INTRODUCTION

Carpal tunnel syndrome (CTS) results from localized compression of the median nerve within the carpal tunnel and is the most commonly encountered peripheral neuropathy. There has been considerable question regarding the work-relatedness of the disorder due to the number of non-occupational risk factors linked to CTS including gender, age, obesity, reduced fitness, smoking, alcohol and caffeine use, diabetes, renal disease, thyroid disease, pregnancy, lactation, sports participation, and genetics. A recent review of over 30 epidemiological studies of workplace factors and CTS determined that, on balance, the evidence supported an association between CTS and highly repetitive work, forceful work, and combinations of risk factors.

A few animal models of chronic median nerve compression are presented in the literature. A recent rat model where subjects perform a voluntary, repetitive grasping or pulling task has been used to study early inflammatory stages of injury due to repetitive use of the front paw. Another model uses anesthetized rabbits in which the FDP m. is repeatedly stimulated to elicit a specific amount of force against a load cell. An alternative to this model is one in which a semi-permanent catheter is inflated to a known pressure. The rabbit is free to amble, and over a period of days or weeks, median nerve impairment develops. Through electrodiagnostic testing, these models have shown median nerve conduction impairment in their subjects similar to that seen in humans with CTS. A monkey model of CTS, based on the anatomic similarities to humans and which uses the performance of a voluntary task, could offer some advantages over these other animal models while complementing the results from those models. If successful, such a model would clearly show that median nerve impairment could occur as a direct result of hand use that is similar to repetitive human hand use in occupational settings. Hence, the objective of the current study was to demonstrate a non-human primate model for the study of CTS caused by chronic overuse.

METHODS

Four adult female Macaca fascicularis monkeys were used in the study. Experimental procedures were approved by the University’s IACUC and subject care was according to the NIH Guide for the Care and Use of Laboratory Animals.

The subjects performed a task that required a sustained pinch grip of 20% maximum voluntary exertion (MVE) for 3 s, with the wrist flexed about 60 deg, at a rate of up to 6/min. Task parameters were based on risk factors commonly identified in the epidemiological literature. The task apparatus (figure 1) was attached to each subject’s cage in such a way that it could only be accessed with the left hand. To perform a pinch, subjects reached through a tube and flexed the wrist to about 60° to grasp a pair of tongs in a pad-pad pinch. Resistance was provided by a compression spring between the tongs. Closure of the tongs required a combined effort from the thumb and fingers (pad-pad pinch). A successful pinch resulted in delivery of a food pellet. To avoid an acute inflammatory response to an extreme change in hand use, pinch force and daily exposure duration to the task were gradually increased during the training period.

The primary dependent variable in the study was median sensory nerve conduction velocity (SNCV) which has been described previously. The median nerve testing was conducted bilaterally, biweekly during which the subjects were initially sedated with Ketamine hydrochloride (13 mg/kg i.m) and were anesthetized with Isoflurane (1-2%) inhaled through a mask. To limit the time of anesthesia for routine testing, ulnar nerve stimulation was only performed at baseline prior to training and for confirmation when a positive diagnosis of median mononeuropathy was suspected.

The latency of the sensory nerve action potential’s onset and peak denervation were measured from the averaged response to the five stimuli. SNCVs were calculated from onset and peak latencies. We have found the measurements based on the peak latencies to be more stable longitudinally, even though measurements based on the onset latencies appear to be more sensitive to the early onset of nerve conduction impairment. The peak-to-peak amplitude was measured but not used due to the amount of longitudinal variability. Compound motor action potentials (CMAP) served primarily as a control for the production of recruitment curves and to verify responses specific to the nerve stimulated.

In this study, a case of CTS was operationally defined as a 25% decrease in median SNCV derived from peak latency. This exceeds the 2 standard deviation decline typically used in human diagnostic testing (2 sd corresponds to a 9-14% decline in SNCV from peak latency and an 11-27% decline in SNCV from onset latency). Two consecutive readings at or greater than the 25% decline were required before the subject was removed from the task and allowed to recover.

RESULTS

Three of the four subjects developed CTS in the working hand as a result of exposure to the repetitive pinching task, as defined by reduction in SNCV (figure 2) after performing the task for 12 to 19 weeks. No changes in conduction velocity were detected in the ulnar nerve of the working hand or in the median and ulnar nerves of the non-working hand. Regression analyses showed highly significant relationships between cumulative workload and decline in SNCV for the working (left) hands of the three affected subjects ($R^2$: 0.86, 0.91, 0.89, respectively; all p-values <0.001), and no significant relationships for the non-working hands or for either of unaffected subject’s hands.

Figure 1. The pinch task required 60 degrees of wrist flexion.

Figure 2. The decline in median nerve conduction velocity over time.

DISCUSSION

The objective of this study was achieved in that a manual task containing several risk factors associated with occupationally-related CTS in human epidemiological research induced a median mononeuropathy in the monkey. This is in contrast to our pilot work for this project in which none of a prior cohort of four monkeys, who performed a low force pinch task with flexed wrist but without a required pinch duration, developed a median nerve impairment. This supports the concept that it is not simply any repetitive use of the hand that leads to CTS but rather exposure to tasks with certain physical characteristics. Hence, these results point to the need for studies describing dose-response relationships between various task factors (force, repetition, and posture) and CTS onset. Given that we were able to demonstrate the development of CTS through an occupationally relevant voluntary pinching task with multiple risk factors, it is our conclusion that the monkey model is well suited for this endeavor.

REFERENCES


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