NEWS

Molecular mechanisms: Autism gene regulates brain structure

BY **JESSICA WRIGHT**

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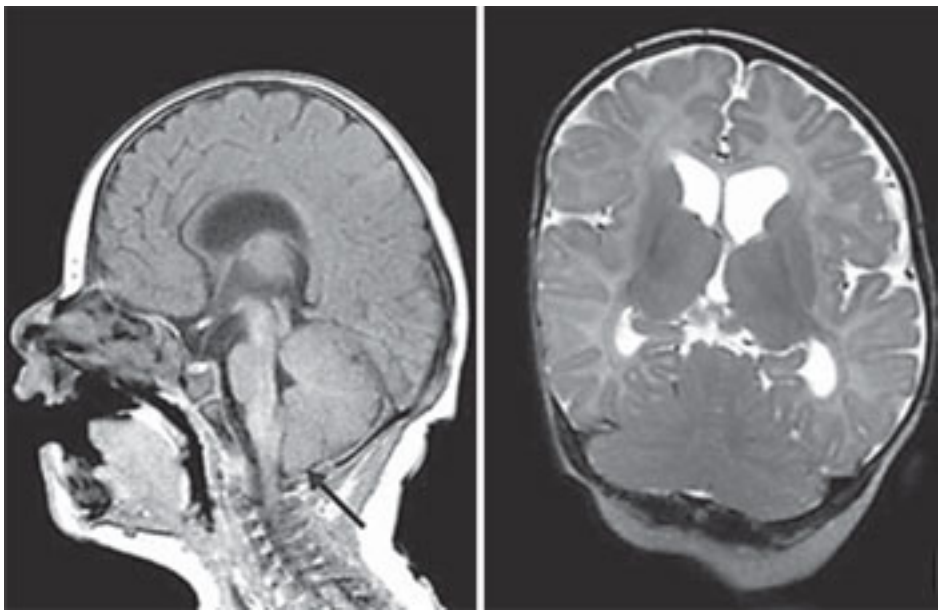

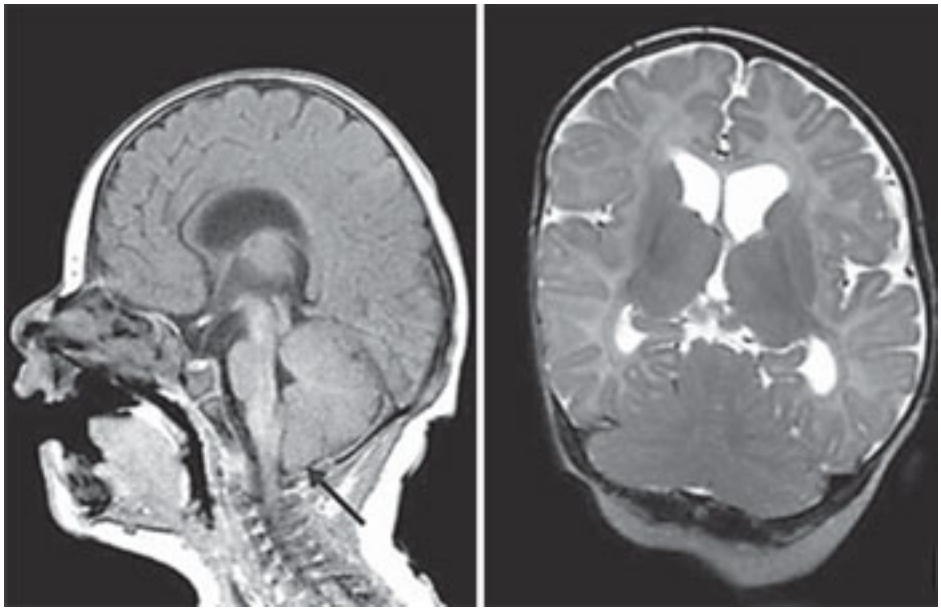

Altered image: A boy lacking the autism-linked TBR1 has brain tissue in the spinal canal (left) and abnormalities in the cortex (right).

Loss of one copy of TBR1, an autism-linked gene involved in fetal brain development, leads to brain malformations, according to a study published in the September issue of *Molecular Syndromology*[1].

TBR1 regulates the development of the cortex — a brain region involved in higher-order cognitive functions — by controlling the expression of other genes. These include the autism candidates **RELN** and **AUTS2**. One of TBR1's primary roles is directing the number and location of neurons that inhibit brain signals. Neurons in the cortices of mice lacking both copies of the gene are **located in the wrong brain layers**.

A study published this month in *Science* found that TBR1 is one of six genes that together may account for **up to one percent of cases** of autism.

In the *Molecular Syndromology* study, researchers characterized four boys who have a deletion of the 2q24 chromosomal region, which that encompasses the TBR1 gene. All four boys have intellectual disability and developmental delay. One 8-year-old has a diagnosis of pervasive developmental disorder–not otherwise specified, and a 33-month-old has features of autism.

All four boys have brain malformations, but of varying severity. Two of them have a thick corpus

callosum, which connects the brain's hemispheres. One of these two boys, and a third, have Chiari malformations, in which brain tissue enters into the spinal canal. All four have slightly dilated ventricles, brain structures that contain cerebrospinal fluid.

Only one of the four, a boy who died at 16 months of age (probably as the result of a seizure) has abnormalities in the cortex. Together, the results suggest that TBR1 only affects development of the cortex in combination with other genetic risk factors.

References:

1: Traylor R.N. *et al. Mol. Syndromol.* **3**, 102-112 (2012) **PubMed**