# AMPA- and GABA(A) receptor signalling and corticospinal motor neuron excitability in mouse models of ALS

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**Country**

United Kingdom

**Title of project or programme**

AMPA- and GABA(A) receptor signalling and corticospinal motor neuron excitability in mouse models of ALS

**Source of funding information**

MRC

**Total sum awarded (Euro)**

€ 656,803

**Start date of award**

01/07/2013

**Total duration of award in years**

3.0

**The project/programme is most relevant to:**

Motor neurone diseases

**Keywords**
**Research Abstract**

We will determine functional characteristics of excitatory and inhibitory influences on identified CSMNs in brain slices prepared from SOD1(G93A) ‘ALS’ mice at different stages of disease

progression. Cells will be retrogradely labelled with FluoroGold or latex beads applied to the cervical spinal cord. We will determine the active and passive electrical properties of the neurons and establish any general alterations in their properties at different stages of the disease. We will then examine the contribution of calcium-permeable AMPARs and their auxiliary proteins (TARPs and CNIHs) to synaptic and extrasynaptic signalling. We will record pharmacologically isolated AMPAR-mediated macroscopic currents and synaptic currents. The contribution of specific proteins will be determined by comparing the kinetics, voltage-dependence, calcium-permeability, conductance and pharmacology of synaptic and extrasynaptic receptors with those of recombinant receptors expressed with specific auxiliary subunits in tsA201 cells. To determine how GABAergic signalling is altered during disease progression, we will quantify the relative contribution to charge transfer of phasic and tonic GABA(A)R activation. We will distinguish between pre- and postsynaptic changes by examining pharmacologically isolated mIPSCs (amplitude and kinetics, and the conductance of the underlying channels). To determine the origin of changes in tonic GABA(A)R-mediated currents will examine the properties of native receptors in outside-out somatic patches and compare these with those of recombinant GABA(A)Rs expressed in tsA201 cells. We will assess the impact of GABA(A)R activation on cell excitability and potential changes in chloride homeostasis in recordings using the gramicidin perforated-patch technique to preserve intracellular chloride. Our research will contribute to the understanding of normal brain function and highlight potential strategies for limiting excitotoxic damage of motor neurons in ALS.

**Lay Summary**
**Further information available at:**

**Types:**
Investments > €500k

**Member States:**
United Kingdom

**Diseases:**
Motor neurone diseases

**Years:**
2016

**Database Categories:**
N/A

**Database Tags:**
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