109 PATHOLOGICAL MECHANISMS OF GLYCINE RECEPTOR ANTIBODIES

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Antibodies against glycine receptors (GlyRAbs) have been found in patients with acquired neuro-logical syndromes, which include oculomotor and autonomic disturbance, rigidity and other evidence of disturbance of spinal inhibitory circuits. However, as with other neuropil autoantibodies, the relationship between the identified antibody and neurological disease remains unclear.

Using whole-cell patch-clamp we have recorded spontaneous miniature inhibitory postsynaptic currents (mIPSCs) from motoneurons in rat dissociated spinal cord cultures. GABA and glycine are co-released at interneuron-motoneuron synapses, both contributing to mIPSCs. We separate the two components (on the basis of time-course) to quantify the contribution of glycinergic neurotransmission to the average mIPSC for motoneurons incubated in patient IgG and control IgG. We will use this system to investigate the cellular mechanisms of disrupted glycinergic neurotransmission. We will also explore whether this functional assay can be used to detect antibodies in sera from patients suspected to have antibody-mediated deficiency in glycinergic neurotransmission, without an identified antigenic target (seronegative 'stiff person plus' and opsoclonus-myoclonus).

Alongside the in vitro investigations we will use clinical neurophysiology to identify affected circuits in GlyRAb patients, and monitor changes with disease progression and recovery. Findings will be compared to patients with genetic defects in glycinergic pathways (hereditary hyperekplexia).