

# A 15q11.2 microdeletion first identified in a pair of autistic monozygotic twins with regression

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Copy number variation (CNV) in 15q11.2, especially between BP1 and BP2, has been reported to be pathogenic and associated with autism spectrum disorder in White populations (Madrigal *et al.*, 2012; Sorte *et al.*, 2013). The segment between BP1 and BP2 contains four evolutionarily conserved genes, *TUBGCP5*, *NIPAI*, *NIPAI2*, and *CYFIP1*, which are widely expressed in the neuronal tissue. Here, we report a microdeletion of chromosome 15q11.2 in a pair of Chinese autistic monozygotic twins.

Diagnoses were made on the basis of a clinical evaluation using the *Diagnostic and Statistical Manual of Mental Disorders*, 4th ed. (DSM-IV) and Autism Diagnostic Observation Schedule (ADOS). Genomic DNA was extracted from peripheral blood using the QIAamp DNA Blood Mini Kit (Cat# 51104; Qiagen, Hilden, Germany). We screened for the dosage of *TUBGCP5*, *NIPAI*, and *CYFIP1* by real-time quantitative PCR to identify the copy number changes between BP1 and BP2 in 15q11.2. Whole-genome CNV analysis was then carried out using Agilent SurePrint G3 Human CGH Microarray 1 × 1 mol/l (Cat# G4824A-021529; Agilent Santa Clara, California, USA) to confirm these changes. Data analysis and CNV identification were carried out on Agilent Genomic Workbench Lite, edition 6.5. All CNVs were checked against the Database of Genomic Variants (<http://projects.tcag.ca/variation>) to determine whether they have been reported previously in autism spectrum disorder patients. The study was approved by the ethical committee of the Children's Hospital of Fudan University.

The monozygotic twins were found to carry a 434.4 kbp deletion in 15q11.2 (22 756 650–23 191 062), spanning five genes (*TUBGCP5*, *CYFIP1*, *NIPAI2*, *NIPAI*, and *WHAMML*, the former four expressed widely in the neuronal tissue). Besides this, a duplication of 15q11.1-11.2 (20 432 851–22 586 951), often identified in the

general population, was also detected. The duplicated region starts with *HERC2P3* and ends with *REREP3*. None of the genes in the duplicated region have been reported to be associated with autism or other neurodevelopmental disorders. The monozygotic twin boys were 3 years old at the time of examination, born by Cesarean section after a natural pregnancy of 31 weeks' gestation with low birth weight. Their height, weight, and head circumference were in the normal range at the time of examination. Phenotypically and clinically, the Chinese identical twins with autistic disorder bear a close resemblance to previously described patients in the White population. Principal among these are typical autistic features, mental retardation, language and motor delay, seizures, and slightly hypotonic. However, the two patients with the 15q11.2 deletion had no obvious dysmorphic features, no high/narrow forehead, no downturned mouth, no almond-shaped eyes, or small hands and feet. Interestingly, developmental regression characterized by a loss of previously acquired abilities and the appearance of autistic behaviors was observed in the twins (Lainhart *et al.*, 2002; Baird *et al.*, 2008). There was no family history for neurodevelopmental or neuropsychiatric disorders.

In conclusion, our study indicates that the 15q11.2 deletion is present in Chinese Han autism patients, with clinical characteristics similar to those reported in patients of American or European descent. The identification of the 15q11.2 deletion provides additional support for the pathogenic nature of this CNV. Importantly, autistic regression observed in these twins with the 15q11.2 deletion had not been reported. Thus, this report may provide new insight into the pathogenesis of the 15q11.2 deletion.

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### **Conflicts of interest**

There are no conflicts of interest.

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