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Neuropathic Pain and Ectopic Spontaneous Action Potential Activity of Human Primary Sensory Neurons

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Introduction

Hyperexcitability of primary sensory neurons and its most extreme form, spontaneous activity, are key cellular-level drivers of neuropathic pain. Though extensively studied in animal models of neuropathic pain and established as a phenomenon occurring in human primary sensory neurons, this altered electrophysiology has not been rigorously studied for human primary sensory neurons nor has its relationship to clinical symptoms of neuropathic pain been established [1-10].

Methods

The study was approved by the M.D. Anderson IRB. Written informed consent for participation was obtained from each tissue donor.

Human dorsal root ganglia and medical histories were obtained from patients undergoing oncological spine surgery that necessitated sacrifice of spinal nerve roots as part of standard of care. Clinical data regarding presence of radicular/neuropathic pain was obtained through retrospective review of medical records or collected at time of study enrollment.

Conclusions

Utilizing whole-cell patch clamp of dissociated human primary sensory neurons from patients both with and without neuropathic pain this study presents two important new findings: 1) first demonstration of a statistically significant association between in vitro spontaneous activity of dissociated human primary sensory neurons and neuropathic pain 2) the first characterization of the altered intrinsic membrane properties associated with spontaneous activity in human primary sensory neurons.

Results

Electrophysiological recordings were obtained from a total of 110 neurons, dissociated from 23 dorsal root ganglia, donated by 13 patients.

Spontaneous activity was noted in 15% (12/79) of neurons from ganglia with pain in a corresponding dermatome vs 0% (0/31) of neurons from pain free ganglia ($P < 0.05$)

Compared to neurons without spontaneous activity, human sensory neurons with spontaneous activity had significantly altered intrinsic membrane properties;

Learning Objectives

By the conclusion of this session, participants should be able to:

1)Understand the utility and basic methodology of harvest, culture, and experimentation with human dorsal root ganglion neurons.

2)Understand the relationship of primary sensory neuron spontaneous action potential activity with human symptoms of neuropathic pain.

3)Understand the association of altered membrane properties associated with spontaneous activity

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