Mirror Neuron Forum

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To what extent does variability in mirror mechanism functioning contribute to the autistic phenotype?

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Perhaps no other application of mirror neuron hypothesizing has been characterized by as much speculation as that of the relation between mirror neurons and the autistic phenotype. Following one highly visible research study (Dapretto et al., 2006), the popular press buzzed that "Autism, Some Researchers Believe, May Involve Broken Mirror Neurons" *(New York Times,* Blakeslee, 2006) and that a "Lack Of 'Mirror Neurons' May Help Explain Autism" *(Scientific American,* Biello, 2005).

These headlines explicitly echoed the claims made by the researchers in their own press release, "UCLA imaging study of children with autism pinpoints broken mirror neuron system as mechanism behind social deficits" *(UCLA Newsroom,* Page, 2005).

Another highly visible research report (Oberman et al., 2005) was similarly heralded in the popular press (including the popular PBS television show, NOVA, 2005) and by the researchers themselves in their *Scientific American* article titled, "Broken Mirrors: A Theory of Autism" (Ramachandran & Oberman, 2006). Because one of these researchers had previously deemed mirror neurons "the driving force behind 'the great leap forward' in human evolution" (Ramachandran, 2000), his subsequent claim that a group of humans lacked this evolutionary mechanism was deemed as "disturbingly … prejudiced" (Corwin, 2007) as similar declarations made about other groups of humans a century ago (Jones, this journal, 2010).

Because autistic persons, by diagnostic definition, are characterized by atypical social communication, the expanding assumptions that mirror neurons underlie everything from speech perception to social interaction makes for an easy leap – as does autistic persons' 'otherness.' Attributions of mirror neuron efficiency and deficiency have been levied against other minority phenotypes, including persons who are sexually attracted to persons of the same sex (Ponseti et al., 2006), persons who stutter (Saltuklaroglu & Kalinowki, 2005), and persons who smoke cigarettes (Pineda & Oberman, 2006), with the latter attribution derived from the same laboratory paradigm as that used to attribute mirror neuron deficiency to autistic persons.

However, of the two most prominent studies promoting the broken mirror neuron hypothesis of autism, one (Dapretto et al., 2006) failed twice to replicate, and the other (Oberman et al., 2005) not only failed twice to replicate but also failed to control one of the most crucial aspects of the study's design.

More specifically, whereas Dapretto et al. (2006) reported that, when imitating, autistic children exhibited significantly less activation "within the pars opercularis of the inferior frontal gyrus (BA 44) – the site with previously identified mirror properties – as well as in the neighboring pars triangularis (BA 45)" (p. 29), Williams et al. (2006), using Iacoboni et al.'s (1999) seminal mirror-neuron-imitation paradigm, and Martineau et al. (2010), using a similar paradigm, reported no differences between autistic and typically developing children in "the site with previously identified mirror properties."

In fact, in neither Williams et al.'s (2006) nor Martineau et al.'s (2010) attempt to replicate Dapretto et al. (2006) did even typically developing children exhibit a reliable amount of activation in "the site with previously identified mirror properties," a finding

supported by a recent meta-analysis by Molenberghs et al. (2009): Of 20 fMRI studies testing samples of typical participants, only two studies reported significant activation in this site (and one of the two studies was from Dapretto et al.'s own lab, i.e., Iacoboni et al., 1999). The vast majority of studies (90%) with typical participants did not report imitation-specific activity in BA 44/45.

Thus, Dapretto et al.'s (2006, p. 30) conclusion that the autistic children's lack of imitation-specific activity in BA 44/45 indicated "dysfunction" that "may be at the core of … autism" and Iacoboni and Dapretto's (2006, p. 949) recommendation that lack of imitation-specific activity in BA 44/45 could be "an effective bio-marker" for autism lack empirical justification.

As for Oberman et al.'s (2005) study, an attempted replication by Rayemakers et al. (2009) found no significant differences between autistic and typically developing participants in mu suppression when executing or observing hand actions; neither did Fan et al. (2010), who measured their participants' eye movements to ensure that both groups of participants were attending equally to the stimuli (a design feature absent in Oberman et al., 2005; see also Bernier et al., 2007, who reported no significant main effect of group or interaction between group and task during execution, imitation, and observation of hand actions).

In contrast to these two highly visible but non-replicated studies, much larger and more firmly established bodies of data contradict predictions made by mirror neuron theory. For example, it has been repeatedly demonstrated that autistic persons of all ages (from preverbal children to mature adults) have no difficulty understanding the intention of other people's actions (Aldridge, Stone, Sweeney, & Bower, 2000; Carpenter, Pennington, & Rogers, 2001; Falk-Ytter, 2010; Hamilton, Brindley, & Frith, 2007; McAleer, Kay, Pollick, & Rutherford, 2010; Russell & Hill, 2001; Sebanz, Knoblich, Stumpf, & Prinz, 2005). Such well-established data argue against empirically unsupported speculations that autistic persons suffer from "defective intentional attunement" (Gallese, 2006, p. 15).

As another example, alongside ample empirical documentation that autistic participants are less precise (than non-autistic participants) when they imitate other people, there are 30 years of empirical documentation that autistic participants are highly responsive when they are imitated *by* other people (Dawson & Adams, 1984; Dawson & Galpert, 1990, Escalona, Field, Nadel, & Lundy, 2002; Field, Field, Sanders, & Nadel, 2001; Heiman, Laberg, & Nordøen, 2006; Katagiri, Inada, & Kamio, 2010; Nadel et al., 2000; Tiegerman & Primavera, 1981; 1984).

Such well-established and repeatedly replicated data contradict the core tenet of most mirror neuron proponents' assumptions about autistic people, for example, Gallese's (2006, p. 21) conjecture that autistic persons suffer from an "incapacity to establish a motor equivalence between demonstrator and imitator, most likely due to a malfunctioning of the mirror neuron system."

The "broken mirror neuron" hypothesis likely represents an unfortunate detour in the quest to provide autistic persons with the support and assistance that they need. Countless unusual interventions have sprung up – from synchronized dance therapy (Ramachandran & Seckel, 2011) to playing with virtual pets (Atlschuler, 2008) -- based on a hypothesis with a faulty empirical foundation and eroding empirical support (cf., Avikainen, Kulomaki, & Hari, 1999; Leighton, Bird, Charman, & Heyes, 2007; Dinstein et al., 2010; Gowen, Stanley, & Miall, 2008; Press, Richardson, & Bird, 2010).

The support and assistance that autistic persons deserve should be based on the results of well-replicated studies that bear the empirical stamina to aid not deter advances.

To what extent does variability in mirror mechanism functioning contribute to the autistic phenotype?
Response to Vittorio Gallese (VG) by *Morton Ann Gernsbacher, University of Wisconsin-Madison*

VG (this issue) claims that autistic persons are characterized by an "incapacity to organize and directly grasp the intrinsic goal-related organization of motor behavior," in other words, VG claims that autistic persons are characterized by an incapacity to understand the intentions of theirs and other persons' motor behavior.

VG supports his claim by referencing head-growth studies (e.g., Courchesne et al., 2007), a cortical thickness study (Hadjikhani et al., 2006), which I review in my response to MI, two motor-control studies (Fabbri-Destro et al., 2008; Schmitz et al., 2003), and a study measuring muscle activation (Cattaneo et al., 2008). But none of those studies directly assess whether, as VG conjectures, autistic persons are incapable of understanding the intentions of action.

Indeed, missing in VG's list of empirical evidence are all but one of a decade's worth of studies, which do in fact directly assess autistic children and adults' understanding of the intentions of theirs and other persons' motor behavior (Aldridge, Stone, Sweeney, & Bower, 2000; Carpenter, Pennington, & Rogers, 2001; Falck-Ytter, 2010; Hamilton, Brindley, & Frith, 2007; McAleer, Kay, Pollick, & Rutherford, 2010; Russell & Hill, 2001; Sebanz, Knoblich, Stumpf, & Prinz, 2005).

The studies VG fails to mention are unanimous in demonstrating that autistic individuals of all ages are perfectly able to understand the intentionality of their own actions and of other humans' actions; there is neither "incapacity" nor impairment in understanding of the intentions of action (Gernsbacher, 2007; Gernsbacher, Stevenson, Khandakar, & Goldsmith, 2008a, 2008b; Gernsbacher et al., in press).

As just a few examples, in Aldridge et al.'s (2000) study. prelinguistic autistic children "showed the expected deficits on [the conventional] imitation tasks but were *significantly better* than [pre-linguistic typically developing children] on the intentionality" tasks (p. 294, emphasis added); in Hamilton et al.'s (2007) study, autistic grade-school-age children "performed *significantly better* than the control" children in "interpreting the meaning of gestures" (p. 1866, emphasis added); in Sebanz et al.'s (2005) study, using a complex spatial compatibility reaction time task, autistic adults were deemed "far from action blind," when they capably represented a co-actor's task, showing the same pattern of results as the matched control group" (p. 433).

Not one of seven studies (Aldridge et al., 2000; Carpenter et al., 2001; Falck-Ytter, 2010; Hamilton et al., 2007; McAleer et al., 2010; Russell & Hill, 2001; Sebanz et al., 2005, which directly assess autistic individuals' understanding of the intentions of theirs and other persons' actions, support VG's claim (in this issue and elsewhere) that autistic persons are incapable of such understanding or that autistic individuals have "defective intentional attunement" (Gallese, 2006a, b; Gallese et al., 2007). But these studies were not cited by VG. Instead, he cited only one study that directly assessed autistic individuals' understanding of action.

In that study (Boria et al., 2009), grade-school-age autistic and non-autistic children didn't differ when the task was to explain why a photographed hand was touching an object (e.g., "to touch" it), and the two participant groups didn't differ when the task was to explain why a hand was grasping an object in such a way as to use it (e.g., "to make a telephone call"). However, both groups performed significantly worse when the task was to explain why a hand was grasping an object not to use it but "to place" it – and the autistic children performed even worse than the non-autistic children. When cues such as containers in which to place the objects were shown, both groups improved significantly, and the two groups didn't differ.
Thus, these data from Boria et al. (2009) don't provide a very strong counterweight to the multiple other data sets that have repeatedly demonstrated that autistic individuals of all ages do not differ from non-autistic individuals in understanding the intentions of actions, contra VG's proposal otherwise.

To what extent does variability in mirror mechanism functioning contribute to the autistic phenotype?
Response to Marco Iacoboni (MI) by *Morton Ann Gernsbacher, University of Wisconsin-Madison*

When answering the question of whether "abnormal" mirror neuron function contributes to the autistic phenotype, MI reports that in the neuroimaging literature, "there are 20 published papers that support the idea," and only "four studies [that] do not." However, MI's tally appears to be based on a rather incomplete survey of the existing literature;

fMRI: Imitation

MI identifies only eight fMRI studies relevant to the question of mirror neuron function and the autistic phenotype. Three of those studies, Dapretto et al. (2006), Williams et al. (2006), and Martineau et al. (2010), are imitation studies that I discussed in my initial response when I stated that neither Martineau et al. (2010) nor Williams et al. (2006) replicate Dapretto et al. (2006). Indeed, as illustrated in Table 1, the three autism-imitation fMRI studies MI cites not only fail to replicate each other, they fail to provide consistent evidence concerning the putative function of mirror neurons during imitation.

fMRI/PET: Face Processing

In addition to the three fMRI studies of imitation MI cites as evidence that "abnormal" mirror neuron function contributes to the autistic phenotype, he cites three fMRI studies of face/emotion processing (Bookheimer, Wang, Scott, Sigman, & Dapretto, 2008; Hadjikhani, Joseph, Snyder, & Tager-Flusberg, 2007; Schulte-Rüther et al., 2010). However, these three studies that MI cites comprise less than 10% of the published autism-face-processing literature, and the results of the studies MI cites are unreflective of that larger literature.

As illustrated in Table 2, in contrast to Hadjikhani et al.'s (2007) report of less activation in autistic vs. non-autistic superior temporal sulcus, 36 other data sets report no differences between autistic and non-autistic participants in superior temporal activation, four data sets report more activation in autistic participants' superior temporal sulcus.

Only a tiny fraction of the data sets – two – corroborate Hadjikhani et al.'s (2007) report of less activation for autistic participants in the putative mirror neuron region of superior temporal sulcus. Similarly, while 12 data sets report less inferior frontal activation for autistic participants, three data sets report more, and the clear majority, 28, of the data sets report no differences between autistic and non-autistic participants in the putative mirror neuron region of inferior frontal cortex.

Structural MRI: Cortical Thickness

MI cites two structural MRI studies as evidence that "abnormal" mirror neuron function contributes to the autistic phenotype. One of these study measures cortical thickness (Hadjikhani et al., 2005) and reports that autistic participants exhibit thinner cortices in three regions of the putative mirror neuron system: inferior frontal, inferior parietal, and superior temporal. Presumably, the assumption is that thinner cortex means fewer mirror neurons.

But what about three other studies that MI doesn't cite (as illustrated in Table 3)? These three studies report that autistic participants have *thicker* cortices in regions of the putative mirror neuron system. Does autistic persons' thicker cortices mean they have more mirror neurons than non-autistic people? More likely, as Table 3 suggests and as reviewed recently by Stevenson and Kellett (2010), the whole set of cortical thickness studies are too inconsistent to allow drawing such conclusions.

Structural MRI: Grey Matter Density and Volume

The other structural MRI study that MI cites is Yamasaki et al.'s (2006) ROI-based morphometry study, which reports that autistic participants have smaller Broca's areas. However, as illustrated in Table 4, a study that MI doesn't cite (Knaus et al., 2009) reports that autistic participants have larger Broca's areas, and another study that MI doesn't cite (DeFosse et al. 2004) reports no difference between autistic and non-autistic participants in volume of Broca's area or its right-hemisphere equivalent.

No difference between autistic and non-autistic participants in either left- or right-hemisphere pars triangularis or pars opercularis is also the conclusion drawn from virtually every voxel-based morphometry study, as also illustrated in Table 4.

EEG: mu Rhythm Suppression

MI also cites several EEG studies, most particularly those that measure mu rhythm suppression, and claims that these studies illustrate "reduced mirroring in autism during action observation." I discussed these studies in my initial response when I noted that Oberman et al.'s (2005) original mu rhythm suppression study has not replicated (Bernier et al., 2007; Fan et al., 2010; Oberman et al., 2008; Raymaekers et al., 2009).

Because MI cites some of these studies, not as failures to replicate, which they are, but instead as evidence of "reduced mirroring in autism during action observation," let me quote directly from these studies.

Bernier et al. (2007, p. 232) report: "Significant attenuation in mu from baseline was found for both groups [autistic and non-autistic] for each condition [observe, execute, and imitate]." There was "a main effect of condition … but no main effect for group or interaction effects." Oberman et al. (2008, p. 1562) report: "There was no significant main effect of … group." There was "a significant main effect of familiarity … [but] there was not a significant group by familiarity interaction."

Fan et al. (2010; p. 981) report: "The mu suppression over the sensorimotor cortex was significantly affected by experimental conditions [observation of hand actions, observation of a moving dot, execution of hand actions], but not by group membership [autistic vs. non-autistic], nor by the interaction between groups and conditions."

Raymaekers et al. (2009, p. 113) report: "Both groups [autistic and non-autistic] show significant mu suppression to both self and observed hand movements. No group differences are found in either condition."

Conclusion

The nearly 70 studies listed in Tables 1 through 4 argue against MI's assertion that only a few brain imaging studies fail to support the proposal of "mirror neuron abnormalities" in autistic persons. Rather, numerous studies – indeed, the bulk of existing brain imaging studies -- fail to support that proposal.

Given the extraordinary federal, private, and international funds spent on identifying the neural basis of the autistic phenotype and the large bodies of research those funds have generated, it's important to examine entire bodies of data, not selective pockets.

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Table 1. Summary of activation reported in three regions of the putative mirror neuron system during imitation experiments

	Region of Putative Mirror Neuron System					
	Inferior Frontal		Inferior Parietal		Superior Temporal	
Study	imitation	observation	imitation	observation	imitation	observation
Dapretto et al. (2006)	⇓	⇓	⇑	(=)	=	(=)
Williams et al. (2006)	(=)	(=)	⇓	=	⇑	(=)
Martineau et al. (2010)	(=)	⇑	(=)	=	(=)	(=)

⇓ Autistic participants' activation significantly less than that of non-autistic participants
⇑ Autistic participants' activation significantly greater than that of non-autistic participants
= Autistic participants' activation not significantly different from that of non-autistic participants
(=) Neither autistic nor non-autistic participants exhibit a reliable amount of activation

Table 2. Summary of activation reported in three regions of the putative mirror neuron system during face processing/emotion experiments

Study	Region of Putative Mirror Neuron System		
	Inferior Frontal	Inferior Parietal	Superior Temporal
Hadjikhani et al. (2007)	⇓	(=)	⇓
Bookheimer et al. (2008)	⇓	(=)	(=)
Schulte-Ruther et al. (2010; other emotions)	⇓	(=)	=
Schulte-Ruther et al. (2010; self emotions)	⇑	(=)	=
Ashwin et al. (2007)	(=)	(=)	⇑
Bird et al. (2006)	(=)	(=)	(=)
Bölte et al. (2006)	(=)	(=)	(=)
Corbett et al. (2009)	(=)	(=)	(=)
Critchley et al. (2000)	(=)	(=)	⇑
Dalton et al. (2005; study 1)	(=)	(=)	(=)
Dalton et al. (2005; study 2)	(=)	(=)	(=)
Dalton et al. (2008)	(=)	(=)	(=)
Deeley et al. (2007)	(=)	(=)	(=)
Greimel et al. (2005; other faces)	(=)	(=)	(=)
Greimel et al. (2005; self face)	⇓	(=)	(=)
Grelotti et al. (2005)	⇓	(=)	(=)
Hadjikhani et al. (2004)	(=)	(=)	(=)
Hall et al. (2003)	⇓	(=)	(=)
Hubl et al. (2003)	(=)	(=)	(=)
Humphreys et al. (2008)	(=)	(=)	⇓
Kleinhaus et al. (2008)	(=)	(=)	(=)
Kleinhaus et al. (2010)	⇓	(=)	(=)
Kleinhaus et al. (2011)	(=)	(=)	(=)
Koshino et al. (2008)	⇓	⇓	(=)
Loveland et al. (2008)	(=)	(=)	⇓
Ogai et al. (2003; disgust)	⇓	(=)	(=)
Ogai et al. (2003; fear)	(=)	(=)	(=)
Ogai et al. (2003; happiness)	(=)	(=)	(=)
Pelphrey et al. (2007; dynamic)	(=)	(=)	(=)
Pelphrey et al. (2007; static)	(=)	(=)	⇑
Pierce et al. (2001)	(=)	(=)	(=)
Pierce & Redcay (2004)	(=)	(=)	(=)
Pierce & Redcay (2008)	⇓	(=)	(=)
Piggot et al. (2004)	(=)	(=)	(=)
Pinkham et al. (2008; trustworthiness)	⇓	(=)	(=)
Pinkham et al. (2008; age judgment)	⇑	(=)	⇑
Scherf et al. (2010; Non-Aut ROIs)	(=)	(=)	(=)
Scherf et al. (2010; Aut ROIs)	⇑	(=)	(=)
Schultz et al. (2000; sample 1)	(=)	(=)	(=)
Schultz et al. (2000; sample 2)	(=)	(=)	(=)

Uddin et al. (2008)	⇓	(=)	(=)	Wang et al. (2004; labeling)	(=)	(=)	(=)
Wang et al. (2004; matching)	(=)	(=)	(=)				

⇓ Autistic participants' activation significantly less than that of non-autistic participants
⇑ Autistic participants' activation significantly greater than that of non-autistic participants
= Autistic participants' activation not significantly different from that of non-autistic participants
(=) Neither autistic nor non-autistic participants exhibit a reliable amount of activation

Table 3. Summary of cortical thickness reported in three regions of the putative mirror neuron system.

Study	Region of Putative Mirror Neuron System					
	Inferior Frontal		Inferior Parietal		Superior Temporal	
	left hemi-sphere	right hemi-sphere	left hemi-sphere	right hemi-sphere	left hemi-sphere	right hemi-sphere
Hadjikhani et al. (2005)	⇓	⇓	⇓	⇓	=	⇓
Chung et al. (2005)	=	=	=	=	⇓	=
Ecker et al. (2010)	⇓	=	⇑	⇑	=	⇑
Hardan et al. (2006)	=	=	⇑	⇑	⇑	⇑
Hutsler et al. (2006)	=	=	=	=	=	=
Hyde et al. (2010)	=	⇑	=	=	⇑	⇑
Jiao et al. (2010)	⇓	⇓	⇓	⇓	=	=
Wallace et al. (2010)	=	=	⇓	⇓	=	=

⇓ Autistic participants' cortices significantly thinner than non-autistic participants'
⇑ Autistic participants' cortices significantly thicker than non-autistic participants'
= Autistic participants' cortices not significantly different from non-autistic participants'

Table 4. Summary of volumetric and grey matter density reported in inferior frontal gyrus

	Putative Mirror Neuron Region			
	left pars triangularis	right pars triangularis	left pars opercularis	left pars opercularis
Study	ROI-based Morphometry			
Yamasaki et al. (2006)	⇓	⇓	⇓	⇓
DeFosse et al. (2004)	=	=	=	=
Knaus et al. (2009)	⇑	⇑	⇑	⇑
	Voxel-based Morphometry			
Abell et al. (1999)	⇓	=	=	=
Craig et al. (2007)	=	=	=	=
Kosaka et al. (2010)	=	⇓	=	=
Kwon et al. (2004)	=	=	=	=
McAlonan et al. (2002)	=	=	=	=
McAlonan et al. (2005)	=	⇓	=	=
Rojas et al. (2006)	=	=	=	=
Toal et al. (2010)	=	=	=	=
Waiter et al. (2004)	=	=	=	=
Wilson et al. (2009)	=	=	=	=

⇓ Autistic participants exhibit significantly smaller volume (ROI-based)/less grey matter density (voxel-based morphology) than non-autistic participants
⇑ Autistic participants exhibit significantly larger volume (ROI-based)/greater grey matter density (voxel-based morphology) than non-autistic participants
= Autistic and non-autistic participants exhibit significantly equivalent volume (ROI-based)/grey matter density (voxel-based morphology)