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Presentation Abstract

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Presentation Title:	Defective GABAergic neurotransmission in the nucleus tractus solitarius in Mecp2-null mice
Location:	WCC Hall A-C
Presentation time:	Tuesday, Nov 18, 2014, 8:00 AM -12:00 PM
Presenter at Poster:	Tue, Nov. 18, 2014, 11:00 AM - 12:00 PM
Topic:	++C.06.f. Rett syndrome
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Abstract:	Respiratory dysfunction is one of the major clinical features of Rett syndrome (RTT), a devastating neurodevelopmental disorder caused by loss-of-function mutations in the X-linked methyl-CpG binding protein 2 (*Mecp2*) gene. GABAergic dysfunction has been implicated contributing to the respiratory dysfunction. The NTS is

the first central site receives and integrates respiratory sensory inputs. Plasticity in the NTS can change the nature of the reflex output. We test the hypothesis that deficiency in *Mecp2* gene reduces GABAergic neurotransmission in NTS. Using whole cell patch clamp technique, we recorded spontaneous inhibitory postsynaptic currents (sIPSCs), miniature IPSCs (mIPSCs), evoked IPSCs (eIPSCs), and agonist-induced whole cell currents from NTS neurons in brainstem slices acutely prepared from age-matched male *Mecp2*-null mice and wild-type littermates. Using qPCR, we determined GABA-A receptor subunit gene expression from NTS punches. Compared to those from wild-type mice (n=11), NTS neurons from *Mecp2*-null mice (n=12) had significantly (P<0.05) smaller sIPSC and mIPSC amplitudes without significant changes in frequencies. There was no significant difference in eIPSC amplitude and pair pulse ratio (PPR) between WT and *Mecp2*-null mice (n=4-6) albeit a greater PPR variability was observed in *Mecp2*-null mice. *Mecp2*-null mice had enhanced response to exogenous GABA-A agonist application (n=4-6) and elevated GABRA1 gene expression (n=3) in the NTS. The data suggest that reduced GABAergic signaling via a post-synaptic mechanism(s) in the NTS contributes to respiratory dysfunction in RTT.

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RESPIRATION

SYNAPTIC TRANSMISSION

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