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Evidence that glutamate induced neurite retraction of reticulospinal neurons is dependent on calcium influx

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Locomotor systems of vertebrates consist of a command system in the brain that activates central pattern generators in the spinal cord to initiate locomotor behavior. Reticulospinal (RS) neurons are the output neural elements of the command system. Following spinal cord injury, axons of RS neurons are severed and must regenerate to restore behavioral functions below the lesion. In higher vertebrates, such as birds and mammals, axonal regeneration is very limited, and spinal cord injury usually results in permanent paralysis below the lesion. In contrast, in the lamprey and a few other lower vertebrates, axonal regeneration is robust following spinal cord injury, and this results in virtually complete behavioral recovery. Therefore, identification of the mechanisms for axonal regeneration in lower vertebrates might provide information about the requirements for regenerating neurons in higher vertebrates. Examination of neurite outgrowth in culture is often used to identify the cellular and molecular mechanisms for axonal regeneration. In our laboratory, we have shown that application of glutamate, an excitatory neurotransmitter, to growth cones of RS neurons in culture causes neurite retraction, presumably by causing depolarization and calcium influx. Intracellular calcium levels are thought to be one of the important regulatory factors for neurite outgrowth. Glutamate might mediate calcium influx via at least two types of channels: chemically-gated channels (e.g. NMDA channels); or voltage-gated calcium channels. The purpose of the present study was to determine if calcium influx via voltage-gated channels is necessary for neurite retraction. The anatomical tracer DiI was applied to the spinal cord to pre-label RS neurons. Following transport, RS neurons were isolated and placed in cell culture. Glutamate was pressure ejected onto the growth cones of RS neurons in the presence of w-conotoxin MVIIC, which is a specific blocker for N and P voltage-gated calcium channels. Under these conditions, conotoxin reduced but did not block glutamate-induced neurite retraction. In conclusion, glutamate-induced neurite retraction of lamprey RS neurons probably is mediated by calcium influx via both chemically-gated and voltage-gated channels. Determination of the factors that regulate neurite outgrowth in culture may provide insights into the mechanisms for axonal regeneration and behavioral recovery following spinal cord injury in whole animals.