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Nerve growth factor-induced hyperexcitability of rat sensory neuron in culture

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ABSTRACT

Abnormal spontaneous firing of primary sensory neurons is considered to be a cause of neuropathic pain. However, pathogenic mechanisms of hyperexcitable sensory neurons in neuropathic model animals are unclear. We examined effects of chronic treatment of nerve growth factor (NGF), one of candidate mediators for the pathogenesis, on excitability of sensory neurons by voltage-clamped recording in a cell-attached configuration. From rat dorsal root ganglion (DRG) neurons cultured without NGF, only stable holding currents without spontaneous firing activity were recorded. On the other hand, more than 20% neurons cultured in the presence of NGF for more than 3 days showed spontaneous current spikes at frequencies between 0.1 and 5 Hz. Each spikes had an initial inward phase followed by the outward phase, resulted from spontaneous transient depolarization followed by transient hyperpolarization. These spontaneous spikes were abolished by tetrodotoxin, lidocaine and reduction of extracellular concentration of Na^+ from 154 mM to 100 mM, in all-or-none fashion, suggesting that spontaneous current spikes reflected spontaneous action potentials. From these results, it became evident that DRG neurons of adult rats had a nature to respond to NGF and obtained the abnormal hyperexcitability to fire spontaneously.

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