

Impaired coordination of brain activity in autism involves local, as well as long-range, signaling

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A study based at the Martinos Center for Biomedical Imaging at Massachusetts General Hospital (MGH) finds that the local functional connectivity of the brain – the extent to which the activity of within a small brain region appears to be coordinated – is reduced in individuals with autism spectrum disorders (ASD). Although it has been recognized for several years that functional connectivity between separate areas of the brain was reduced in ASD, it had been assumed that local functional connectivity was actually higher in the brains of autistic individuals.

"Functional connectivity reflects connections that actually play a role in the processing of information in the cortex," says Tal Kenet, PhD, of the Martinos Center, corresponding author of the study appearing in *PNAS* Online Early Edition. "Imagine the [brain](#) is like an orchestra. When the violins are coordinated with the woodwinds and the trumpets with the violas, the orchestra will play in harmony – that's a version of long-range connectivity. Local functional connectivity is like focusing on the violins and whether they are all playing together.

"What has commonly been believed about autism is that the 'orchestra' isn't very well coordinated between sections but that the 'instruments' within sections were highly coordinated with each other, as though they were playing their own tune independent of the rest of the orchestra. We found that the opposite is true and that even the timing within sections is off. It's like each violin is playing independently from not only the rest

of the orchestra but from all the other violins."

Because the distances involved in communication between nearby neurons or groups of [neurons](#) are on a scale of millimeters to centimeters, it has been very difficult to study local connectivity through noninvasive imaging methods. The current study took advantage of a [brain activity](#) shown by previous invasive studies to reflect local communication – measurement of what are called nested oscillations, which occur when one aspect of a particular brain rhythm affects a different aspect of another brain rhythm. In this instance they focused on phase-amplitude coupling, in which the phase of a lower-frequency rhythm changes the amplitude of a higher-frequency rhythm, measured by magnetoencephalography (MEG), an imaging technique that detects the location as well as the timing of brain activity with high precision.

The research team used MEG to measure both local phase-amplitude coupling and longer range coordination of brain rhythms in 17 young men diagnosed with an ASD and in 20 volunteers with typical neurodevelopmental histories. Functional connectivity was measured while participants viewed faces with neutral expressions, faces with emotional expression – angry or fearful – and as a control, images of houses.

Local functional connectivity was measured in an area of the brain known to be important for the recognition of faces, while long-range connectivity was determined by looking for the coordination of brain rhythms between the facial recognition area and other, more distant areas of the cortex. Results were scored based on two statistical measures: for local connectivity, whether phase-amplitude coupling in the facial recognition area was stronger when participants viewed faces than when they viewed houses, and for long-range connectivity, whether there was a difference in how rhythms in the monitored areas corresponded with those in the facial recognition area while viewing the

two types of images.

As expected, typically developing participants had greater long-range functional connectivity – reflected by increased correspondence of brain rhythms between monitored areas – than did participants with autism. Contrary to previous assumptions, however, participants with [ASD](#) also had reduced local functional connectivity, in that phase-amplitude coupling was not increased in their [facial recognition](#) area while viewing facial images. In addition, local functional connectivity was reduced to the same extent that long-range connectivity was reduced, and greater reductions were seen in participants whose autism-related symptoms were more severe. A combination of the local and long-range functional connectivity measures was 90 percent accurate in distinguishing participants with autism from those who were typically developing.

An instructor in Neurology at Harvard Medical School, Kenet notes that other studies are required to investigate local [functional connectivity](#) in contexts such as memory and language and that better understanding of the mechanisms underlying phase-amplitude coupling is needed. "That sort of work would have to be done invasively in animal models," she explains. "But if we can figure out a way of disrupting phase-amplitude coupling in animals that mimics what we see in autism, that could be an important clue towards what goes wrong in [autism spectrum disorders](#). In addition, investigating whether disrupted phase-amplitude coupling occurs in children with autism could lead us to a biomarker for early diagnosis."

Provided by Massachusetts General Hospital

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