

National Science Foundation Workshop Report

Neurocognitive Development and Autism: The Mirror Neuron Hypothesis

July 23-24, 2007

Executive Summary

Typical developmental processes can often be studied productively by comparing them with disordered development. One such example is autism spectrum disorder (ASD), in particular because it has recently been proposed that its multiple aspects can be attributed to failure in a single system: the mirror neuron system. Mirror neurons activate both when the person performs an action and sees it performed by another. They apparently assist in imitation, important for language development and social connectedness. Because this hypothesis is tractable (though potentially incorrect), it provided a useful target for organizing a workshop to explore possibilities in using autism as a tool for studying neurocognitive development. The workshop, sponsored jointly by the National Science Foundation and Autism Speaks, brought ten senior researchers and 19 junior researchers and students together to address whether the mirror neuron hypothesis could help us understand development. Although there were brief presentations of experimental results (lectures and posters), the main work was done in two working groups devoted to asking whether testable predictions could be generated for further research. Workshop attendees proposed several avenues to explore:

- Do measures of mirror neuron activity correlate with, and perhaps explain, differences in imitation ability between typically developing children those with ASD?
- To what extent are mirror neurons involved only in goal-directed activity, and does this differ across populations?
- Does imitation itself change the mirror neuron system, and equally in both populations?
- Are there mirror neurons for social aspects (emotion, empathy, altruism) as well as actions?

Given that these basic issues have not been fully explored, the working groups recommended that researchers take this opportunity to simultaneously test a provocative theory—that a complex disorder can be attributed to gradience in mirror neuron development—and provide a greater understanding both of typical development and the challenging disorder of autism.

Part I: Background of the Workshop

The complex interplay of gene-directed development and the environment has recently become a central area of research in neurocognitive development. The human brain is one of the most complex structures in nature, and its development in the child relies on an

intricate set of interactions to make this complexity a reality. As with all natural processes, development is a variable process, taking on a wide range of traits due to individual and environmental differences. Aphasia gave us the first important information about specialization for language within the brain. In much the same way, developmental delays and their causes can be quite informative about typical development. Although there are many such developmental difficulties, one in particular offers immediate possibilities for understanding neurocognitive development: autism.

Autism is a developmental disorder that is manifest in a number of atypical behaviors. Given that these differences may occur in varying degrees, it is more accurate to label it Autism Spectrum Disorder (ASD). Children with ASD show deficits in "social interaction, language as used in social communication, or symbolic or imaginative play" (Diagnostic and Statistical Manual of Mental Disorders), and they do so to differing degrees. Such a disorder provides a valuable perspective on the range of variability seen in typical development.

One deficit in ASD is a reduction in the amount of imitation shown by persons of all ages and functioning levels (see Rogers and Williams (2006) for a review). This is true both of spontaneous and elicited imitation. There are several hypotheses that attempt to explain the onset of ASD, but there is as yet no consensus. One recent hypothesis, and the focus of this workshop, is that the lack of imitation is central to autism (first suggested by Rogers and Pennington, 1991) and due to a failure of the mirror neuron system (first suggested by Altschuler and colleagues, 2000, and Williams and colleagues, 2001; see Ramachandran and Oberman, 2006, for a review). A series of experiments has shown that there are "mirror neurons" within the macaque brain that are active when the monkey either performs an action or sees another (human or monkey) perform that action (Rizzolatti et al. 1996). Non-visual mirror neurons have been found as well, for example, ones that respond to seeing a peanut being cracked open but also to hearing a peanut cracking (Kohler et al., 2002). The high concentration of these neurons in the macaque analog of Broca's area in humans has led to the proposal that mirror neurons facilitate the acquisition of shared movement and meaning (Gallese and Lakoff 2003). A similar mirror system also exists in humans, demonstrated through single cell recording and various neuroimaging procedures. In humans, unlike other animals, the mirror neuron system responds to gestures and facial movements as well as intentional actions on objects (Carr et al., 2003).

Difficulty with imitation is one of the signatures of ASD. Persons with ASD show decreased spontaneous imitation, decreased precision of intentional imitation, and decreased automatic imitation, than comparison persons, including those with other developmental disorders. This pattern is present in the first years of life and continues into adulthood, even in very mildly affected persons. The lack of automatic imitation of facial and postural movements may contribute to the lack of emotional and social reciprocity in ASD, which is particularly striking and, unlike motor stereotypies and repetitive behavior, is unique to this disorder. Persons with autism also appear to have atypical brain activation in mirror neuron areas, both when observing others and when imitating others, and there is recent evidence that the degree of atypical mirror neuron

activation is directly related to the severity of autism symptoms (Dapretto et al. 2006). Thus, the mirror neuron system may be an important part of the biological foundation for the behavioral impairments seen in autism.

Goal of the meeting

Although there is as yet no clear hypothesis about how the mirror neuron system in particular would be disturbed, the phenomena point to a coherent and testable explanation of how ASD differs from typical development. The goal of the meeting was to frame the most important scientific questions that can inform our knowledge concerning the relationship of mirror neuron system function to development. A nucleus of senior researchers in autism and neurocognitive development was brought together with a broader group of young researchers to explore ideas in depth and to examine this and other basic science questions that can be addressed through the lens of autism. This report represents a working document that provides abstracts of the science that was shared. It also provides research hypotheses and ideas generated by the group which can be used to build a potential program of research for use by funding groups. The goal is to stimulate the advancement of scientific knowledge concerning bio-behavioral ties between mirror neuron system functions in humans and social behavior.

Part II: Scientific Presentations

Sally J. Rogers (University of California, Davis)

“Autism, imitation, and intentions: questions for mirror neuron studies”

Intersubjective impairments in ASD are the result of disordered self-other mapping (Rogers & Pennington, 1991). There are at least four different phases of the information processing sequence involving imitation at which the autism-specific impairment might show itself: visual input, memory, MNS cross-modal response from observation to action, and intentional motor execution. My lab group has been working to examine each step of this sequence. Visual Input: in a current eye tracking study of gestural and action imitations, the gaze patterns of 18 high functioning 8-12 year olds with ASD was compared to that of 13 typically developing (TD) children. There were no group differences in the pattern of gaze to the salient actions of the model in both the gestural and the action imitations (Vivanti et al., in prep.). Working memory: no memory differences have been found across several different studies using varied delay periods (Bennetto, 1999; Rogers, Bennetto, McEvoy, & Pennington, 1996; Rogers, Young, Giolzetti, & Ozonoff, 2007). Motor execution: The level at which ASD specific differences have been identified involves the motor execution level, using tasks involving manual and facial gestures and actions on objects, in both young children and in older higher functioning children and adolescents (Rogers et al 1996; 2003; Bennetto 1999; Vivanti et al, in review). In addition to intentional execution, automatic imitation, or mimicry, involving facial expressions, has also been found to be abnormal in ASD, in two year olds with autism (Scambler, Hepburn, Rutherford, Wehner, & Rogers, 2005)

and in high functioning adults using EMG (McIntosh, Reichmann-Decker, Winkielman, & Wilbarger, 2005).

The impairments in motor execution in ASD support a MNS hypothesis. However, other findings in autism imitation are not easily reconciled with a MNS hypothesis. The ability to read other's intentions in meaningful actions appears to be intact in autism, and this is an ability that also generates MNS response in animals and in people. People with autism also perform imitation tasks differentially depending on the meaningfulness of the task – a variable that should differentially activate MNS. Two models of meaningful (MF) versus meaningless (ML) imitation processing have been proposed (Rumiati et al., 2005; Iacoboni, 2005).

Several questions emerging from current autism research may lead to a deeper understanding of the relationship of MNS activation and imitation to autism: (1) How do the MNS of persons with autism respond to meaningful versus meaningless imitation tasks? Is there MNS response in ASD to observation of intentional actions on objects? Can socially based treatments normalize mimicry and imitation in early ASD? Does such treatment also normalize MNS activation? Underactivation of the MNS may be a cause or an effect of autism, and the directionality of this relationship must be defined in order to fully understand the significance of MNS activation and response patterns and their possible causal role in autism.

Eric Lewin Altschuler (University of California, San Diego) and **Lindsay M. Oberman** (University of California, San Diego; Harvard)

"Mirror neurons in autism: Pre-history, past, present and future"

Altschuler and Oberman described a range of collaborative work with V.S. Ramachandran, University of California, San Diego. EEG measures show a decrease in the "mu wave" associated with both action and perception of that action (Altschuler et al., 1997). This "mu wave suppression" is considered to indicate involvement of the MNS (Altschuler et al., 2000). Skills like lip reading, and the presence of the McGurk effect, should involve MNS responses. Recent work with typical adults has shown that the mu wave suppression occurs when observing a robotic arm (Oberman & Ramachandran, 2007). A human hand that is manipulated rather than moving voluntarily elicits suppression as well. A recent experiment involving social interaction with typically developing subjects involved observing a video in which a ball is being thrown in a social game. The observer perceives the ball being thrown either to another or to the self. Mu wave suppression was stronger when there was the perception of social interaction between the self and another, as opposed to interactions between other people and not the self, demonstrating differential responses to social engagement involving self versus others' actions. While previous studies in this lab have found relative lack of mu wave suppression in ASD compared to controls, (Altschuler et al., 2000; Oberman et al., 2005). A possible approach to treatment might involve TMS to mirror neuron system, to improve functioning through changes in plasticity (Oberman, Fecteau, & Pascual-Leone,

BIDMC). Webkinz® (an on-line, virtual pet) might be another treatment approach (Altschuler, 2007).

Robert Schulz (Yale University)

“The social brain in ASD: Studies of brain function and structure”

FMRI studies of face processing in higher functioning older persons with ASD show consistent abnormalities, with effect sizes of 1.0 in studies of face recognition and effect sizes of .70 in studies of emotion recognition. Hypoactivation of the fusiform face area (FFA) in response to face stimuli has been demonstrated and replicated in adults with ASD, and the degree of FFA activation correlates inversely with the severity of autism as indexed by ADOS scores. The Social Attribution Task, involving attribution of human qualities to moving geometric shapes, activates the entire social network involving amygdala, orbital PFC, DLPFC, FFA, and STS, just like face and emotion recognition tasks, even though there are no human stimuli involved.

In ASD, the biggest anatomical brain differences occur in the social network and involve temporal lobe enlargement and increased white matter in the FFA. All differences in the DTI measures involve long fiber tracts. The FFA area differences were central in the group differences that emerged in this comparative study of ASD. The differences involved the visual areas and the temporal areas. Thus, there is convergence in ASD among behavioral differences, brain function differences, and brain structure differences involving social responses.

A major research challenge is to disentangle the cause and effect relations from the correlational analyses in the brain-behavior and MNS studies of ASD. Two main ways to accomplish this involve using treatment studies, and through TMS lesions. This is a very important aspect of the MNS approach to autism at this time.

Mirella Dapretto (University of California, Los Angeles)

“Mirror neuron dysfunction relates to core deficits in autism”

Many recent publications have indicated a deficit in the MNS associated with ASD, using a variety of tasks and measures: EEG studies of observation - execution of hand actions (Altschuler et al 2000, Oberman et al 2005, Bernier et al 2007); MEG study of imitation of static mouth and lip forms (Nishitani et al 2004); TMS study of observation of finger movements (Theoret et al 2005); fMRI study of observation - imitation of finger movements (Williams et al 2006); Structural MRI abnormalities in fronto-parietal MNS areas (Hadjikhani et al 2006, 2007); EMG study of observation - imitation of facial expressions (McIntosh et al 2006); fMRI studies of observation - imitation of facial expressions (Dapretto et al 2006, Cox et al 2007). Further, in normals, there is a correlation between socialness (Interpersonal Competence Scale (ICS: Cairns et al 1995) and limbic activity during imitation of emotion (Dapretto et al., in prep.).

Dapretto et al.'s (2006) fMRI study involving imitation and MNS activation in ASD revealed no activity in the key MNS regions in the ASD group to human movement stimuli; there was reduced activation in other key areas of the social brain: amygdala, insula, striatum, and basal ganglia. There was increased activation during observation in visual association cortex and left parietal cortex in ASD compared to controls. There were no group differences in fusiform face area (FFA), but there were decreases in the inferior frontal gyrus (IFG) and pars opercularis. The FFA activity did not correlate with MNS activity as measured in IFG. These differences were not due to differences in observation of the stimuli. The ASD and typical groups spent the same amount of time fixating on the eyes during the observation period, and there was no correlation between eye fixation patterns and MNS activation.

In the typical comparison group, there was a significant correlation between interpersonal competence and MNS activity, and also between reported imitation and empathy responses in the ASD group and MNS activation in anterior cingulate cortex (ACC) and amygdala. In addition, reports of social motivation, including shared enjoyment and social reciprocity, were all negatively correlated with MNS activation in ASD. One possible inconsistency in their report and MNS hypotheses concerned their evidence of normal imitation in the ASD subjects. However, in this talk she stated that their imitation skills were not unaffected.

Finally, the issues of cause and effect need to be sorted out. She raised questions concerning the ventral striatum reward circuitry and MNS, given current theories about decreased social reward in ASD, and this is an area for future research. In terms of treatment studies, a legitimate question involves "training" the MNS.

Michael Arbib (University of Southern California)

“Autism – more than the mirror system”

The MNS does not “understand”. The neural system as a whole “understands”. Arbib's position is that he stresses the importance of mirror neuron systems (note plural) but denies that mirror neurons do “it” (imitation, language, prevent autism) all by themselves. We must go “beyond the mirror” to seek larger neural systems *of which mirror neurons are a part*.

Are MNSs inherently social? He suggests yes, that the MNS systems evolved as a social system. He suggests that the system began as a self-monitoring device and expanded to respond to others.

Neonatal imitation is not really imitation. It is the neural system gearing up to solve the correspondence problem. Intentional imitation is a capacity that is first observed at 8-12 months. The developmental sequence begins with a crude mapping of self and other, then to the developments of grasp and joy in social exchanges – both of which motivate the organism, then to the development of affordances of objects via grasping, then recognizing one's own grasp and objects, then mapping self and other's acts.

In addition to continuing study of normal and autistic children, we need more research on *neurophysiological*, *behavioral* and *comparative/evolutionary* research on monkeys. Dapretto et al. (2006) found differences in use of pars opercularis between autistic and non-autistic children, but there was no difference in the ability to imitate. This highlights the importance (Rutter, 2005) of research not just on deficits but rather also on “the compensatory cognitive strategies that individuals with autism use.” Williams et al. (2001) attribute autism to a failure of the MNS, but do repetitive actions and stereotypy introduce a paradox?

Oztop & Arbib (2002) developed a computational model of the MNS, with emphasis on how recognition of novel actions may be acquired. This was used to highlight goals for new computational models to ground new empirical studies: In addition to aspects of the MNS, we need to understand processes involved in selective attention; recognizing the object; recognizing the agent; broadening the linkage to motivational systems; going beyond recognition of single actions to recognition of sequences and hierarchical actions (paving the way for simple & complex imitation); and integrating the study of transitive and intransitive actions and language .

What is the role of the amygdala in these processes? We need incremental computer modeling of language and language systems coupled with data from early development to build better developmental models.

Marco Iacoboni (University of California, Los Angeles)

"Mirror neurons: Basic findings and implications for autism"

The discovery of premotor and parietal cells known as mirror neurons in the macaque brain that fire not only when the animal is in action, but also when it observes others carrying out the same actions provides a plausible neurophysiological mechanism for a variety of important social behaviors, from imitation to empathy. F5 is embedded in a huge area of sensorimotor neurons in animals. It is a social response of sensorimotor neurons. Multiple regions of frontal lobes modulate MN . Is this what dampens imitative responses? Recent data also show that dysfunction of the mirror neuron system in humans might be a core deficit in autism, a socially isolating condition (Iacoboni and Dapretto, 2006). Deep electrode research in humans has found further that there are cells that are "super mirror neurons" in that they are active during action but completely shut down - but inhibitory - during observation /perception (Iacoboni et al, in prep.). Although the existence of such cells is theoretically necessary (so that not all actions are imitated), this is the first demonstration of them in the human Are these the inhibitory neurons? In human subjects, 12% of motor neurons are MN in ACC and SMA. 1/3 are classically excitatory, 1/3 are classically inhibitory, and 1/3 are super mirror neurons. These super MN are in the “theory of mind” area – the social MN area is broader in humans than in monkeys, and is involved in more functions. Why would MN respond to photos and static stimuli? Perhaps because the brain is predicting motion, anticipating

actions in order to judge what will happen next – and this involves MNS . Further work will be necessary to pursue the full implication of the MNS for ASD.

Catherine Lord (University of Michigan)

“Trajectories of social communicative development in ASD”

Social deficits are as seen as the “core” of ASD, so all individuals with ASD have them. Any given behavior can be defined on multiple levels. In a study of coordination of basic behaviors, children with ASD did less of each single behavior and less coordination, but coordination was related to directing behavior.

There are differing patterns of social growth in ASD over time, even though it is the core of ASD, involving both worsening and improving. Overall, socialization at age two improved over time but social functioning at 2 predicted a continuing deficit found through age 17. In her large longitudinal study from age 2 into adolescence, four patterns were found: consistently impaired, mild and improving, mild and worsening, and consistent and mild. Can understanding social behaviors associated with mirror neurons help us explain these changes? Acquisition of other prosocial skills needs to be examined. Can we use these data to better understand the neurobiological phenomena? Developmental/experimental approaches are needed, and the dimension of meaning needs attention; face recognition is only one component.

Andrew N. Meltzoff (University of Washington, Seattle)

“Understanding social cognition: Typical development and implications for autism and mirror neurons “

Children with autism exhibit deficits in imitation and other aspects of social cognition (Dawson et al., 1998; Lord et al., 2000; Rogers, 1999; Rogers & Williams, 2006). Research in typically developing children has described the psychological mechanisms underlying infant imitation (‘the AIM hypothesis, Meltzoff & Moore, 1997) and made progress in specifying the neural correlates of imitation in adults (Iacoboni, 2005; Jackson et al., 2006). In typically developing children, the behavioral data establish that imitation is present in neonates in a primitive form (Meltzoff & Moore, 1977, 1997). This demonstrates a close coupling between the perception and production mediated by what psychologists have called a ‘supramodal’ representation (a common code) for human acts (e.g., Meltzoff & Prinz, 2002). Current debate focuses on whether the MNS provides the initial neural substrate for the supramodal code, or whether the MNS is built up through associative experience (e.g., Meltzoff & Decety, 2003). More specifically, a key question is whether the MNS in humans underlies early imitation or is a consequence of prior

imitative experience (parents imitating infants and vice versa). Moreover, imitation has been linked to other aspects of social cognition in infants such as gaze following (Brooks & Meltzoff, 2002), emotional understanding (Repacholi & Meltzoff, 2007), and using self-knowledge to understand the mental experiences of others who behave ‘Like Me’ (Meltzoff, 2007). Interestingly, this suite of behaviors comprises key elements of the deficits of children with autism (e.g., Rogers & Williams, 2006; Toth et al., 2006). Future research will be needed to determine whether the hypothesized dysfunction in the MNS in children with autism (Dapretto et al., 2006; Iacobani & Dapretto, 2006; Williams et al., 2001) covers this suite of behaviors or whether MNS dysfunction is a downstream consequence of other more fundamental deficits in social cognition. A developmental approach is indicated. Imitation, gaze following, and other social cognitive behaviors provide powerful leverage guiding future research: They can be studied at 2 levels of analysis (neuroscientific and behavioral) in 2 populations (children with autism and typically developing infants and children). Each cell in this 2x2 table informs the other; by exploring all 4 cells from a developmental viewpoint future work can better illuminate fundamental mechanisms of human cognition.

Jaime A. Pineda (University of California, San Diego)

“Mu rhythms, mirror neurons and autism spectrum disorders”

Does mu suppression reflect mirror activity? One study (Pineda et al., 2000) showed that power in the 8-13 Hz band (mu rhythm) showed suppression to self movement and the observation of movement. To what degree does this mu oscillation reflect the social dimension of stimulus presentation? Oberman et al. (2007) showed graded responses in mu suppression to the observation of videos that varied in the degree of social interaction. If mu suppression reflects MNS activity and the capacity to understand actions as well as learning through imitation, then children with autism should show differences in mu suppression compared to controls. In one experiment, TD children showed mu suppression both to moving their hands and to watching other hands move; in contrast, ASD showed it only for self moving (Oberman et al., 2005). Is the link between mu suppression and MNS direct? That is, do sensorimotor mu rhythms reflect downstream modulation from cells in premotor (IFG) cortex? In a study using TMS to inhibit IFG activity, accuracy on perception of emotion was reduced but not for gender determination. Mu suppression was eliminated as well (Pineda et al., in prep). If changing the dynamics of mu oscillation can produce a temporary “autism” then perhaps operant conditioning training on mu rhythm can result in normalization of function. In a study using neurofeedback training for 10 weeks, children with autism showed positive changes in behavior and recovery of mu suppression (Pineda et al., in prep), though no differences in imitative responses.. The correlations between mu rhythms and mirror neurons are striking and allow us to treat mu suppression as an index of MNS involvement.

Justin H. G. Williams (University of Aberdeen)

“Contributions of orbitofrontal cortex to imitation in autism”

Williams et al, (2001) noted impairments of ‘theory of mind’ and dysfunctional imitation in autism (too much or too little), as well as previous theory (Rogers and Pennington, 1991) that self-other matching mechanisms associated with motor control may undermine social development. They suggested that ‘mirror neurons’ may serve ‘self-other mapping’, be important in developing these functions, and be dysfunctional in autism. Imitation is a form of motor learning that utilizes an inverse dynamic model of motor control.

Experiments using simple actions will be more helpful than those using complex actions because complex acts involve too many skills. Control tasks in MNS experiments need to involve making actions to active stimuli.

Williams et al. (2007) measured brain activity during congruent (imitative) and incongruent finger movements. Results showed that imitation utilizes both cortical systems (including the ‘mirror neuron’ system) and subcortical systems of motor control. Imitation was also associated with activity in lateral orbitofrontal cortex (OFC) and amygdala. Williams suggests that imitation relies on detecting differences between self and other, which leads to behavioral modification. OFC is closely connected with the ‘mirror neuron’ system and there is evidence that OFC is implicated in autism (Bachevalier and Loveland, 2006; Waiter et al, 2004) leading us to predict that differential involvement of OFC in autism could underlie ‘mirror neuron’ dysfunction. The brain substrate was consistent with Wolpert’s model of inverse control. The OFC, amygdala circuit for behavioral conditioning is linked to motor control

The developmental process of imitation is incremental. Over time there is increasing flexibility through motor learning and incremental learning.

A region of interest analysis carried out on a previous data set collected during a test of the ‘mirror neuron’ hypothesis (Williams et al. 2006) found reduced midline activity and left lateral activity but increased medial activity bilaterally in the group with Asperger’s syndrome. OFC function is thought to be differentiated by laterality and these findings would predict that imitation learning in autism would be more repetitive but less adaptive. Abnormal OFC function could be important in determining abnormal ‘mirror neuron’ function in autism as well as the unusual patterns of imitation learning. Three aspects seem importantly involved in ASD: (1) diminished self monitoring; (2) more rigid learning; (3) more repetitive. The OFC control of goal detection is critical from imitation.

Poster Presentations:

- Bencini, Giulia (Hunter College, CUNY) “Syntactic Priming in Young Children: A Proposal to Investigate Language Function in Autism”
- Bennetto, Lotsa; Laura Silverman; Elizabeth Smith (University of Rochester) “Integration of Speech and Nonverbal Cues in Autism”
- Brenier, R., G. Dawson; M. Murias; S. Webb; S. Lunde (University of Washington, Seattle) “EEG Correlates of Mirror Neuron Activity and Imitation in Autism”
- Catella, Stephanie Jaye; Lauren Lafrance; Latoya M Burden; Peter J. Marshall; Thomas Shipley (Temple University) “Behavioral and Neurophysiological Assessment of Perception-Action Interactions in Pre-school Children”
- Colombi, Contanza, Sally Rogers (University of California, Davis) “Imitation, Intentions, Social Development, and Mirror Neurons in Autism”
- Gotham, K S.; Risis; C. Lord (University of Michigan) “Measuring ASD Severity with Calibrated ADOS Scopes”
- Helt, Molly; Inge-Marie Eigst; Peter Sayder; Hilary Boorstein; Deborah Fein (University of Connecticut) “Are Children with Autism Susceptible to Contagious Yawning?”
- Irwin, Julia (Haskins Laboratories) “Audiovisual Speech Perception in ASD and TD Perceivers: Neurobiological and Behavioral Implications”
- Kana, Rahesh; Timothy Keller; Dave Williams; Valdmir Cherkassky; Nancy Minshew; Marcel Adam Just (Carnegie Mellon University; University of Pittsburg School of Medicine) “Mind Reading, Mirror Neurons, and Cortical Midline Structures in Autism”
- McCleery, Joseph P.; Elizabeth Allman; Leslie J. Arier; Karen R. Dobkins (University of California, Davis) “Abnormal Mangocellular Pathway Visual Processing in Infants at Risk for Autism: Precursor to Mirror Neuron System Abnormalities?”
- Morris, James; Kevin Pelphrey; George McArthur (Duke University Medical Center) “The Superior Temporal Sulcus Region and Social Perception: Studies of Biological Motion Perception”
- Murias, Michael; Pahael Brenier; Geraldine Dawson (University of Washington, Seattle) “Slower Motor Rhythms Frequencies in Adults with Autism”
- Oberman, Lindsay M. (University of California, San Diego) “The Mu Wave: An EEG Index of the Mirror Neuron System”
- Vivant, Gacomo; Aparna Nadig; Sally Rogers (University of Sienna; University of California, Davis; The MIND institute, University of California, Davis Medical Center) “The Role of Visual Attention in Imitation Impairment in Autism”
- Yerys, Benjamin; Phillip Lee; Jenn Foss-Feig; Anne Della-Rosa; Joetta James; Sara McCracken; William Gaillard; Chandan Vaidya; Lauren Kenworthy (Children's National Medical Center; Children's Research Institute - Neuro Science) “Functional Connectivity for Response Inhibition in Autism Spectrum Disorders”

Part III: Questions and suggested areas for research

One main goal of the workshop was to generate questions from existing knowledge concerning various aspects of MNS functioning, autism, and social behavior that would inform and stimulate research in this area. The following questions, and suggested areas for investigation are summarized from the various discussions that occurred during the meeting.

1. What are the developmental origins of MNS deficits in autism? Suggested areas of investigation include:

- Longitudinal studies in young monkeys in order to understand the development of the MNS over time;
- Lesion studies in animal developmental models of MNS deficits to determine effects on social functioning and repetitive movements;
- Training studies with animals to evaluate experiential effects on MNS activation.
- Development of computational methods to model and test the hypothesized role of MNS deficits in social-communicative behaviors affected in autism.

2. Do mirror neuron system deficits distinguish autism from other developmental disorders? Since autism symptoms are dimensional (and not categorical) variables, what is the relationship between mirror neuron system function and the “self-other” or social-communicative dimensional variables seen in autism? Suggested areas of investigation to address the “uniqueness” of MNS activation patterns in ASD include comparative studies of other groups with social difficulties such as FXS or developmental dyspraxia.

3. What patterns of interaction of other neural systems with the MNS occur during social experiences involving self-other mapping? Brain regions that activate in relation to motivational states should demonstrate relationships with MNS activation. Important areas of investigation include:

- Identification of behavioral states that modulate MNS activation patterns;
- Identification of patterns of neural function during self-other experiences at lower (e.g. mimicry, observation of intentional acts) and higher levels (e.g. theory of mind, empathy) to determine if there are neural differences between lower and higher level mapping, involving activation of separate, the same or expanded neural systems;
- Identification of connections among different brain systems that activate together during social experiences, which involve self-other mapping at some level?

4. Is the MNS involved in discriminating object affordances, and if so, how?

5. To what extent does training in one self-other capacity (e.g. imitation) affect behavioral functioning and MNS activation in other self-other capacities (e.g. empathy)?

6. What is the relationship between early experience and MNS development? What is the relation between imitation skills and mirroring experiences?

Conclusion

The rapid progress on research on MNS has been mirrored by equally rapid progress in examination of MNS functioning in ASD. A variety of diverse studies have converged in finding MNS activation patterns to be abnormal in ASD subjects in response to a wide range of stimuli. The idea that MNS abnormalities may underlie the social-communicative deficits in autism is the latest neural model of autism, and unlike many previous neural models, it may underlie the very unique pattern of social-cognitive and communicative deficits that constitute the primary neuropsychological profiles of autism. Autism is a severe and debilitating lifelong disorder that appears to be affecting more and more children. Since successful treatment of a disorder is dependent on understanding the origins and mechanisms involved in causing the disorder, part of the excitement about the MNS hypothesis in autism is the hope that it will lead to much more effective treatments, both behavioral and pharmacological. Rapid progress in MNS research in autism will allow us to determine the usefulness of this model for understanding ASD, and for developing treatments that may normalize neural activation patterns as well as behavioral functioning.

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Workshop Attendees

Altschuler, Eric University of California, San Diego, University of Medicine & Dentistry of New Jersey
Arbib, Michael University of Southern California
Bencini, Giulia Hunter College, City University of New York
Bennetto, Loisa University of Rochester
Bernier, Raphael University of Washington
Colamarino, Sophia Autism Speaks
Columbi, Constanza University of California, Davis
Dapretto, Mirella University of California, Los Angeles
Gotham, Kate University of Michigan
Helt, Molly University of Connecticut
Iacoboni, Marco University of California, Los Angeles
Irwin, Julia Haskins Laboratories
Kana, Rajesh Carnegie Mellon University
Lee, Susan University of Rochester
Liarakos, Chuck Autism Speaks; National Science Foundation
Lord, Cathy University of Michigan
Marshall, Peter Temple University
McCleery, Joseph University of California, San Diego
McWhirr, Morven University of Aberdeen
Meltzoff, Andrew University of Washington
Morris, Jamie Duke University
Murias, Michael University of Washington
Oberman, Lindsay University of California, San Diego
Pineda, Jaime University of California, San Diego
Reynolds, Elizabeth University of California, Los Angeles
Rogers, Sally University of California, Davis
Schultz, Robert Yale University
Spinelli, Simona National Institutes of Health
Vishton, Peter National Science Foundation
Vivanti, Giacomo University of Sienna; University of California, Davis
Whalen, Douglas H. National Science Foundation
Williams, Justin University of Aberdeen
Yerys, Benjamin Children's National Medical Center