Glial cells are known to support neurons, maintain homeostasis in the nervous system or act as an immune defense, to name a few of their physiological functions. In pathological conditions, they change their properties and become active participants with beneficial and/or harmful effects. The exact role they play in Amyotrophic lateral sclerosis (ALS) is not known, but with the urgent need for efficient therapy, there is a constant effort to precisely elucidate their involvement. We examined cortical astrocytes, microglia and oligodendrocytes in the SOD1(G93A) mouse model of ALS with the use of single-cell RNA sequencing and immunohistochemistry, and then further focused on the functional properties of astrocytes in ALS and in Alzheimer's disease (AD) using *in situ* 3D-morphometry and the real-time iontophoretic method. The profiling revealed minimal changes in the cortical glia in the final stage of ALS, suggesting unsuitability of the model for future cortical studies. Nevertheless, with the use of the ALS mouse model on a different background, we were able to detect cortical and spinal astrogliosis and identify diminished K^+ uptake during hyperkalemia and downregulation of Kir4.1 in spinal ALS-affected astrocytes. The investigation in the AD model also showed diminished astrocytic swelling in response to hyperkalemia and hypo-osmotic stress. The overall results provide insights into the astrocytic homeostatic abilities during pathology and highlight the importance of using a reliable animal model.