Reduced cortico-motor facilitation in a normal sample with high traits of autism

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\textbf{Abstract}

Recent research in social neuroscience proposes a link between mirror neuron system (MNS) and social cognition. The MNS has been proposed to be the neural mechanism underlying action recognition and intention understanding and more broadly social cognition. Pre-motor MNS has been suggested to modulate the motor cortex during action observation. This modulation results in an enhanced cortico-motor excitability reflected in increased motor evoked potentials (MEPs) at the muscle of interest during action observation. Anomalous MNS activity has been reported in the autistic population whose social skills are notably impaired. It is still an open question whether traits of autism in the normal population are linked to the MNS functioning. We measured TMS-induced MEPs in normal individuals with high and low traits of autism as measured by the autistic quotient (AQ), while observing videos of hand or mouth actions, static images of a hand or mouth or a blank screen. No differences were observed between the two while they observed a blank screen. However, participants with low traits of autism showed significantly greater MEP amplitudes during observation of hand/mouth actions relative to static hand/mouth stimuli. In contrast, participants with high traits of autism did not show such a MEP amplitude difference between observation of actions and static stimuli. These results are discussed with reference to MNS functioning.

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Mirror neurons are a class of neurons that fire both during action performance and action observation. These neurons have been directly observed by depth electrode recording techniques in primates [9]. Indirect evidence of a mirror neuron system (MNS) in humans has been supported by several studies using various psychophysiological techniques in humans: e.g. fMRI [20], PET [14], MEG [22]. Recently, intracranial recording has provided direct evidence of the existence of mirror neurons in humans [18]. Evidence for the existence of a human MNS also comes from studies using transcranial magnetic stimulation (TMS). It is proposed that while the participant is observing the movement of the muscle embedded in an action, the mirror neuron system activity increases in the pre-motor cortex. This activity modulates the motor cortex (M1) resulting in enhanced motor evoked potential (MEP) amplitude recorded at the participant’s muscle when the corresponding cortical area is stimulated using the TMS. Thus an increase in MEP amplitude during action observation has been interpreted as representing MNS activation [10]. Following this rationale, a number of TMS studies have replicated and characterized this observation-induced motor facilitation [5,11,26].

The human MNS has been proposed to contribute to human action recognition, action understanding, imitation, theory of mind and empathy [24]. However, the precise role of mirror neurons in action understanding and other high order cognitive functions has received considerable criticism (see [17] for a review). The range of social-cognitive abilities ascribed to the MNS seems to overlap to some extent with the several social-cognitive disabilities seen in autism [29]. Consequently, MNS functioning has been investigated in autistic spectrum disorder (ASD) individuals using a variety of techniques. Theoret et al. examined functional differences in MNS between individuals with ASD and controls using TMS. They showed that observation of a hand movement oriented away from the observer failed to modulate the excitability of the motor cortex in ASD individuals whereas they showed comparable motor cortex excitability to the controls when they observed hand movement oriented towards them. This was interpreted as resulting from a defective self-other representation mechanism [27]. Another study carried out by Cattaneo et al. [6], demonstrated that intention understanding may be impaired in ASD individuals. They found that when controls were asked to reach and grasp...
food, during the reaching phase an increase of EMG activity was recorded from the mylohyoid muscle (MH) which controls mouth opening. However, no EMG increase in the MH was observed when controls were asked to reach and grasp an object and place it somewhere else. The same pattern of EMG increase in the MH was found when controls observed a model reaching and grasping food and conversely no EMG increase in the MH was found when the model reached and grasped an object. In ASD children, results were different: during the execution of “reaching and grasping to eat” no EMG activation of MH was observed at all. The MH was activated only in the last stage of the action (bringing to mouth). Also, no EMG activation of MH was recorded in ASD children during the observation of a model performing the bringing-to-the-mouth action or putting an object into a container. Cattaneo et al. suggested that ASD children were unable to understand the intention of others [6].

The above evidence has been interpreted as a dysfunctional MNS in ASD individuals and could represent the neural substrate of the social deficits characteristic of this clinical population. Even though ASD individuals show abnormal MNS activity at the neural level, however there is no evidence that at a behavioural level they show imitation or goal understanding deficits. Hamilton et al., compared ASD and matched controls in an imitation, goal emulation and goal understanding tasks as well as on motor planning and gesture understanding and concluded that ASD children were not impaired in any of these tasks [16]. Hamilton suggests that children with ASD have no problems in emulation tasks (copying the goal of the task). However ASD individuals perform poorly on mimicry tasks in which they are supposed to spontaneously simulate the kinematic features of the observed action [15]. Also Southgate et al. [25] pointed out that some of the studies showing abnormal mirror neuron activity [23,4] did show EEG and cortico-motor abnormalities in ASD relative to controls but they did not test any imitation skills in the ASD individuals, in that ASD were instructed to observe stimuli presentation. Similarly, neuroimaging studies [8,29] have shown to reduce MNS activation in ASD compared to controls but failed to report behavioural differences between ASD and controls in imitating facial expressions or meaningless finger movements.

In the present study, we investigated the activity within the sensorimotor MNS during action observation in relation to autistic traits in the normal population. To this end, the AQ [3] that measures social/communication skills, attention switching, attention to detail, and imagination was administered to healthy individuals from the general population. Two groups were formed according to their scores on this measure: one defined as having high traits of autism and the other as having low traits of autism. The two groups (high & low AQ) were exposed to single pulse TMS while the EMG was recorded from the abductor pollicis brevis (APB) hand muscle. We measured participant’s TMS-induced MEPs while they were watching a blank screen; that served as a baseline to control for cortico-motor excitability differences in the two groups in absence of any stimulus presentation. Then, while they were watching images of static body parts (hand & mouth) and while watching short videos of hand and mouth actions presented either visually + auditory, only visually or only auditory, in a random order. We presented participants with different body parts (hand & mouth) in order to test the APB facilitation speciﬁcity. We predicted that observing hand actions involving the APB muscle would facilitate the participants’ APB muscle because of the automatic observation/execution matching mechanism at play during the action observation and that this would be reﬂected in greater MEP responses to TMS stimulation. On the other hand, during the static hand observation, the participants’ APB should be facilitated to a lesser extent because no action is performed. We presented the stimuli (hand & mouth action) in 4 different modalities (visual/auditory, only visual, only auditory and static) in order to investigate possible differential effects on the visual and the auditory mirror neuron systems [12]. Following the dysfunctional MNS theory of autism we hypothesized that if a link between traits of autism and the observation/execution matching mechanism exists then we should expect that participants with high AQ scores (that suggest traits of autism) would show a different pattern of cortico-motor facilitation as indexed by MEP amplitudes during stimuli observation (static, visual, auditory, visual/auditory) compared to participants with low AQ scores. Specifically we expected the low AQ group to facilitate significantly more during actions observation compared to static stimuli observation and that this difference would not be seen in the high AQ group.

A sample of 207 university students was contacted by e-mail. They were initially screened using the AQ (mean score was 16.2 with a standard deviation of 5.7). Due to the fact that participants’ scores at the AQ were not normally distributed, out of 207 questionnaires received 17 participants qualiﬁed to be included in the low AQ group and 20 in the high AQ group. These participants were then invited to attend the whole TMS experiment and 10 participants per group responded and completed the whole experiment. The final sample was composed of 20 students (12 males). The criterion for group formation was AQ score being at least one standard deviation below (low AQ group) or above (high AQ group) the mean. One group consisted of 6 males and 4 females (mean age 23.7 SD 2.8) with “low scores” (AQ < 10) and the other group consisted of 6 males and 4 females (mean age 24.5, SD 3.1) with “high scores” (AQ > 22). All participants’ AQ score were under the clinical cut-off point (see below). All those participating in the TMS part of the study were screened for TMS suitability using internationally approved safety guidelines [28] and were paid £10 for their participation. Ethical approval was granted by the local ethical committee (Department of Psychology, University of Essex). This is a brief, self-administered scale for identifying the degree to which adult people with normal IQs present ‘autistic traits’. It contains 50 questions.

Participants’ scores could range from 0 to 50. The score of 32 represents the cut-off score that suggests the need for clinical assessment [3].

Stimuli were different types of 3 s video clips. In the “hand condition” stimuli were video clips showing manual goal directed actions, these were: cutting a piece of paper with scissors, ringing a bicycle bell, playing guitar, dialling a number on a cellular phone, clicking fingers, locking a door and crumpling a piece of paper. All actions presented as stimuli were performed with the right hand and involved movement of the abductor pollicis brevis (APB) muscle. In the “mouth condition” stimuli were video clips showing human mouth actions, these were: kissing, sucking through a straw, singing, whistling, rapid lips vibration, talking and blowing. Each stimulus in the “hand” and “mouth” conditions was presented in 3 different modalities—visual (video without sound), auditory (sound with a blank screen) and visual + auditory (video with sound). Static video clips of a hand or a mouth were also included.

Each experimental trial started with a 1000 ms fixation cross, followed by a 3000 ms video clip followed by a 1000 ms black screen. The fixation cross appearing on the screen indicated the beginning of each trial as well as the beginning of the EMG recording. Participants were simply asked to attentively observe the video clips shown on the screen and to control for their stimuli attendance to count and report at the end of each block the number of times a target stimulus was presented. At the beginning of the experiment participants attended a baseline session where they were watching a black screen while 15 single pulse TMS trials were delivered. Then they were shown all the hand and mouth stimuli in a visual-sound mode to familiarise them with the stimuli and to put the sounds into context. Then they attended a block where they observed 30 static hand videos and 30 static mouth videos. Following this they
attended 5 blocks of 3 min and a half each where they observed hand and mouth actions presented in 3 different modalities—visual, auditory and visual + auditory. Each block contained all hand and mouth action types in the 3 different modalities (7 hand actions × 7 mouth actions × 3 different presentation modalities) for a total of 42 stimuli per block.

MEPs were recorded from the abductor pollicis brevis (APB) muscle of the right hand at rest. EMG data were acquired with the Nexus10 system (Mind Media B.V.). A figure-eight coil connected to a Magstim Rapid Transcranial Magnetic Stimulator (Magstim Co. Ltd.) was placed over the left primary motor cortex (M1). The intersection of the coil was placed tangentially to the scalp with the handle pointing backward and laterally at 45° angle away from the midline. The coil was moved nearby the left motor cortex in order to establish the optimal position from where maximal amplitude MEPs was elicited in APB. The intensity of the single pulses used in the experiment was set at 130% of the resting motor threshold, defined as the minimal intensity necessary to produce MEPs with amplitude of approximately 50 μV in at least 5 out of 10 trials [2]. Pulses were randomly delivered between 1.5 s and 2 s after onset of each video clip. Minimum inter-pulse interval = 4.5 s.

Data were collected from 20 participants, 4 participants were discarded: 2 participants because of high variability in the data caused by head movements and 2 because of problems associated with the estimation of the resting motor threshold. Data from 16 participants were analyzed. Eight participants formed the high AQ group and eight the low AQ group.

Each data point in the baseline condition was log (Ln) transformed in order to normalise it. All the data in the other conditions (static hand/mouth, visual + auditory hand/mouth, visual hand/mouth and auditory hand/mouth) were normally distributed (Shapiro–Wilk’s test of normality applied). An independent-samples t-test was performed on the baseline condition with the two low and high AQ being the grouping variable.

For the main analysis a mixed factorial design was employed. The between subjects factor was AQ score: low vs high. One within-subjects factor was body part (hand vs mouth). The second was the presentation mode: visual & auditory, only visual, only auditory and static. The dependent variable was the TMS-induced MEPs (root mean square amplitude) recorded from APB muscle of the right hand. To further explore differences between the two (low and high AQ) groups planned paired-samples t-test comparisons were run: static (hand/mouth) vs visual + auditory actions (hand/mouth); static (hand/mouth) vs visual actions (hand/mouth) and static (hand/mouth) vs auditory actions (hand/mouth).

An independent-samples t-test (2-tailed) was run to compare the two groups (low/high AQ) on the baseline session (low AQ mean amplitude was 212.79 and high AQ mean amplitude was 203.89). It revealed no significant difference [t < 1] and showed that corticomotor excitability at rest was equivalent in the two groups.

The amount of TMS-induced APB muscle facilitation during stimuli observation (hand/mouth goal directed action presented in different modalities: visual, auditory, visual + auditory and static hand/mouth) differed according to the presentation modality [F3,42 = 7.464; p < 0.0004]. The effect of the modality presentation on the TMS-induced APB muscle facilitation differed between the two high and low AQ groups, [F3,42 = 4.127; p < 0.011] (Fig. 1). No other main effects or interactions were significant (the largest F < 1.687).

The significant interaction between presentation modality and AQ score (independent of the body part shown) was further explored using collapsed across body part (hand + mouth) planned paired-samples t-test comparisons (Fig. 2): the first was between static stimuli and visual goal directed actions. This revealed that low AQ participants were significantly more facilitated (APB motor

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**Fig. 1.** Motor evoked potentials measured at the APB during body parts (hand/mouth movement) presented in four different modalities (static, visual + auditory, visual, auditory) in the two groups (low and high AQ). Error bars indicate s.e.m.

**Fig. 2.** Pre-planned (paired-samples t-test) comparisons between high and low AQ groups’ cortico-motor facilitation between static hand/mouth stimuli against visual and auditory hand/mouth actions stimuli observation (action V/A); static hand/mouth stimuli and visual hand/mouth actions (action V) stimuli observation; static hand/mouth stimuli and auditory hand/mouth actions (action A) stimuli observation. Asterisks (*) denote significant difference.
facilitation) when presented with visual goal directed actions compared to when presented with static stimuli \([t(7) = -2.897; p < 0.023]\). In contrast, the high AQ group was not significantly more facilitated (APB motor facilitation) when presented with goal directed actions compared to when presented with the static condition \([t(7) = -3.289; p < 0.013]\). In contrast, high AQ did not show such a motor facilitation \([t < 1]\). The second comparison was between static stimuli and visual/auditory goal directed actions. This also showed the same pattern of results with low AQ participants being more facilitated (APB motor facilitation) when observing visual/auditory goal directed actions than when they observed static stimuli \([t(7) = -2.347; p < 0.06]\); whereas there was no difference between the two conditions in the high AQ group \([t < 1]\). Both groups were 100% accurate on counting the target stimulus that controlled for stimuli attendance.

This study investigated whether there was a relationship between traits of autism in a normal population and the MNS activity as indexed by changes in TMS–induced MEP amplitudes. Results revealed that individuals with low traits of autism had significantly greater cortico–motor APB facilitation when they were presented with videos depicting hand and mouth actions (presented both in visual/auditory or only visual modality) compared to when they were presented with images of a static hand or mouth. As for the individuals with high traits of autism, no such difference in cortico-motor APB facilitation was observed. Our results therefore suggest that the TMS-induced MEP facilitation during hand/mouth action observation is associated with the participants’ AQ scores. Results revealed that participants with low and high traits of autism did not differ when their cortico-motor excitability was assessed at rest. This is interesting because it shows that the resting pyramidal tract is equivalently functioning in the two groups and that the other differences found between the two groups are likely to be related to the experimental manipulations. The fact that mouth actions video observation facilitated the APB motor response was unpredicted. The mouth action videos were introduced in the study in order to test for the specificity of the APB motor facilitation. This result could be due to the high connectivity between hand and mouth regions of the primary motor cortex. Therefore it could well be that the presentation of mouth actions also resulted in increased excitability of the hand regions [13]. In agreement with this, Liuzzi et al. [21], showed facilitation of the leg motor cortex during speech perception suggesting that mouth action stimuli are not an appropriate control for muscle facilitation when exploring limb movement.

Two of the main functions attributed to the MNS are action recognition and action understanding [24]. Evidence coming from TMS studies has given support to that by showing that there is an increase in the amplitude of the TMS-induced MEPs within the muscles involved in the action that is being observed [10,11]. It is hypothesized that actions are recognized and understood when the representation of the action that an individual is observing is mapped onto the observer’s own motor system [19]. In line with these TMS studies, our results show that normal participants with high traits of autism exhibit a reduced activity in this mechanism, which suggests that at the neural level, they may carry out recognition and understanding of the observed action through different mechanisms.

Our results are also in line with the impairment of motion perception documented in ASD individuals. Dakin and Frith [7], suggest that poor motion perception documented in ASD might be related to atypical functioning of the superior temporal sulcus (STS) [7]. Converging evidence points to the STS being the area involved in the integration of biological motion [1]. If this is correct, it follows that dysfunctional STS could contribute to disorders in social communication. This is compatible with the dysfunctional mirror neuron system theory of autism and hence with the results of the present study. The STS along with the inferior frontal gyrus (IFG) and the inferior parietal lobe (IPL) constitute the MNS in humans [19]. One could speculate that if the motion perception integration in the STS is abnormal in ASD then the afferent visual input that originates from the STS and goes through the IPL to the IFG in order to activate the corresponding action from the observer’s motor repertoire will not be functioning properly. This would lead to an impaired recognition and understanding of the action, which might be related to the reduced cortico–motor facilitation observed in ASD by Theoret et al. [27]. This reasoning might also explain the reduced cortico–motor facilitation found in normal individuals with high traits of autism showed by our results. Further research is needed to better understand the behavioral implications of this reduced cortico–motor facilitation during action observation in normal people with high traits of autism.

In summary, we found a difference in cortico–spinal activation dependent on the level of autistic traits found in a normal population sample. Specifically, participants with low scores on a measure of these traits (low AQ) showed greater TMS–induced motor evoked potentials when observing moving hand/mouth actions than still hand/mouth images. This is thought to be an index of mirror neuron system activation [5,11,12,27] and was not observed for participants with high scores on the AQ. These results also suggest that MEP facilitation may be a useful biomarker of autistic traits in the general population.

References