Early postnatal elimination of slow-type motor neurons induces progressive muscle atrophy and kinetic tremor

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Fast muscles (white muscles) are innervated by fast-type motor neurons (MNs); slow muscles (red muscles) are by slow-type MNs. VAcHT-Cre is a Cre-driver mouse line that can direct DNA recombination in postnatal slow-type motor neurons (Misawa et al., *genesis*, 54, 568-572, 2016). To selectively eliminate slow-type motor neurons, VAcHT-Cre mice were crossbred with NSE-DTA mice in which diphtheria toxin A (DTA) was expressed after the loxP-site excision. The VAcHT-Cre;NSE-DTA mice (delta SlowMN mice) were born normally but showed progressive body weight loss, tremor and reduced life-span (average life, ca. 40 weeks). Muscular atrophy was evident in red muscles including the soleus and diaphragm, however white muscles were normal. Complex fiber-type transitions were observed in each muscles. The delta SlowMN mice showed hunched back posture (kyphosis) possibly by reduced trunk muscles. The tremor was kinetic in nature and most conspicuous in head and neck. The observed abnormalities were largely different from those observed in mutant SOD1-expressed ALS model mice in which fast-type motor neurons are known to be preferentially affected. The delta SlowMN mice could be a novel MN disease model characterized in proximal muscle atrophy, tremor and bulbar involvement.