



Article

Passive Transfer of Sera from ALS Patients with Identified Mutations Evokes an Increased Synaptic Vesicle Number and Elevation of Calcium Levels in Motor Axon Terminals, Similar to Sera from Sporadic Patients

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Abstract: Previously, we demonstrated increased calcium levels and synaptic vesicle densities in the motor axon terminals (MATs) of sporadic amyotrophic lateral sclerosis (ALS) patients. Such alterations could be conferred to mice with an intraperitoneal injection of sera from these patients or with purified immunoglobulin G. Later, we confirmed the presence of similar alterations in the superoxide dismutase 1 G93A transgenic mouse strain model of familial ALS. These consistent observations suggested that calcium plays a central role in the pathomechanism of ALS. This may be further reinforced by completing a similar analytical study of the MATs of ALS patients with identified mutations. However, due to the low yield of muscle biopsy samples containing MATs, and the low incidence of ALS patients with the identified mutations, these examinations are not technically feasible. Alternatively, a passive transfer of sera from ALS patients with known mutations was used, and the MATs of the inoculated mice were tested for alterations in their calcium homeostasis and synaptic activity. Patients with 11 different ALS-related mutations participated in the study. Intraperitoneal injection of sera from these patients on two consecutive days resulted in elevated intracellular calcium levels and increased vesicle densities in the MATs of mice, which is comparable to the effect of the passive transfer from sporadic patients. Our results support the idea that the pathomechanism underlying the identical manifestation of the disease with or without identified mutations is based on a common final pathway, in which increasing calcium levels play a central role.

Keywords: ALS; passive transfer; intracellular calcium; synaptic vesicles; SOD1 mutation; C9ORF72 mutation