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Impaired motor facilitation during action observation in individuals with autism spectrum disorder

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It has been suggested that social impairments observed in individuals with autism spectrum disorder (ASD) can be partly explained by an abnormal mirror neuron system (MNS) [1,2]. Studies on monkeys have shown that mirror neurons are cells in premotor area F5 that discharge when a monkey executes or sees a specific action or when it hears the corresponding action-related sound [3–5]. Evidence for the presence of a MNS in humans comes in part from studies using transcranial magnetic stimulation (TMS), where a change in the amplitude of the TMS-induced motor-evoked potentials (MEPs) during action observation has been demonstrated [6–9]. These data suggest that actions are understood when the representation of that action is mapped onto the observer's own motor structures [10]. To determine if the neural mechanism matching action observation and execution is anomalous in individuals with ASD, TMS was applied over the primary motor cortex (M1) during observation of intransitive, meaningless finger movements. We show that overall modulation of M1 excitability during action observation is significantly lower in individuals with ASD compared with matched controls. In addition, we find that basic motor cortex abnormalities do not underlie this impairment.

Ten high-functioning individuals (seven males) with ASD who met a clinical diagnosis for autism or Asperger disorder (age range 23–58, mean 39) and ten age- and gender-matched controls (age range 21–60, mean 39) were studied following a protocol approved by the investigational review board after obtaining informed consent. All patients were diagnosed by a psychiatrist or neurologist and met DSM-IV-R criteria [11] for ASD. TMS-induced MEPs from the right first dorsal interosseus (FDI) and abductor pollicis brevis (APB) muscles were recorded while subjects passively viewed 10 second movie clips of index or thumb movements on a computer screen at a distance of 1 m.

In the control group, observation of index finger movements preferentially facilitated the MEPs recorded from the FDI, whereas observation of thumb movements facilitated the MEPs recorded from the APB, irrespective of hand orientation (Figure 1). In the ASD group, muscle-specific facilitation was absent during observation of movements away from the observer (egocentric view). However, for conditions in which hand orientation and finger movements were towards the observer (allocentric view), MEP facilitation was similar to that seen in controls. The difference between groups was statistically significant. A repeated measures ANOVA revealed a main effect of group (f = 9.97; p = 0.007), and planned comparisons revealed that the two groups differed for the 'index away' (t = -2.20; p = 0.047) and 'thumb away' (t = –2.57; p = 0.022) conditions, whereas both 'toward' conditions were not statistically different (all p > 0.4).

Individuals with autism display atypical patterns of motor cortex activation during simple finger movements [12]. Therefore, the reported cortical abnormalities in ASD during action observation could be related to a low-level dysfunction of primary motor cortex or cortico-spinal projection. To rule out this possibility, we used TMS to study motor threshold, input–output curves, intracortical inhibition and facilitation (paired-pulse TMS) and silent period. No significant difference between groups was revealed (see

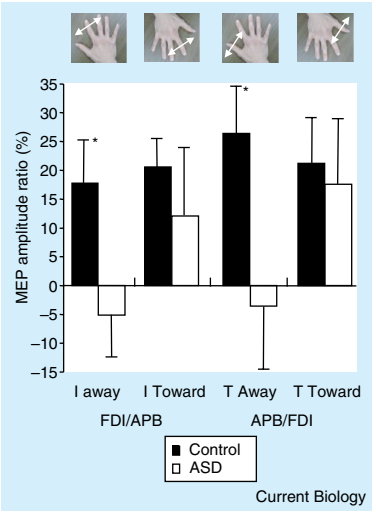

Figure 1. Bar histogram of the muscle ratios of the area-under-the-curve for the motor-evoked potentials depending on viewing condition.
Data are expressed as the percentage increase of MEP size for the target muscle (involved in the observed movement) relative to the other muscle. I: index finger; T: thumb. Four different movie clips were randomly presented to the subjects: 1) index finger moving laterally at 1 Hz, facing away from the subject; 2) index finger moving laterally at 1 Hz, facing toward the subject; 3) thumb moving laterally at 1 Hz, facing away from the subject; 4) thumb moving laterally at 1 Hz, facing toward the subject. Each movie clip was presented 16 times and a single TMS pulse was delivered over the left M1 during each clip presentation at an intensity of approximately 120% motor threshold. The timing of the TMS pulse was varied between 5 and 7 sec after initiation of the movie clip. TMS was performed with a 70 mm figure-of-eight coil and Magstim 200 (Magstim, Dyfed, UK). MEPs were recorded from the first dorsal interosseus (FDI) and abductor pollicis brevis (APB) muscles. Raw data (area under the curve of each MEP) were first converted to muscle ratios to account for the inherent variability between subjects and recorded muscles. Data were analyzed as the ratio of FDI over APB for observation of index finger movement and APB over FDI for observation of thumb movement (in percentage change). Data were evaluated with a two-way repeated measures ANOVA with group and condition as factors.

Supplemental data for Figure S1 and methods).

We show for the first time that the system matching action observation and execution is impaired in ASD, where observation of finger movements failed to normally modulate the excitability of the motor cortex. Specifically, observation of a movement in control subjects selectively enhanced motor ouput to the muscles involved in the movement whereas this modulation was weaker in ASD. The MNS seems to be intricately involved in imitation [13–16] and might form a link between sender and receiver and thus be crucial to the adequate development of social cognition [17]. Therefore, a dysfunction of the MNS in ASD, as demonstrated by our data, could represent the neural underpinnings of the social deficits characteristic of ASD, and ultimately lead to abnormal self–other representations, reduced reciprocal social abilities, and perhaps prevent the development of empathy and full theory of mind [1].

The difference between the toward–away conditions in individuals with ASD may be explained by a self-consciousness deficit resulting in faulty self–other representation. Recent data suggest that individuals with ASD, contrary to normal controls, fail to display a memory advantage for self-referent material over semantic material [18] and are impaired at recalling self-related events [19]. Here, we report that observation of hand movement in the egocentric view failed to properly activate motor structures of the brain, whereas observation in the allocentric view was associated with normal activation of the motor cortex. As such, the self-directed movement (more primary in development) is correctly processed but the more complex 'other-directed' movement is impaired. This might provide a useful strategy to identify and probe the mirror neuron level of self–other impairments.

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Supplemental data

Supplemental data including analysis of motor cortex function in control and ASD groups as well as methodological details are available at http://www.current-biology.com/cgi/content/full/15/3/R84/DC1/

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