Intraepidermal nerve fiber assessment in Macaque fascicularis

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ABSTRACT

Patients with peripheral neuropathy may present with a constellation of symptoms related the fibers that are affected. Small fiber neuropathy causes sensory and autonomic symptoms. Small fiber neuropathy cannot be confirmed with standard clinical neurophysiological investigations. However, small fiber neuropathy can be evaluated with intaepidermal skin biopsy. Neurofilament Protein clone 2F11 antibody was used to label intraepidermal nerve fibers in skin biopsies from an adult Macaca fascicularis. Small fibers were well visualized with this technique. In summary, the preliminary data suggests that this technique can be utilized to evaluate the intraepidermal fibers in the Macaque fascicularis. As in human beings, qualitative and quantitative techniques may be employed to evaluate the images.

KEYWORDS: Immunohistochemistry, small fiber neuropathy, non-human primate.

INTRODUCTION

Peripheral neuropathy is a disabling condition that affects 15 to 20 million people in the USA. Patients may present with a constellation of symptoms related the fibers that are affected (Shy, 2007).

Peripheral nerve fibers can be categorized based on size. Large diameter fibers are myelinated and include A-alpha fibers which supply skeletal muscles and A-beta fibers which mediate the sensation of touch and vibration. Medium size fibers are also myelinated and include A-gamma fibers which are related to muscle spindle function. Small diameter fibers include myelinated A-delta fibers and unmyelinated C-fibers which supply the skin and involuntary muscles. These small fibers mediate pain, thermal sensation and autonomic function (Holland et al., 1997; Tavee and Zhou, 2009).

Small fiber neuropathy causes sensory and autonomic symptoms. Sensory symptoms include pain and dysesthesias. Typically, the legs are initially affected. Autonomic symptoms include orthostatic hypotension, sexual dysfun-
tion as well as bowel and bladder symptoms. Small fiber neuropathy is associated with diabetes mellitus, connective tissue disease, B12 deficiency, paraproteinemia, human immunodeficiency virus, hepatitis C, celiac disease and paraneoplastic syndrome (Shy, 2007).

In human beings, small fiber neuropathy is evaluated in clinical practice and research studies with intraepidermal nerve fiber studies. These studies are performed on small skin samples, which are obtained by punch biopsy. The pathological assessment includes qualitative and quantitative immunohistochemistry techniques to evaluate intraepidermal nerve fibers (Umapathi et al., 2007).

In this brief report, we describe an immunohistochemistry technique to evaluate the intraepidermal nerve fibers in the Macaque fascicularis. To our knowledge, this has not been reported previously in non-human primates. Tissue samples were collected from a cadaveric subject. The investigators’ did not conduct any research on this subject, while the subject was alive.

**MATERIALS AND METHODS**

In a single subject, Neurofilament Protein clone 2F11 antibody (Dako Inc, Carpinteria, California) was used to label intraepidermal nerve fibers in skin biopsies from an adult Macaca fascicularis. A full-thickness skin biopsy was obtained from a cadaveric subject that had recently died. Skin samples were obtained from the outer foot with a 3 mm punch biopsy. The tissue samples were immediately fixed in a 2% buffered paraformaldehyde solution for 24 hrs. The specimens were then cryo-protected with 20% glycerol overnight and frozen for later cryosectioning. Biopsies were then cut into 50-μm sections with a cryostat and then immunostained with Neurofilament Protein antibody.

![Image](image_url)

**Figure 1:** Epidermal nerve fibers were visualized with biopsy samples treated with Neurofilament Protein clone 2F11 antibody, at 40x magnification light microscopy.
RESULTS AND DISCUSSION

In this one subject, the intraepidermal nerve fibers were well visualized. The preliminary data suggests that Neurofilament Protein clone 2F11 antibody can be utilized to evaluate the intraepidermal fibers in the macaque fascicularis. It should be noted that the collection of skin tissue can be undertaken on a serial basis, with minimal morbidity to the subject. As well, this immunohistochemistry technique is relatively straightforward and can be completed at without specialized or expensive equipment.

The most common cause of small fiber neuropathy in human beings is diabetes mellitus. Of note, non-insulin dependent diabetes occurs spontaneously in the macaque fascicularis (Dunaif and Tattersall, 1998). As such, this histological technique may be helpful in advancing the development of non-human primate models of small fiber neuropathy. Qualitative and quantitative techniques may be employed to evaluate the images. With this approach, intraepidermal fiber assessment may be useful in the measurement of the nature and progression of small fiber neuropathy in non-human primates.

Figure 2: Epidermal nerve fibers, at 100x magnification light microscopy.
REFERENCES


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