Spatiotemporal localization of cellular factors is a fundamental feature impacting cell survival and proper function. The cell needs to respond in an accurate manner in both space and time to both intra and inter cellular environment cues. The regulation of this comprehensive process involves the cytoskeleton and the trafficking machinery. Alterations in such mechanisms can lead to cell dysfunction and disease. Motor neurons that can extend over tens of centimeters are a classic example for the importance of such events. Changes in spatiotemporal localization regulated by cytoskeleton processes are thought to play a role in motor neuron degeneration. In this talk I will discuss these mechanisms and argue that alterations in localization events lead to motor neuron degeneration in ALS.