Journal of Clinical Neuroscience 17 (2010) 1239–1243

Contents lists available at ScienceDirect

Journal of Clinical Neuroscience

journal homepage: www.elsevier.com/locate/jocn

Personal View

Mirror neuron dysfunction in autism spectrum disorders

Tom Perkins [a], Mark Stokes [a,*], Jane McGillivray [a], Richard Bittar [b,c,d,e]

[a] Department of Psychology, Faculty of Health, Medicine, Nursing and Behavioural Sciences, Deakin University, 221 Burwood Highway, Burwood, Victoria 3125, Australia
[b] Precision Neurosurgery, Melbourne, Victoria, Australia
[c] Department of Neurosurgery, Royal Melbourne Hospital, Parkville, Victoria, Australia
[d] Department of Surgery, The University of Melbourne, Parkville, Victoria, Australia
[e] Brain and Mind Research Institute, The University of Sydney, Sydney, Australia

ARTICLE INFO

Article history:
Received 6 July 2009
Accepted 17 January 2010

Keywords:
Autistic disorder
Autism spectrum disorders
High functioning autism
Inferior frontal gyrus
Inferior parietal lobule
Mirror neurons
Mu rhythm

ABSTRACT

Autism spectrum disorders (ASDs) are developmental conditions characterized by deficits in social interaction, verbal and nonverbal communication and obsessive/stereotyped patterns of behaviour. Although there is no reliable neurophysiological marker associated with ASDs, dysfunction of the parieto-frontal mirror neuron system has been suggested as a disturbance linked to the disorder. Mirror neurons (MNs) are visuomotor neurons which discharge both when performing and observing a goal directed action. Research suggests MNs may have a role in imitation, empathy, theory of mind and language. Although the research base is small, evidence from functional MRI, transcranial magnetic stimulation, and an electroencephalographic component called the *mu* rhythm suggests MNs are dysfunctional in subjects with ASD. These deficits are more pronounced when ASD subjects complete tasks with social relevance, or that are emotional in nature. Promising research has identified that interventions targeting MN related functions such as imitation can improve social functioning in ASDs. Boosting the function of MNs may improve the prognosis of ASDs, and contribute to diagnostic clarity.

1. Introduction

Autism spectrum disorders (ASDs) are pervasive, developmental, neurological conditions which adversely impact behaviour in three key domains: social interaction, verbal and nonverbal communication, and obsessive and/or stereotyped patterns of behaviour.[1] Abnormal or impaired social interaction is characterized by deficits in joint attention, reciprocity, imitation, empathy, relationships, as well as hyperactive/impulsive behaviour and social anxiety. Communicative deficits in language include odd prosody, failure to understand metaphors or statements with implied meaning, idiosyncratic use of words and delayed speech development. Obsessive interests and stereotyped patterns of behaviour including an intense interest in a particular subject matter, preoccupation with small details as opposed to global functioning, inflexible adherence to non-functional routines and rituals, and abnormal motor and sensory functioning.[2] Although presentation varies considerably across individuals, these core characteristics are defined as deviant relative to the individual's developmental level.

The Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision (DSM IV-TR),[3] describes two major ASDs; Autistic disorder (AD) and Asperger's syndrome (AS).[4] Although subject to ongoing debate, AS is diagnostically differentiated from AD on the basis of normal language development, defined as expression of single words by age 2 years and communicative phrases by age 3 years.[3] Where intellectual functioning is not impaired (IQ > 70–85) in AD, the condition is termed high functioning autism (HFA). A meta-analysis of 43 studies estimates the prevalence of autism (AD and HFA) to be approximately 0.13% of the population, and AS 0.03%.[5]

To date, an important issue confronting clinicians and researchers is the absence of definable and reliable, neurophysiological markers to the disorder. Diagnosis is made on the basis of behavioural symptoms, which reduces diagnostic clarity and limits the capacity to identify these conditions early and accurately. In 1999, two research groups independently suggested that a network of visuomotor cells known as mirror neurons (MNs) may contribute to some of the key symptoms that characterize autism.[6,7]

2. Mirror neurons

MNs are activated by the performance or observation of *object* or *goal* directed actions. What distinguishes MNs from other motor neurons is they not only discharge when an individual performs a particular action (such as reaching for a piece of food), but also

* Corresponding author. Tel.: +61 3 9244 6865.
E-mail address: mark.stokes@deakin.edu.au (M. Stokes).

0967-5868/$ - see front matter © 2010 Elsevier Ltd. All rights reserved.
doi:10.1016/j.jocn.2010.01.026

when an individual watches somebody else perform a similar action (such as a friend reaching for a piece of food).[8]

Studies in primates have identified a MN system consisting of the ventral premotor cortex (area F5) and inferior parietal lobule (IPL).[9] Although MNs have not been directly observed in humans, there is indirect evidence that MNs may exist in homologous areas. These are the ventral premotor cortex, IPL, and inferior frontal gyrus (IFG; which corresponds to the pars opercularis).[10] This network has been named the parieto-frontal mirror system.[8] A large body of evidence using fMRI has identified activity in these regions when *observing* motor actions such as grasping an object.[11–16]

3. Mirror neuron dysfunction in autism

3.1. Initial theory

Prior to the discovery of MNs, a theory was penned that suggested a deficit in self-other matching may contribute to autism.[17] This ability involves forming and coordinating mental representations of the self and others. Understanding others behaviours and social rules is achieved by extracting patterns of similarity between the self and other. It has now been acknowledged that this theory of autism is similar to the key role of MNs. Disruption of MN functioning may contribute to this self-other matching deficit.[7] However, it is unlikely that this alone would account for the entire presentation of autism. We argue here that MN function may constitute a neurophysiological marker of autism.

MN deficits were first thought to be linked to autism due to their purported role in behaviours and abilities that are commonly disturbed in autism. The first studies of MNs by Rizzolatti and his colleagues identified their key function as most likely facilitating understanding of motor actions.[9] Because the same pattern of MNs are activated when performing or observing an action, primates can recognize the goal of a motor act performed by others.[6] More recent evidence suggests that this execution/observation matching system may have evolved conjointly with other networks to allow for more complex functions in humans. These include, imitation, empathy, theory of mind and language,[18] all of which can be disturbed in autism.

3.2. Imitation and empathy

The ability to imitate the actions of others is commonly disturbed in autism.[19] Neuroimaging studies in normal individuals have furnished evidence of a role for MNs in motor imitation. One study used repetitive Transcranial Magnetic Stimulation (rTMS) to disrupt function in particular cortical areas during imitative tasks. The authors identified a significant increase in error rate during imitation when either the left or right pars opercularis was activated.[20] In other words, disruption of an area believed to be populated with MNs led to a decrement in imitative performance. Other studies support the hypothesis that MN areas are involved in imitation.[21–23]

Empathy refers to the ability to understand and vicariously experience the emotional state of others. Empathy is linked to imitation, and is commonly disturbed in autism.[24] Those with autism have more difficulty interpreting others emotions such as discriminating between a sad and happy face.[25]

Anatomical studies have revealed connectivity between the dysgranular field of the insula and the frontal and parietal MN areas.[26] Further, insula neurons with mirror-like properties have been identified. Utilizing fMRI on 14 healthy males, overlap of activity in the insula was found whilst subjects inhaled a foul smelling odorant (execution condition), and when they watched a video of someone emotionally expressing disgust (observation condition).[27] Two other studies have found similar concordance of neural activity between the performance and observation of disgusting stimuli.[28,29] A study in which subjects had to identify or imitate faces depicting six emotions (happy, angry, sad, surprise, disgust and fear) also found increased activity in MN areas.[30] Although this research base provides evidence for mirror-like activity, the methodology of correlating brain activity to a task does not necessarily prove whether MNs are involved.

3.3. Theory of mind

MNs have been linked to theory of mind (TOM) abilities. TOM requires an inference of what other people are thinking, and allows people to evaluate the behaviour of others within the context of their mental states. This includes their goals, desires, emotions and opinions.[4] Impaired TOM is a prominent cognitive theory of autism, with a large body of research identifying TOM deficits among those with autism.[31–33] The possibility that MNs have a role in TOM has yet to be directly tested. However a theoretical link has been made. Proposed more than a decade before the discovery of MNs, this theory suggests people use their own mental representations to predict and comprehend the mental processes and behaviours of others.[34] Indirect attempts to support this claim have been undertaken with limited success to date,[35] yet these have not directly assessed the hypothesis that MNs are involved in TOM. Nonetheless, recent research has identified MNs can selectively respond to specific intentions in both monkeys and humans, indicating that they are involved in the internal representation of another.[36,37]

3.4. Language development and communication

A more speculative link has been made between MNs and language development. A broad range of language deficits can occur in autism, and form part of the diagnostic criteria.[38] Communicative MNs have been discovered in the lateral region of area F5 of Macaques (homologous to Broca's area).[39] These cells respond to performed or observed actions with communicative intent such as tongue protrusion or lip-smacking.

Additionally, MNs with audio properties in Macaques have been identified.[40] A substantial number of MNs fired in response to a goal directed action (such as breaking a peanut) and also to the sound itself with the action out of sight. It has been speculated that MNs that match observed and executed actions with communicative significance provided a basis for gestural communication.[41]

4. The case against mirror neurons

Despite this promising research base, numerous criticisms have been made toward the study of MNs in humans. Firstly, MNs have yet to be *directly* observed in humans.[42] Secondly, MNs make up a small minority of observed cells in Macaques (approximately 6%; yet the distribution in humans remains unknown),[9] which means interpretation of homologous areas in humans is not exclusively measuring suspected MN activity. Thirdly, it has been suggested that an exclusive MN explanation of imitation is too simple for such a complex ability.[43] Fourthly, movement selectivity (a key characteristic of MNs) has not been adequately assessed in humans.[44] It is worth noting these issues raised are predominantly methodological in nature.

5. Evidence for mirror neuron dysfunction in autism

5.1. Electroencephalograph (EEG)

One method to investigate MN activity in humans is via EEG. The *mu* wave measures large amplitude oscillations of the synchro-