., Baeumler, D., & Holthoff, V. A. (2010). Age and the neural network of personal familiarity. *PLoS ONE, 5*(12), 1–7. [https://doi.org/10.](https://doi.org/10.1371/journal.pone.0015790) [1371/journal.pone.0015790](https://doi.org/10.1371/journal.pone.0015790)
- Elliot, C. (2007). *Diferential abilities scale (DAS-II) Manual* (2nd ed.). San Antonio, TX: Harcourt Assessment, Inc.
- Estes, A., Munson, J., Rogers, S. J., Greenson, J., Winter, J., & Dawson, G. (2015). Long-term outcomes of early intervention in 6-year-old children with autism spectrum disorder. *Journal of the American Academy of Child and Adolescent Psychiatry, 54*(7), 580–587.<https://doi.org/10.1016/j.jaac.2015.04.005>
- Fan, Y.-T., Decety, J., Yang, C.-Y., Liu, J.-L., & Cheng, Y. (2010). Unbroken mirror neurons in autism spectrum disorders. *Journal of Child Psychology and Psychiatry, and Allied Disciplines, 51*, 981–988. <https://doi.org/10.1111/j.1469-7610.2010.02269.x>
- Filimon, F., Nelson, J. D., Hagler, D. J., & Sereno, M. I. (2007). Human cortical representations for reaching: Mirror neurons for execution, observation, and imagery. *NeuroImage, 37*(4), 1315–1328.<https://doi.org/10.1016/j.neuroimage.2007.06.008>
- Gillespie-Smith, K., Doherty-Sneddon, G., Hancock, P. J. B., & Riby, D. M. (2014). That looks familiar: Attention allocation to familiar and unfamiliar faces in children with autism spectrum disorder. *Cognitive Neuropsychiatry, 19*(6), 554–569. [https://](https://doi.org/10.1080/13546805.2014.943365) doi.org/10.1080/13546805.2014.943365
- Heyes, C., & Catmur, C. (2020). What happened to mirror neurons? *Perspectives on Psychological Science*. [https://doi.org/10.](https://doi.org/10.31234/osf.io/dtnqg) [31234/osf.io/dtnqg](https://doi.org/10.31234/osf.io/dtnqg)
- Hobson, H. M., & Bishop, D. V. M. (2016). Mu suppression – A good measure of the human mirror neuron system? *Cortex, 82*, 290–310.<https://doi.org/10.1016/j.cortex.2016.03.019>
- Hobson, H. M., & Bishop, D. V. M. (2017). The interpretation of mu suppression as an index of mirror neuron activity: Past, present and future. *Royal Society Open Science*. [https://doi.org/](https://doi.org/10.1098/rsos.160662) [10.1098/rsos.160662](https://doi.org/10.1098/rsos.160662)
- Iacoboni, M. (1999). Cortical mechanisms of human imitation. *Science, 286*(5449), 2526–2528. [https://doi.org/10.1126/science.](https://doi.org/10.1126/science.286.5449.2526) [286.5449.2526](https://doi.org/10.1126/science.286.5449.2526)
- Iacoboni, M. (2005). Neural mechanisms of imitation. *Current Opinion in Neurobiology*.<https://doi.org/10.1016/j.conb.2005.10.010>
- Iacoboni, M., & Dapretto, M. (2006). The mirror neuron system and the consequences of its dysfunction. *Nature Reviews Neuroscience, 7*, 942–951.<https://doi.org/10.1038/nrn2024>
- Iacoboni, M., Molnar-Szakacs, I., Gallese, V., Buccino, G., & Mazziotta, J. C. (2005). Grasping the intentions of others with one's own mirror neuron system. *PLoS Biology*. [https://doi.org/10.](https://doi.org/10.1371/journal.pbio.0030079) [1371/journal.pbio.0030079](https://doi.org/10.1371/journal.pbio.0030079)
- Key, A. P. F., & Stone, W. L. (2012). Processing of novel and familiar faces in infants at average and high risk for autism. *Developmental Cognitive Neuroscience, 2*(2), 244–255. [https://doi.org/](https://doi.org/10.1016/j.dcn.2011.12.003) [10.1016/j.dcn.2011.12.003](https://doi.org/10.1016/j.dcn.2011.12.003)
- Kilner, J. M., & Lemon, R. N. (2013). What we know currently about mirror neurons. *Current Biology*, *23*(23), R1057–R1062. [https://](https://doi.org/10.1016/j.cub.2013.10.051) doi.org/10.1016/j.cub.2013.10.051
- Liew, S. L., Han, S., & Aziz-Zadeh, L. (2011). Familiarity modulates mirror neuron and mentalizing regions during intention understanding. *Human Brain Mapping, 32*(11), 1986–1997. [https://](https://doi.org/10.1002/hbm.21164) doi.org/10.1002/hbm.21164
- Lord, C., Risi, S., Lambrecht, L., Cook, E. H., Leventhal, B. L., DiLavore, P. C., & Rutter, M. (2000). Autism diagnostic observation schedule (ADOS). *Journal of Autism and Developmental Disorders*. <https://doi.org/10.1007/BF02211841>
- Marshall, P. J., & Meltzof, A. N. (2011). Neural mirroring systems: Exploring the EEG mu rhythm in human infancy. *Developmental Cognitive Neuroscience*, *1*(2), 110–123. [https://doi.org/10.1016/j.](https://doi.org/10.1016/j.dcn.2010.09.001) [dcn.2010.09.001](https://doi.org/10.1016/j.dcn.2010.09.001)
- Martineau, J., Cochin, S., Rémy, M., & Barthelemy, C. (2008). Impaired cortical activation in autistic children: Is the mirror neuron system involved? *International Journal of Psychophysiology*, *68*(1), 35–40. <https://doi.org/10.1016/j.ijpsycho.2008.01.002>
- McPartland, J., Dawson, G., Webb, S. J., Panagiotides, H., & Carver, L. J. (2004). Event-related brain potentials reveal anomalies in temporal processing of faces in autism spectrum disorder. *Journal of Child Psychology and Psychiatry, and Allied Disciplines, 45*(7), 1235–1245. [https://doi.org/10.1111/j.1469-7610.](https://doi.org/10.1111/j.1469-7610.2004.00318.x) [2004.00318.x](https://doi.org/10.1111/j.1469-7610.2004.00318.x)
- Morrison, I., Lloyd, D., di Pellegrino, G., & Roberts, N. (2004). Vicarious responses to pain in anterior cingulate cortex: Is empathy a multisensory issue? *Cognitive, Afective and Behavioral Neuroscience, 4*(2), 270–278.<https://doi.org/10.3758/CABN.4.2.270>
- Muthukumaraswamy, S. D., & Johnson, B. W. (2004). Changes in rolandic mu rhythm during observation of a precision grip. *Psychophysiology, 41*(1), 152–156. [https://doi.org/10.1046/j.1469-](https://doi.org/10.1046/j.1469-8986.2003.00129.x) [8986.2003.00129.x](https://doi.org/10.1046/j.1469-8986.2003.00129.x)
- Muthukumaraswamy, S. D., Johnson, B. W., & McNair, N. A. (2004). Mu rhythm modulation during observation of an object-directed grasp. *Cognitive Brain Research, 19*(2), 195–201. [https://doi.org/](https://doi.org/10.1016/j.cogbrainres.2003.12.001) [10.1016/j.cogbrainres.2003.12.001](https://doi.org/10.1016/j.cogbrainres.2003.12.001)
- Nakahachi, T., Yamashita, K., Iwase, M., Ishigami, W., Tanaka, C., Toyonaga, K., & Takeda, M. (2008). Disturbed holistic processing in autism spectrum disorders verifed by two cognitive tasks requiring perception of complex visual stimuli. *Psychiatry Research, 159*(3), 330–338. [https://doi.org/10.1016/j.psychres.](https://doi.org/10.1016/j.psychres.2005.08.028) [2005.08.028](https://doi.org/10.1016/j.psychres.2005.08.028)
- Oberman, L. M., Hubbard, E. M., McCleery, J. P., Altschuler, E., Ramachandran, V. S., & Pineda, J. A. (2005). EEG evidence for mirror neuron dysfunction in autism spectrum disorders. *Cognitive Brain Research*, *24*(2), 190–198. [https://doi.org/10.1016/j.](https://doi.org/10.1016/j.cogbrainres.2005.01.014) [cogbrainres.2005.01.014](https://doi.org/10.1016/j.cogbrainres.2005.01.014)
- Oberman, L. M., McCleery, J. P., Hubbard, E. M., Bernier, R., Wiersema, J. R., Raymaekers, R., & Pineda, J. A. (2013). Developmental changes in mu suppression to observed and executed actions in autism spectrum disorders. *Social Cognitive and Afective Neuroscience, 8*(3), 300–304. [https://doi.org/10.1093/scan/](https://doi.org/10.1093/scan/nsr097) [nsr097](https://doi.org/10.1093/scan/nsr097)
- Oberman, L. M., Ramachandran, V. S., & Pineda, J. A. (2008). Modulation of mu suppression in children with autism spectrum disorders in response to familiar or unfamiliar stimuli: The mirror neuron hypothesis. *Neuropsychologia, 46*(5), 1558–1565. [https://](https://doi.org/10.1016/j.neuropsychologia.2008.01.010) doi.org/10.1016/j.neuropsychologia.2008.01.010
- Perkins, T., Stokes, M., McGillivray, J., & Bittar, R. (2010). Mirror neuron dysfunction in autism spectrum disorders. *Journal of*

Clinical Neuroscience, 17(10), 1239–1243. [https://doi.org/10.](https://doi.org/10.1016/j.jocn.2010.01.026) [1016/j.jocn.2010.01.026](https://doi.org/10.1016/j.jocn.2010.01.026)

- Pfurtscheller, G., Neuper, C., Andrew, C., & Edlinger, G. (1997). Foot and hand area mu rhythms. *International Journal of Psychophysiology, 26*(1–3), 121–135. [https://doi.org/10.1016/S0167-8760\(97\)](https://doi.org/10.1016/S0167-8760(97)00760-5) [00760-5](https://doi.org/10.1016/S0167-8760(97)00760-5)
- Pierce, K. (2001). Face processing occurs outside the fusiform `face area' in autism: Evidence from functional MRI. *Brain, 124*(10), 2059–2073.<https://doi.org/10.1093/brain/124.10.2059>
- Pierce, K., Haist, F., Sedaghat, F., & Courchesne, E. (2004). The brain response to personally familiar faces in autism: Findings of fusiform activity and beyond. *Brain, 127*(12), 2703–2716. [https://doi.](https://doi.org/10.1093/brain/awh289) [org/10.1093/brain/awh289](https://doi.org/10.1093/brain/awh289)
- Pierce, K., & Redcay, E. (2008). Fusiform function in children with an autism spectrum disorder is a matter of "Who." *Biological Psychiatry, 64*(7), 552–560. [https://doi.org/10.1016/j.biopsych.](https://doi.org/10.1016/j.biopsych.2008.05.013) [2008.05.013](https://doi.org/10.1016/j.biopsych.2008.05.013)
- Raymaekers, R., Wiersema, J. R., & Roeyers, H. (2009). EEG study of the mirror neuron system in children with high functioning autism. *Brain Research*, *1304*, 113–121. [https://doi.org/10.1016/j.](https://doi.org/10.1016/j.brainres.2009.09.068) [brainres.2009.09.068](https://doi.org/10.1016/j.brainres.2009.09.068)
- Rizzolatti, G., & Craighero, L. (2004). The Mirror-neuron system. *Annual Review of Neuroscience*, *27*(1), 169–192. [https://doi.org/](https://doi.org/10.1146/annurev.neuro.27.070203.144230) [10.1146/annurev.neuro.27.070203.144230](https://doi.org/10.1146/annurev.neuro.27.070203.144230)
- Rogers, S., Cook, I., & Greiss-Hess, L. (2005). *Mature imitation task*. M.I.N.D. Institute, University of California, Davis (Unpublished coding manual.).
- Rogers, S. J., Estes, A., Vismara, L., Munson, J., Zierhut, C., Greenson, J., & Talbott, M. (2019a). Enhancing low-intensity coaching in parent implemented early start Denver model intervention for early autism: A randomized comparison treatment trial. *Journal of Autism and Developmental Disorders, 49*(2), 632–646. [https://](https://doi.org/10.1007/s10803-018-3740-5) doi.org/10.1007/s10803-018-3740-5
- Rogers, S. J., Estes, A., Lord, C., Munson, J., Rocha, M., Winter, J., & Talbott, M. (2019b). A multisite randomized controlled two-phase trial of the early start Denver model compared to treatment as usual. *Journal of the American Academy of Child and Adolescent Psychiatry, 58*(9), 853–865. [https://doi.org/10.1016/j.jaac.2019.](https://doi.org/10.1016/j.jaac.2019.01.004) [01.004](https://doi.org/10.1016/j.jaac.2019.01.004)
- Rogers, S. J., Estes, A., Lord, C., Vismara, L., Winter, J., Fitzpatrick, A., Mengye, G., Dawson, G. (2012). Efects of a Brief Early Start Denver Model (ESDM)–based parent intervention on toddlers at risk for autism spectrum disorders: A randomized controlled trial. *Journal of the American Academy of Child and Adolescent Psychiatry*, *51*(10), 1052–1065.
- Ruysschaert, L., Warreyn, P., Wiersema, J. R., Oostra, A., & Roeyers, H. (2014). Exploring the role of neural mirroring in children with autism spectrum disorder. *Autism Research, 7*(2), 197–206. <https://doi.org/10.1002/aur.1339>
- Schreibman, L., Dawson, G., Stahmer, A. U., Landa, R., Rogers, S. J., McGee, G. G., Kasari, C., Ingersoll, B., Kaiser, A. P., Bruinsma, Y., McNerney, E., Wetherby, A., & Halladay, A. (2015). Naturalistic Developmental Behavioral Interventions: Empirically Validated Treatments for Autism Spectrum Disorder. *Journal of Autism and Developmental Disorders*, *45*(8), 2411–2428. [https://](https://doi.org/10.1007/s10803-015-2407-8) doi.org/10.1007/s10803-015-2407-8
- Schultz, R. T., Gauthier, I., Klin, A., Fulbright, R. K., Anderson, A. W., Volkmar, F., & Gore, J. C. (2000). Abnormal ventral temporal cortical activity during face discrimination among individuals with autism and Asperger syndrome. *Archives of General Psychiatry, 57*(4), 331.<https://doi.org/10.1001/archpsyc.57.4.331>
- Shah, N. J., Marshall, J. C., Zafris, O., Schwab, A., Zilles, K., Markowitsch, H. J., & Fink, G. R. (2001). The neural correlates of person familiarity. A functional magnetic resonance imaging study with clinical implications. *Brain: A Journal of Neurology, 124*, 804–815.<https://doi.org/10.1093/brain/124.4.804>
- Sterling, L., Dawson, G., Webb, S., Murias, M., Munson, J., Panagiotides, H., & Aylward, E. (2008). The role of face familiarity in eye tracking of faces by individuals with autism spectrum disorders. *Journal of Autism and Developmental Disorders, 38*(9), 1666–1675. <https://doi.org/10.1007/s10803-008-0550-1>
- Taylor, M. J., Arsalidou, M., Bayless, S. J., Morris, D., Evans, J. W., & Barbeau, E. J. (2009). Neural correlates of personally familiar faces: Parents, partner and own faces. *Human Brain Mapping, 30*(7), 2008–2020. <https://doi.org/10.1002/hbm.20646>
- Vanderwert, R. E., Fox, N. A., & Ferrari, P. F. (2013). The mirror mechanism and mu rhythm in social development. *Neuroscience Letters, 540*, 15–20.<https://doi.org/10.1016/j.neulet.2012.10.006>
- Ventola, P., Yang, D. Y. J., Friedman, H. E., Oosting, D., Wolf, J., Sukhodolsky, D. G., & Pelphrey, K. A. (2015). Heterogeneity of neural mechanisms of response to pivotal response treatment. *Brain Imaging and Behavior, 9*(1), 74–88. [https://doi.org/10.1007/](https://doi.org/10.1007/s11682-014-9331-y) [s11682-014-9331-y](https://doi.org/10.1007/s11682-014-9331-y)
- Voos, A. C., Pelphrey, K. A., Tirrell, J., Bolling, D. Z., Wyk, B. V., Vander, B., Kaiser, M. D., & Ventola, P. (2013). Neural mechanisms of improvements in social motivation after pivotal

response treatment: Two case studies. *Journal of Autism and Developmental Disorders, 43*(1), 1–10. [https://doi.org/10.1007/](https://doi.org/10.1007/s10803-012-1683-9) [s10803-012-1683-9](https://doi.org/10.1007/s10803-012-1683-9)

- Wang, Y., Veluvolu, K. C., Cho, J. -H., Defoort, M. (2012). Adaptive estimation of EEG for subject-specifc reactive band identifcation and improved ERD detection. *Neuroscience Letters*, *528*(2), 137–142.<https://doi.org/10.1016/j.neulet.2012.09.001>
- Webb, S. J., Jones, E. J. H., Merkle, K., Murias Jessica, M., Greenson, J., Richards, T., Aylward, E., & Dawson, G. (2010). Response to familiar faces newly familiar faces and novel faces as assessed by ERPs is intact in adults with autism spectrum disorders. *International Journal of Psychophysiology*, *77*(2), 106–117. [https://doi.](https://doi.org/10.1016/j.ijpsycho.2010.04.011) [org/10.1016/j.ijpsycho.2010.04.011](https://doi.org/10.1016/j.ijpsycho.2010.04.011)

Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.