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Crosstalk between left and right brain is key to language development

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Proper communication between the left and right sides of the brain is critical for the development of advanced language skills, according to new research by UC San Francisco scientists. In most people, areas related to language processing are located in the brain's left hemisphere. The researchers suggest that autism-like problems with language comprehension seen in people with defective connections between the two hemispheres may occur because these individuals tend to use the right side of the brain to process language instead of the left.

The research—published in the April 20, 2016 issue of the *Journal of Neuroscience*—is the first large-scale study of rare individuals born missing key connections between the brain's left and right hemispheres and suggests that the left-hemisphere's normal specialization for language processing may be more important for the development language skills than was previously realized.

The study was led by UCSF neurologist Elliott Sherr, MD, PhD, and UCSF neuroscientist Srikantan Nagarajan, PhD, and focused on the role of the corpus callosum—a tight bundle of nerves containing as much as 200 million signaling fibers that transmit information between the left and right sides of the brain. To see whether the loss of the corpus callosum affected which hemisphere was dominant for language, the UCSF team tracked brain activity in people lacking a normal corpus callosum by measuring magnetic fields in while administering linguistic tests that required participants to name verbs and pictures.

The researchers found that in contrast to 21 normal control subjects, who relied on the left hemisphere for key aspects of these tasks, 13 research subjects born completely lacking a corpus callosum were more likely to use the right hemisphere, while 12 subjects born with only a partial corpus callosum fell squarely between the two.

According to Sherr, a professor in the Departments of Neurology and Pediatrics at UCSF, "This study is the first real evidence that one of the functions of the corpus callosum is to establish laterality between the two halves of the brain, which is most evident in the way that you see language form. This has broad implications for understanding how the brain is organized during development."

"Our study also showed that having speech localization on the right side of the brain was associated with lower performance on verbal tasks, as measured by the verbal IQ," he said.

Lack of hemisphere-linking corpus callosum is tied to autism-like language delay

As a pediatric neurologist Sherr has for more than a decade treated and studied children born without a corpus callosum, a condition that affects between one-in-three-thousand and one-in-four-thousand newborns. The corpus callosum normally develops between the 10th and 14th weeks of gestation, and its failure to develop—called "agenesis"—can be routinely detected during prenatal ultrasound examination. "Almost all who are born with this condition, even the highest functioning, have delays in language acquisition, although most of them learn to speak eventually," Sherr said.

Agenesis of the corpus callosum also is associated with intellectual disability and autism-like social and cognitive deficits. Sherr counsels parents and treats newborns and children with the condition. He also has led research studies that have implicated mutations in single genes as potential causes of agenesis.

Some neurologists are beginning to clinically manipulate brain signaling between the two hemispheres to treat stroke patients, Sherr said, but it is currently unclear how brain stimulation could be used to mimic actions of the corpus callosum to stimulate normal language development.

Nagarajan, a professor with the Department of Radiology and Biomedical Imaging at UCSF, is a leading research expert in magnetoencephalographic (MEG) imaging, which relies on the measurement of tiny magnetic fields about a billion-fold smaller than the earth's own magnetic field, produced by simultaneous bursts of electrical activity occurring in tens of thousands of neurons at the same time. Detecting these magnetic fields requires the use of superconducting sensors bathed in liquid helium to allow detection and amplification of

the magnetic signal, and the experiments are conducted in shielded rooms.

MEG can be used to detect changes in localization of brain activity that occur over one tenth of a second, sufficient to observe language localization. It takes about half a second for the intention to speak to result in the production of speech, Nagarajan said.

"We knew that the corpus callosum was a potential candidate as a means to promote lateralization of brain function," Nagarajan said, "but nobody had ever assembled a large cohort of healthy individuals with agenesis of the corpus callosum to do this test, and nobody had used MEG, which is much more time-sensitive than functional MRI."

The researchers also noted an interesting association between language localization in the brain and right- or left-handededness, though the research does not specifically address this connection.

"In almost all right handed individuals language is localized to the left hemisphere, as it is in a smaller majority of left-handed people." Sherr said. Research suggests that many left-handed individuals with language localized to the right side of brain are developmentally normal, he said, but some of the right-side language localization in left-handers may be associated developmental difficulties.

More information: L. B. N. Hinkley et al. The Contribution of the Corpus Callosum to Language Lateralization, *Journal of Neuroscience* (2016). DOI: 10.1523/JNEUROSCI.3850-14.2016

K. M. Jasmin et al. Cohesion and Joint Speech: Right Hemisphere Contributions to Synchronized Vocal Production, *Journal of Neuroscience* (2016). DOI: 10.1523/JNEUROSCI.4075-15.2016