Imaging Can Match Brain Structure to Behavior

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IRVINE, CALIF. — Neuroimaging is offering a window into the brain structure abnormalities that underlie the unique mental and behavioral features of some rare genetic disorders, Allan Reiss, M.D., said at the annual conference of the EEG and Clinical Neuroscience Society.

In some cases, these studies may allow researchers to match specific genes with certain neurologic functions, Dr. Reiss said.

He described some of the studies he and his colleagues at Stanford (Calif.) University have conducted on individuals with Turner's and Williams syndromes.

The clinical features of Turner's syndrome (the loss of an X chromosome), which affects 1 of every 2,500 live female births, include short stature, delayed or absent puberty, and a high risk of diabetes and osteoporosis.

Affected girls usually have an IQ that is normal but may be 5-8 points lower than that of a same-sex sibling. They exhibit problems with basic emotional processing beyond what might be expected for their IQ, Dr. Reiss said. Their verbal development is normal, but they have marked deficits in visual-spatial processing.

Functional MRI studies in his lab have shown that parietal and occipital cortical volume is smaller in patients with Turner's syndrome than in controls, which could explain the visual-spatial weaknesses. Significant volume losses in the inferior parietal lobule and, in some patients, the postcentral gyrus, account for most of the parietal deficits in these patients. The hippocampus also displays mild losses of volume.

In a series of functional MRI studies comparing brain activation in 13 patients with Turner's syndrome to that of 13 normal controls, Dr. Reiss and his colleagues found that both groups activated the parietal-occipital and frontal cortices in response to a visual orientation task, but the activation was significantly less among subjects with Turner's syndrome. When confronted with a more difficult task, the controls recruited executive frontal areas, but the patients showed no such recruitment. The investigators concluded that problems in activating and deactivating neurons in the relevant brain regions may underlie the visual-spatial deficits that characterize this condition (Cereb. Cortex 2004;14:174-80).

Dr. Reiss and his associates evaluated a pair of monozygotic twins, one of whom had Turner's syndrome and the other who developed normally. Both girls had a verbal IQ in the mid-140s. However, the unaffected twin had a performance IQ of 139; her sister's was 121.

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Imaging studies showed that portions of the parietal lobe and the frontal and prefrontal gyri were smaller in the affected than the nonaffected twin, yet the twin with Turner's syndrome performed as well as her sister on visual-spatial tests. She accomplished this through significantly greater activation of her parietal lobe, Dr. Reiss said.

All in all, the evidence to date suggests that structural and functional abnormalities of the parietal-occipital cortex underlie the nonverbal deficits that characterize Turner's syndrome, he said. The twin study sheds a glimmer of light on possible compensatory strategies some patients may use to overcome those deficits and raises the possibility that those strategies could be taught to other patients as well.

Boys as well as girls may have Williams syndrome (WS), which is caused by the deletion of several genes from the q11.23 region of chromosome 7. Conventional estimates place its incidence at 1 in every 20,000 live births, but the actual occurrence is probably closer to 1 in 8,000.

In one study, Dr. Reiss and his associates used volumetric analysis and voxel-based morphometry to compare the brain anatomy of 43 patients with WS to that of 40 healthy age- and sex-matched controls. The children with WS had reduced gray matter volume in the thalamus and occipital lobe and reduced gray matter density in the subcortical and cortical regions comprising the visual-spatial system. Their brains were about 13% smaller than those of the controls, with reduced occipital volume accounting for most of that difference. ■