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Nerve Excitability Studies of Peripheral Neuropathies: Charcot-Marie-Tooth Disease 1A

This thesis set out to better characterize excitability changes that occur with demyelination and specifically focused on the most common inherited demyelinating polyneuropathy: Charcot-Marie-tooth 1A disease (CMT1A). Tail nerves of wild-type and CMT1A female rats were compared for their accommodations to polarizing conditions using threshold tracking. Abnormalities were consistently detected in CMT1A rats, which were representative of changes seen in previously to occur in humans. Disease progression was tracked at three time points representative of adolescence, adulthood, and aging, during which CMT1A rats showed clear excitability differences. Throughout aging, however, the trends seen in accommodating depolarizing conditions paralleled WT rats, whereas there was abnormally almost no change in accommodating hyperpolarizing conditions.

In addition to disease progression, efficacies of two therapeutic approaches were also tested. A dietary increase in either cholesterol or curcumin in CMT1A rats showed to have no significant effects on the CMT1A abnormalities detected with threshold tracking. Contrarily, in the mouse model of CMT1A, an overexpression of axonal Neuregulin-1 type I proved to ameliorate the abnormal responses to hyperpolarization back to WT levels.

Therefore, this thesis provides new data supporting the strength of the CMT1A rat model, and also suggests that Neuregulin-1 type I overexpression in the nerve had beneficial effects on the abnormal CMT1A nerve excitability.