Neuroprotective Role of Testosterone

Neuroprotective Effect of Testosterone Treatment on Motoneuron Recruitment Following the Death of Nearby Motoneurons

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Motoneuron loss is a significant medical problem, capable of causing severe movement disorders or even death. We have previously shown that motoneuron death induces marked dendritic atrophy in surviving nearby motoneurons. Additionally, in quadriceps motoneurons, this atrophy is accompanied by decreases in motor nerve activity. However, treatment with testosterone partially attenuates changes in both the morphology and activation of quadriceps motoneurons. Testosterone has an even larger neuroprotective effect on the morphology of motoneurons of the spinal nucleus of the bulbocavernosus (SNB), in which testosterone treatment can completely prevent dendritic atrophy. The present experiment was performed to determine whether the greater neuroprotective effect of testosterone on SNB motoneuron morphology was accompanied by a greater neuroprotective effect on motor activation. Right side SNB motoneurons were killed by intramuscular injection of cholera toxin-conjugated saporin in adult male Sprague-Dawley rats. Animals were either given Silastic testosterone implants or left untreated. Four weeks later, left side SNB motor activation was assessed with peripheral nerve recording. The death of right side SNB motoneurons resulted in several changes in the electrophysiological response properties of surviving left side SNB motoneurons, including decreased background activity, increased response latency, increased activity duration, and decreased motoneuron recruitment. Treatment with exogenous testosterone attenuated the increase in activity duration and completely prevented the decrease in motoneuron recruitment. These data provide a functional correlate to the known protective effects of testosterone treatment on the morphology of these motoneurons, and further support a role for testosterone as a therapeutic agent in the injured nervous system.

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Neuroprotective effects of testosterone on dendritic morphology following partial motoneuron depletion: efficacy in female rats.

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Motoneuron loss is a significant medical problem, capable of causing severe movement disorders and even death. We have previously demonstrated that partial depletion of motoneurons induces dendritic atrophy in remaining motoneurons, with a concomitant reduction in motor activation. Treatment of male rats with testosterone attenuates the regressive changes following partial motoneuron depletion. To test whether testosterone has similar effects in females, we examined potential neuroprotective effects in motoneurons innervating muscles of the quadriceps of female rats. Motoneurons were selectively killed by intramuscular injection of cholera toxin-conjugated saporin. Simultaneously, some saporin-injected rats were given implants containing testosterone or left untreated. Four weeks later, surviving motoneurons were labeled with cholera toxin-conjugated HRP, and dendritic arbors were reconstructed in three dimensions. Compared to normal females, partial motoneuron depletion resulted in decreased dendritic length in remaining quadriceps motoneurons, and this atrophy was greatly attenuated by testosterone treatment. These findings suggest that testosterone has neuroprotective effects on morphology in both males and females, further supporting a role for testosterone as a neurotherapeutic agent in the injured nervous system.

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