Mirror Neuron Activity Associated with Social Impairments but not Age in Autism Spectrum Disorder

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Background: The neurobiology of autism spectrum disorder (ASD) is not particularly well understood, and biomedical treatment approaches are therefore extremely limited. A prominent explanatory model suggests that social-relating symptoms may arise from dysfunction within the mirror neuron system, while a recent neuroimaging study suggests that these impairments in ASD might reduce with age.

Methods: Participants with autism spectrum disorder (i.e., DSM-IV autistic disorder or Asperger's disorder) ($n = 34$) and matched control subjects ($n = 36$) completed a transcranial magnetic stimulation study in which corticospinal excitability was assessed during the observation of hand gestures.

Results: Regression analyses revealed that the ASD group presented with significantly reduced corticospinal excitability during the observation of a transitive hand gesture (relative to observation of a static hand) ($p < .05$), which indicates reduced putative mirror neuron system activity within ventral premotor cortex/inferior frontal gyrus. Among the ASD group, there was also a negative association between putative mirror neuron activity and self-reported social-relating impairments, but there was no indication that mirror neuron impairments in ASD decrease with age.

Conclusions: These data provide general support for the mirror neuron hypothesis of autism; researchers now must clarify the precise functional significance of mirror neurons to truly understand their role in the neuropathophysiology of ASD and to determine whether they should be used as targets for the treatment of ASD.

Key Words: Asperger's disorder, autism, electromyography, mirror neuron system, primary motor cortex, transcranial magnetic stimulation

Autism spectrum disorder (ASD) is characterized by severe social, communicative, and behavioral impairments. The precise neuropathophysiology of ASD is unclear, but a recent account suggests that dysfunction of mirror neurons might underlie aspects of ASD, particularly with respect to social relating (1). Originally discovered via depth electrode recordings in macaque monkeys (2), mirror neurons are brain cells that become active not only when a behavior is performed but also when that same behavior is observed. Mirror neurons and mirror systems have since been established in humans using a range of techniques (e.g., functional magnetic resonance imaging [fMRI], electroencephalography [EEG], transcranial magnetic stimulation [TMS]) and in a range of modalities (e.g., behavior, sensation, pain, emotion) (3,4). Theoretical accounts propose that mirror systems provide an embodied simulation that not only allows an understanding of the actions of others but also facilitates broader social cognitive processes, including empathy and understanding others' mental and emotional states (5).

It has been widely suggested that dysfunction of mirror neurons may underlie ASD (i.e., the broken mirror hypothesis) (6–8). Evidence for reduced activation of elements of the mirror system in autism comes from a range of noninvasive techniques, including fMRI (9), structural magnetic resonance imaging (10,11), EEG indices of mu suppression (12–14), and TMS indices of corticospinal excitability during action observation (15). Stimuli used to elicit a mirror neuron response in these studies have been similarly varied but include static emotional facial expressions (9), static nonemotional facial expressions (16), and intransitive hand movements (12,13,15,17). Another study demonstrated that the observation of an action led to mirrored activity of a muscle that was soon to be used by the observed individual to complete a goal (e.g., activation of mouth-opening mylohyoid muscle when viewing an object grasped for the purpose of eating) but that this mirrored anticipation was absent in ASD (18); this implies a deficit in linking or representing motor chains for understanding intention. While generally supportive of reduced mirror system activity in ASD and links with social relating (9), these studies have nevertheless been characterized by small sample sizes, thereby limiting further analyses (e.g., regression).

More recently, Bastiaansen *et al.* (19) used fMRI to investigate responses to facial expressions among adults with ASD; while there were no overall group differences, the authors found reductions in inferior frontal gyrus (IFG) activity for younger individuals with ASD (mean age: 22 years) and an age-related increase in IFG activity for the ASD group. These age patterns were not apparent among the control group. This is a particularly interesting and novel finding, as it suggests that individuals with ASD may outgrow any mirror neuron deficit by early-mid adulthood, raising questions about the importance of the mirror neuron system (MNS) among adults with ASD, many of whom nevertheless continue to experience pronounced social difficulties.

Despite this evidence for a mirror neuron impairment, ASD is increasingly recognized, from clinical, genetic, and neurobiological perspectives, as a heterogeneous group of disorders. Accordingly, one neurobiological model, such as the mirror neuron account, is unlikely to provide an explanatory account that applies to all indi-

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viduals with ASD. It is therefore possible that only a subgroup of individuals with ASD experience a reduction in mirror neuron activity, which would be crucial to future efforts to individualize treatments. Indeed, some studies have reported no activation in individuals with ASD in regions thought to comprise the MNS (9), while others provide evidence to suggest enhanced activation of the MNS in ASD (17) or no mirror neuron deficit in ASD at all (20,21). Whether a lack of mirror neuron activity in ASD is associated with a different clinical profile (e.g., more pronounced social-relating impairments) to those with ASD who do not show evidence for a mirror neuron deficit is not clear.

The current study aimed to use TMS to better understand the MNS in ASD. To our knowledge, there has been only one other study that has used TMS to investigate the MNS in ASD: Theoret *et al.* (15) administered TMS to 10 adults with ASD and 10 matched control subjects during the observation of intransitive thumb and index finger movements. These were presented from both egocentric (self) and allocentric (other) perspectives. Motor evoked potentials (MEPs) were recorded from the contralateral first dorsal interosseous (FDI; index finger-relevant) and abductor pollicis brevis (thumb-relevant). Individuals with ASD failed to show motor facilitation for the relevant muscle but only when the action was presented from the egocentric view. The authors suggest that this may reflect a mirror-related deficit in self-consciousness that affects self-other processing in ASD. In the current study, we sought a relatively large sample size to allow us to examine, via regression analyses, associations with potential modulating variables, including social relating and age. Transcranial magnetic stimulation is somewhat unique in that it can be used to determine, for each individual, whether or not there is evidence of MNS activity. Specifically, increased motor corticospinal excitability (CSE) during action observation (compared with CSE during a control condition) is thought to reflect measurable MNS activity in the premotor cortex/IFG, whereas unchanged or decreased CSE amplitude does not (22–24). Transcranial magnetic stimulation is also advantageous as, unlike fMRI and EEG, it provides high temporal resolution, giving an index of mirror neuron activity with millisecond precision (i.e., at a specific phase in the observed movement) (24,25). The current study employed transitive stimuli (i.e., hand interacting with object in a goal-directed fashion), which appear critical to the mirror neuron response (26,27) but to our knowledge have not been employed in studies of ASD. It was hypothesized that individuals with ASD would be associated with reduced positive modulation of CSE during the observation of a transitive movement and that this would be negatively associated with age. It was also hypothesized that in ASD, greater social symptom severity would be associated with reduced positive modulation of CSE during the observation of a transitive movement.

Methods and Materials

Participants

Participants were 34 individuals diagnosed with ASD (either high-functioning autism or Asperger's disorder) and 36 neurotypical (NT) (healthy) control subjects matched for gender and age. Individuals with ASD were recruited via the Monash Alfred Psychiatry Research Centre participant database (comprised of clinically diagnosed research participants who had given permission to be contacted in relation to future research) and advertisements in ASD support group newsletters and websites. All clinical participants had a confirmed DSM-IV diagnosis of autistic disorder or Asperger's disorder. Where a participant had not been diagnosed through our clinical service, the diagnosis was confirmed by participants providing a copy of their diagnostic report or by one of the researchers speaking with the diagnosing clinician (psychiatrist, pediatrician, or psychologist). Eleven of these participants were medicated (6 selective serotonin reuptake inhibitor [SSRI], 2 SSRI/atypical antipsychotic [AP], 2 SSRI/atypical AP/benzodiazepine, 1 tetracyclic antidepressant, 1 atypical AP, 1 serotonin-norepinephrine reuptake inhibitor). Neurotypical participants reported no history of substance abuse, psychiatric disorder, or neurological illness and were recruited via advertisements placed at The Alfred Hospital and Monash University. Demographics are presented in Table 1; there were no significant differences in age, gender, or IQ (as assessed by the Kaufman Brief Intelligence Test, Second Edition). All participants were screened to ensure that they did not meet safety-based exclusion criteria for TMS (26). Written informed consent was obtained from all participants (and a parent for those under the age of 18). The project was approved by the research ethics committees of The Alfred, Monash University, and Southern Health.

Table 1. Participant Demographics

	ASD	NT
n	34	36
Age (Years)	26.32 (10.70)	26.86 (6.38)
Gender (M:F)	26:8	20:16
Formal Education (Years)[a]	14.66 (4.04)	17.82 (3.49)
Handedness (EHI) (R : L : ambi)	25:5:4	31:4:0
KBIT-2 VIQ	101.03 (17.11)	108.09 (12.90)
KBIT-2 PIQ	108.09 (19.35)	113.29 (13.64)
KBIT-2 FSIQ	105.47 (19.33)	112.41 (13.75)
AQ[b]	31.49 (8.46)	13.11 (5.60)
RAADS		
Social relating[b]	41.31 (14.36)	15.36 (11.12)
Language communication[b]	33.77 (13.58)	8.61 (6.38)
Sensorimotor[b]	31.08 (16.33)	9.46 (8.42)
Total[b]	106.15 (40.50)	33.42 (22.21)
DBC Total	53.00 (28.46)	1.00 (-)
DBC Autism Screen	18.25 (9.62)	1.00 (-)

Standard deviations in parentheses.

ambi, ambidextrous; AQ, Autism Spectrum Quotient; ASD, autism spectrum disorder; DBC, Developmental Behaviour Checklist; EHI, Edinburgh Handedness Inventory; F, female; FSIQ, full-scale intelligence quotient; KBIT-2, Kaufman Brief Intelligence Test, Second Edition; L, left; M, male; NT, neurotypical; PIQ, performance (nonverbal) intelligence quotient; R, right; RAADS, Ritvo Autism-Aspergers Diagnostic Scale; VIQ, verbal intelligence quotient.

[a] $p < .01$.

[b] $p < .001$.

Procedure

Participants (and their parents for those under 18) completed several measures related to autistic symptomatology, including the Autism Spectrum Quotient (AQ)/Autism Spectrum Quotient Adolescent Version (28,29), the Ritvo Autism and Asperger's Diagnostic Scale (for those aged 18 or above) (30), and the parent-completed Developmental Behaviour Checklist (for those aged below 18) (31).

Consistent with previous research (22–24), putative mirror neuron activity was assessed via the administration of TMS to the left primary motor cortex (and subsequent electromyography [EMG] recordings of the contralateral FDI muscle) during the observation of a series of short video clips depicting a static hand or a hand movement (e.g., grasping a mug). Importantly, these stimuli involve the presentation of a transitive (i.e., goal-directed, object-related) movement, an essential act when attempting to elicit a mirror neuron response among healthy individuals.

Single pulse TMS (Magstim-200 stimulator, Magstim Company Ltd., United Kingdom) was administered to the primary motor cortex using a hand-held, 70 mm figure-of-eight coil that was placed against the scalp in the conventional manner. The site of the pri-

mary motor cortical stimulation was that which, following stimulation, produced the greatest EMG response in the contralateral FDI muscle. Resting motor threshold was the lowest stimulator intensity at which at least three out of five consecutive pulses elicited a response of at least 50 μV.

Electromyography was recorded from the FDI muscle using self-adhesive electrodes. All EMG signals were amplified and filtered (low pass: 500 Hz, high pass: 10 Hz) using PowerLab/4SP (AD Instruments, Colorado Springs, Colorado) and sampled via a CED Micro 1401 mk II analog-to-digital converting unit (Cambridge Electronic Design, Cambridge, United Kingdom).

Briefly, participants viewed a quasi-random sequence of five different video clips: a static hand (dorsal view), a static hand with a mug present, a pantomimed grasping motion, a pantomimed grasping motion with the mug present, and a transitive movement where the hand grasped the handle of the mug (see Enticott *et al.* [23] for screen shots of each condition and further details). All videos were presented from an egocentric perspective. A TMS pulse (120% resting motor threshold) was delivered during each clip; for the motion videos, this was immediately before the completion of the grasp (which is the phase in this movement that is typically associated with the most pronounced increase in CSE) (25). Each clip was of 3 seconds duration and presented 10 times, with the entire sequence of 4 minutes 39 seconds duration. Stimuli were presented on a 22-inch LCD monitor (aspect ratio: 16:9) that was positioned at eye level and 120 cm ahead of the participant.

Participants were monitored by a second experimenter throughout the video presentation to ensure that visual gaze was directed toward the monitor. Participants were also asked a series of questions at the conclusion of the video presentation, for which they were not forewarned, to assess whether they had been attending to the videos (e.g., name the object present in the videos, imitate the hand movement seen). All participants were able to answer these questions successfully.

Data Analyses

Consistent with our previous study, in which enhanced CSE among NT individuals was only seen during the observation of a transitive hand movement (indicating putative mirror neuron activity) (23), median MEP responses were extracted for the static hand and transitive movement conditions. The MEP response during the observation of a transitive hand movement was then converted to an MEP percentage change relative to the MEP response during the observation of a static hand. The formula for calculating this variable is presented below:

*MEP Percentage Change (MEP-PC) = [(MEP transitive –MEP static)/MEP static] * 100*

This provides not only an index of relative mirror neuron activity but also the opportunity to differentiate between those who do show evidence of mirror neuron activity (i.e., MEP-PC > 0) and those who do not show evidence of mirror neuron activity (i.e., MEP-PC ≤ 0).

Standard and logistic regression were used to investigate the effect of group (ASD vs. NT) on our index of mirror system activity (i.e., MEP-PC). Additional predictors that have been shown or speculated to modulate mirror neuron activity in ASD (verbal IQ, age, and gender) were also added to the model. Because of multicollinearity, the ASD diagnosis and self-reported social-relating impairments (i.e., social relating subscale of AQ/Autism Spectrum Quotient Adolescent Version) were considered in separate regression analyses. Subsequent logistic regression analyses investigated the association between the mirror neuron response and predictors AQ social relating, gender, verbal IQ, and age. We examined both the mirror neuron response (i.e., CSE increase during action observation) and the presence or absence of a mirror neuron response (i.e., whether or not CSE was increased during action observation); the former assesses a spectrum view of mirror neuron activity, whereas the latter assesses the possibility of abnormal mirror neuron activity (i.e., absent MNS response) as a possible neurobiological subtype of ASD.

Table 2. Regression Examining the Influence of Four Predictors, Group (ASD Versus Control), Verbal IQ, Gender, and Age, on MEP-PC

IV	MEP-PC β (*p*)
Group	−24.71 (.045)[a]
Verbal IQ	−.04 (.923)
Gender	9.25 (.467)
Age	.41 (.547)

ASD, autism spectrum disorder; IQ, intelligence quotient; IV, independent variable; MEP-PC, motor evoked potentials-percentage change.
[a]Significant results.

Table 3. Regression for Examining, Among All Participants, the Effect of Predictors AQ Social, Verbal IQ, Gender, and Age on MEP-PC and Logistic Regression Examining the Effect of These Same Predictors on the Presence/Absence of a Putative MNS Response

IV	MEP-PC β (*p*)	MNS Response Odds Ratio (*p*)
AQ Social	−3.77 (.088)	.81 (.027)[a]
Verbal IQ	.10 (.787)	1.01 (.617)
Gender	8.06 (.541)	1.85 (.295)
Age	.37 (.596)	1.00 (.894)

AQ, Autism Spectrum Quotient; IQ, intelligence quotient; IV, independent variable; MEP-PC, motor evoked potentials-percentage change; MNS, mirror neuron system.
[a]Significant results.

Results

Results of the regression analyses are presented in Tables 2, 3, and 4. As demonstrated in Table 2, an ASD diagnosis is significantly associated with reduced MEP-PC during transitive action observation (Figure 1), thus providing support for reduced mirror system activity in ASD during the observation of transitive behavior. (Analysis of all five observation conditions by group is presented in Figure S1 in Supplement 1.) Within this model, there was no effect of age, verbal IQ, or gender.

When examining predictors of MEP-PC during action observation (Table 3), AQ social failed to reach significance (see Figure 2 for scatter plot), while the remaining variables, verbal IQ, gender, and

Table 4. Logistic Regression Examining, Separately for Each Group, the Influence of Predictors on the Presence or Absence of Putative MNS Activity

IV	ASD MNS Response Odds Ratio (*p*)	Control Subjects MNS Response Odds Ratio (*p*)
AQ Social	.53 (.018)[a]	1.01 (.959)
Verbal IQ	1.04 (.216)	1.00 (.912)
Gender	.76 (.783)	3.75 (.109)
Age	.98 (.573)	1.04 (.523)

ASD, autism spectrum disorder; AQ, Autism Spectrum Quotient; IQ, intelligence quotient; IV, independent variable; MNS, mirror neuron system.
[a]Significant results.

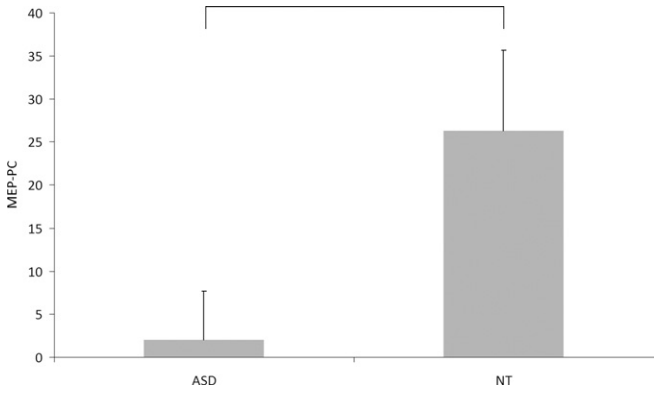

Figure 1. Motor evoked potentials-percentage change (+ standard error) during observation of a transitive hand movement for autism spectrum disorder and neurotypical groups. ASD, autism spectrum disorder; MEP-PC, motor evoked potentials-percentage change; NT, neurotypical.

age, were again not associated. When, however, examining the influence of factors on the presence or absence of a mirror neuron response (i.e., MNS response), there was an effect of AQ social score, suggesting that having a discernable mirror neuron response is associated with an increased score on the AQ social relating subscale, but there was no effect of verbal IQ, gender, or age.

When considering ASD and control groups separately (Table 4), there was an effect of social on the MNS response for the ASD group, suggesting that the absence of a putative mirror neuron response in ASD is linked to greater social symptom severity but no effect of verbal IQ, gender, or age. By contrast, among control subjects, there was no effect of any of the variables AQ social relating, verbal IQ, gender, and age, suggesting that the presence or absence of recordable putative mirror neuron activity has no relationship to these variables among this group. (Remaining scatter plots and bar charts presenting relationships described here are presented in Figures S2–S16 in Supplement 1.)

Discussion

The current study supports the notion that the MNS is disrupted among individuals with ASD. When viewing a human hand performing a transitive action, individuals with ASD showed reduced CSE (relative to viewing a static hand) when compared with NT individuals. Although we did not compare different visual orientations, because our videos were presented from an egocentric perspective, this should be considered consistent with the findings of Theoret *et al.* (15). Among ASD participants, self-reported social impairments were negatively associated with the presence of MNS activity, a relationship that did not exist among control subjects. Finally, unlike Bastiaansen *et al.* (19), we found no association with age, nor did we find any link to gender or verbal IQ. Although we used different methodology to assess the MNS, both with respect to recording technique and stimulus presentation, our results are not in agreement with the view that any mirror neuron impairment in ASD is absent or corrected by early-mid adulthood.

There is good evidence, both in primates and humans, that the MNS plays a vital role in allowing a first-hand understanding of the goals and intentions associated with others' behavior (32). From a theoretical perspective, then, our findings add strong support to the broken mirror hypothesis of autism, specifically, that a deficit within mirror neurons, or impairment within the broader MNS, significantly limits one's ability to understand the behavior of others and might then contribute to ASD and its social-relating difficulties. As demonstrated by Cattaneo *et al.* (18), this presumably in-

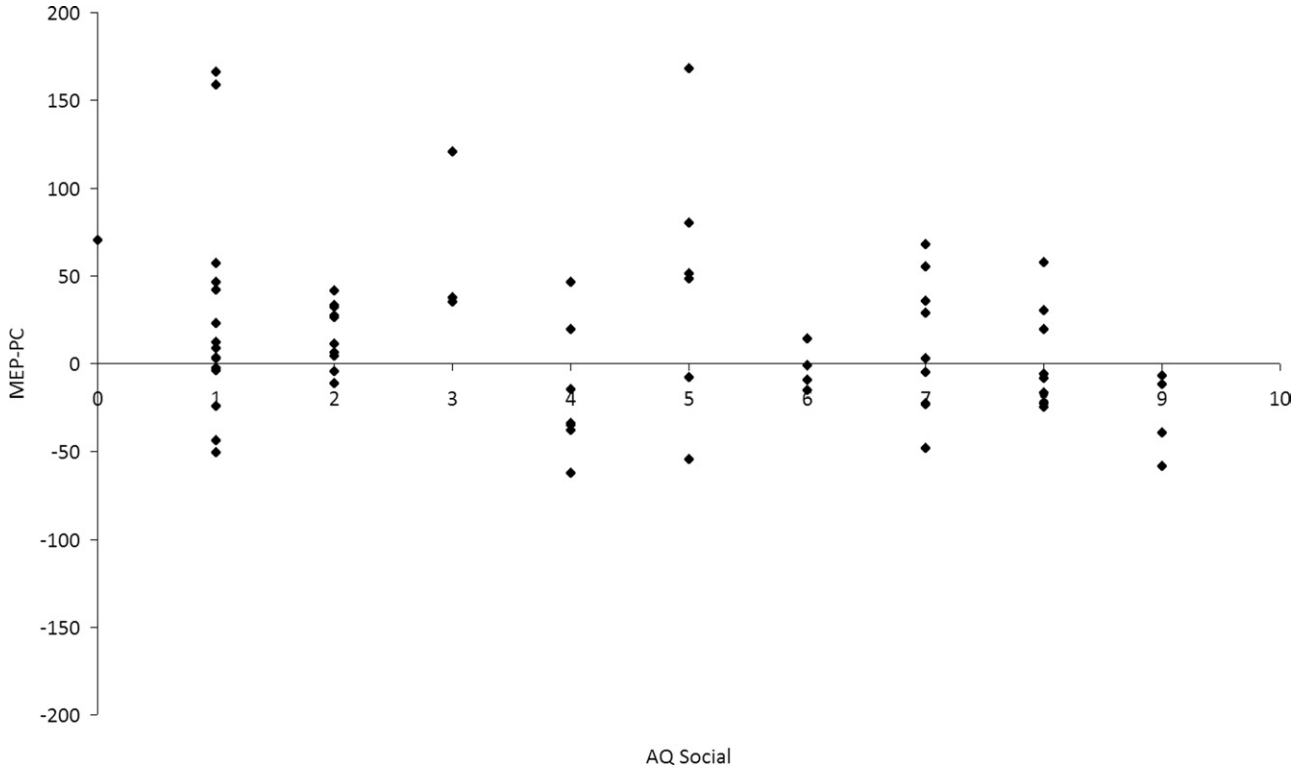

Figure 2. Scatter plot demonstrating relationship between motor evoked potentials-percentage change and Autism Spectrum Quotient social for all participants. AQ, Autism Spectrum Quotient; MEP-PC, motor evoked potentials-percentage change.

cludes the ability to infer intention by linking motor events to infer goals and intentions. The MNS is therefore considered integral to the neuropathophysiology of social-relating impairments in ASD, where the ability to infer others' intentions is impaired.

Beyond intention understanding and in further support of our results within the broken mirror hypothesis, there is also evidence to support a link between the MNS and higher-order social cognitive processes related to action and emotion understanding. For example, Neal and Chartrand (33) demonstrate that when administered Botox to block automatic facial mimicry, a presumed consequence of mirror system activation, healthy individuals are less able to successfully infer others' emotional facial expressions. Furthermore, there is mounting evidence for a link between mirror neurons and higher-order social cognitive processes that are typically impaired in ASD, such as empathy (34–36), facial affect recognition (37,38), and the interpretation of action (26). Thus, mirror neurons might form a critical link in the neural chain from behavior observation to understanding others' mental and emotional states. In addition, inhibitory TMS applied to a prefrontal region of the MNS (pars opercularis) disrupts subsequent imitation (39), which has been linked to the mirror neuron system and is often disrupted in autism (40). Thus, our findings of reduced MNS activity in ASD and an association with social relating seem entirely consistent with the broken mirror model.

The neuropathophysiology of the broken mirror account might be best understood in the context of motor impairments in ASD; mirror neurons, after all, are also motor neurons. Although not a core symptom, impaired motor coordination is widely recognized as a feature of ASD (see Fournier *et al.* [41] for a recent meta-analysis and review). This includes, for example, dyspraxia (42,43), disturbances of gait and posture (44), and impaired movement preparation (45,46). Neuroimaging and electrophysiological research has allowed our understanding of this dysfunction to extend to structural and functional abnormalities in key motor cortical and subcortical regions, including parietofrontal (i.e., mirror system) networks, premotor cortex, supplementary motor area, basal ganglia, thalamus, and the cerebellum (47–51). Moreover, as with mirror neurons in the current study, dyspraxia in ASD is associated with clinical characteristics, including impaired social relating (42,43). Thus, the observed mirror neuron deficit may reflect, at a cortical level, impaired motor function in ASD and result from the disrupted development of neural circuitry involving key motor regions. Related to this, the observed mirror neuron deficits in ASD might otherwise be a by-product of the well-documented disruptions of neural connectivity in ASD (52), a possibility that we have previously discussed in relation to both ASD and schizophrenia (53). This does not argue against the broken mirror hypothesis, but it does provide a sound neurobiological basis for reduced mirror neuron activity in ASD.

Despite our findings, it cannot be conclusively suggested that dysfunctional mirror systems cause some forms of autism or that they contribute to social impairments in autism, even among those who display no evidence of mirror system activity. The broken mirror hypothesis of autism has been highly controversial since its inception, largely because of what it attempts to explain and the limitations of extant research, and a number of researchers have suggested that a mirror neuron-based explanation of autism is premature or grossly undersupported (54,55). In the broken mirror model, mirror neurons are viewed as a neurobiological substrate for social cognition, providing an embodied simulation of others' minds that allows interpersonal understanding. A recent, alternative model, however, suggests that mirror neurons might arise from Hebbian sensorimotor associations, whereby the mirror properties of these neurons and brain regions develop because motor actions and the observation of these same or similar motor actions often co-occur (e.g., parental imitation of a child in infancy, visually self-guided motor movements) (55). Within this association model, it is conceivable that there is an underlying nonmirror mechanism in autism that produces the social and communicative impairments but that these impairments also prevent the necessary social orienting and attention toward others that are crucial to the effective formation of these mirror associations. The data from the current study are not inconsistent with this model; nevertheless, the sensorimotor model seems less well equipped to account for findings linking the MNS to intention understanding (18,32,33) and requires substantial testing in relation to the broken mirror hypothesis of autism. Others still have attempted to integrate the two competing models, claiming an important role for experience in the development of mirror neurons but attesting to their capacity to understand goals and other aspects of behavior (27).

Accordingly, the issue of causation in this study remains unresolved, with mirror neuron impairment either a cause or consequence of social impairments in ASD. This uncertainty, however, is not specific to the broken mirror hypothesis. The correlational nature of neuroimaging and neurophysiologic data for this and other clinical populations ensures that we must be cautious when attempting to infer causality. In another example, the apparent reductions in structural and functional connectivity between certain brain regions in ASD (52) may actually be a product of a lifelong pattern of altered engagement with one's environment, social and otherwise. Large-scale longitudinal studies will be critical to addressing these concerns.

In the current study, we examined mirror neuron activity both as a continuous variable (i.e., MEP amplitude when observing transitive relative to static videos) and as a categorical variable (i.e., whether or not the MEP amplitude was greater for transitive than static videos). That a significant association was seen for social symptoms and the categorical (rather than continuous) mirror neuron index may speak to the heterogeneous nature of ASD; that is, rather than mirror neuron impairments affecting all individuals with ASD, it may indicate a neurobiological subtype of ASD that is associated with more severe social symptoms. It should be noted, however, that the influence of AQ social on the continuous mirror neuron variable approached significance. While this finding might be seen as supporting the broken mirror hypothesis, it could also be viewed as consistent with a sensorimotor learning account, whereby greater social impairments might prohibit the effective formation of associations between neural processes related to self-movements and others' movements (i.e., mirror neurons). In any case, the current findings should be pursued further, as establishing neurobiological subtypes of ASD is of particular importance to developing biomedical treatments.

Limitations to this study include investigation of only one cerebral hemisphere, the inclusion of some medicated participants (although the impact of psychotropic medication on recordings of putative mirror neuron activity is not known), and a relatively broad age range of participants. It might be argued that our results could reflect attentional impairments (i.e., that the group that did not show facilitation displayed poorer attention to the stimuli); this is certainly possible but is not supported by participants' responses to questions about the stimuli and the monitoring of participant eye gaze. The use of self-report for determining symptom severity might also be criticized; however, we lack strong measures for third-party symptom ratings in ASD that are appropriate for both children and adults. Furthermore, many of our adult participants live alone, and in this respect self-report was considered most appropriate. Nevertheless, the current findings provide support for

the contention that, on the whole, there is an MNS impairment in ASD. This impairment does not appear to affect all individuals with ASD but is associated with greater social symptom severity. We now need to determine the neurobiological source of this impairment (e.g., motor systems, neural connectivity, neurotransmitter systems) and, more importantly, determine the functional significance of this impairment (which will arise through continued study of mirror neuron activity in both healthy and disordered human populations). This will allow us to decide whether the human MNS should be pursued in relation to developing new ways of diagnosing and treating autism and associated disorders, or simply be considered a by-product of impaired social relating.

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Supplementary material cited in this article is available online.

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