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Excitation-inhibition imbalance in the respiratory network of a mouse model of Rett Syndrome

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ABSTRACT OF THE TALK

Rett Syndrome, an Autistic Spectrum Disorder (ASD), is a debilitating neurodevelopmental condition that affects 1 in 10000 young females. It is caused by mutations in the X-chromosomal gene of the transcriptional repressor methyl-CpG-binding protein 2 (MeCP2). MeCP2-mutant mice have been generated to study the molecular mechanisms of the disease. It has been suggested that an imbalance in synaptic transmission was the underlying cause for the behavioral abnormalities, one of them being the severe respiratory impairments in both Rett patients and mice models. It remained unclear, however, which transmitter and receptor systems are predominantly involved, and when the cellular defects become apparent. We report that MeCP2 KO mice present an imbalance between inhibitory and excitatory synaptic transmission in the respiratory network already at postnatal day 7, long before the manifestation of characteristic symptoms (>P20). We show also that specific alterations at the pre- and postsynaptic site of GABAergic and glutamatergic synapse may be the basis of the general network imbalance. These observations mandate the search for more refined diagnostic tools and may provide a rationale for the timing of future therapeutic interventions in Rett patients.