# PROGRESS IN NEUROSCIENCE PINS

**Seminar Series of the**
**Brain & Mind Research Institute**
**Weill Cornell Medical College (WCMC)**
**&**
**The Graduate Program in Neuroscience of**
**WCMC and Sloan Kettering Institute**

**Thursday, 1/26/17, 4 PM, coffee at 3:45 PM**
**Weill Auditorium**

## "Reduced sensory-motor synaptic excitation impairs motor neuron function through the potassium channel Kv2.1"

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## Abstract

The demise of normal behavior in neurodegenerative diseases is often attributed to the selective dysfunction of vulnerable neurons via cell-autonomous mechanisms. Vulnerable neurons however, are embedded in neuronal circuits but the contribution exerted by their synaptic partners to the disease process is largely unknown. In a mouse model of spinal muscular atrophy, an inherited neurodegenerative disease, we show that sensory-motor synaptic dysfunction exerts a powerful influence on the excitability and functional output of motor neurons by reducing their spiking ability in a non-autonomous manner. The synaptic dysfunction is caused by impairment of glutamate release presynaptically from proprioceptive neurons and mediated by a reduction of the potassium channel Kv2.1 on motor neurons, which can be reversed by increasing neuronal network activity pharmacologically. Our results demonstrate a key role of excitatory synaptic drive in shaping the function of motor neurons during development and the contribution of its disruption to neurodegenerative diseases.

**Recent Relevant Publications:**

1. Mentis GZ, Blivis D, Liu W, Drobac E, Crowder ME, Kong L, Alvarez FJ, Sumner CJ, O'Donovan MJ. Early functional impairment of sensory-motor connectivity in a mouse model of spinal muscular atrophy. Neuron. 2011; 69:453-67.
2. Lotti F, Imlach WL, Saieva L, Beck ES, Hao le T, Li DK, Jiao W, Mentis GZ, Beattie CE, McCabe BD, Pellizzoni L. An SMN-dependent U12 splicing event essential for motor circuit function. Cell. 2012; 151:440-54.
3. Mentis GZ, Blivis D, Liu W, Drobac E, Crowder ME, Kong L, Alvarez FJ, Sumner CJ, O'Donovan MJ. Early functional impairment of sensory-motor connectivity in a mouse model of spinal muscular atrophy. Neuron. 2011; 69:453-67.

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