COMPARING AXONAL EXCITABILITY IN PAST POLIO TO AMYOTROPHIC LATERAL SCLEROSIS

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ABSTRACT: *Introduction*: Poliomyelitis causes selective destruction of anterior horn cells and usually has a stable disease course post-infection. We assessed the excitability characteristics in patients with a stable course after past poliomyelitis and compared them with changes described in amyotrophic lateral sclerosis (ALS). *Methods*: The excitability characteristics of motor and sensory nerves were studied in 10 subjects with stable past poliomyelitis. *Results*: Motor rheobase was increased, but there were no significant changes in strength–duration properties or depolarizing threshold electrotonus, as have been seen in previous studies of ALS. *Conclusions*: There is minimal change in axonal excitability properties in patients with stable past poliomyelitis. The results may signify sufficient compensation in the stable state of the disease. Increased subexcitability in 1 subject with demonstrable hyperexcitability may represent compensation for increased ectopic activity rather than a different process in surviving motor neurons.

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Poliomyelitis occurs in 0.6–1.6% of people infected by the polioviruses, with a selective destruction of anterior horn cells.[1,2] Between 25% and 60% of motor neurons are lost in patients with prior polio, as assessed by motor unit number index (MUNIX) and macro-electromyography (macro-EMG).[3] The superimposed physiological loss with aging has been purported to cause the post-polio syndrome (PPS) due to the increasing demands placed on surviving motor neurons controlling the enlarged motor units.[4–6] The lower motor neuron features in past polio survivors are similar to those of amyotrophic lateral sclerosis (ALS) patients, and the progressive form of the former, PPS, is difficult to distinguish from ALS clinically and electrophysiologically. However, acute poliomyelitis tends to not affect the corticospinal tract.[7] Patients frequently have enlarged motor units with EMG evidence of chronic denervation over several segments, including limbs that were not wasted.

In axonal excitability studies, increased strength–duration time constant (τ_{SD}) was noted in patients with ALS, spinal muscular atrophy (SMA), and Kennedy disease, which was thought to be related to axonal regeneration and sprouting.[8–13] In patients with ALS, there were also greater changes in depolarizing threshold electrotonus and greater supernormality in the recovery cycle. This is suggestive of increased persistent Na^+ and reduced K^+ conductance[8–10] causing axonal hyperexcitability, the extent of which is related to the size of the compound motor action potential (CMAP) and disease progression.[9]

In this study we attempted to characterize axonal excitability characteristics of peripheral nerves in patients with past poliomyelitis and compare them with those noted in ALS.

METHODS

Ten patients (6 men, 4 women), aged 30–77 (mean 58.7) years, were diagnosed with past polio by clinical history and needle EMG. All had a stable clinical course. The study was approved by the local ethics committee, and all participants provided informed consent. Both motor and sensory studies in each individual were assessed in the patient and control groups. The methodology of excitability testing has been described in full elsewhere.[14] Student *t*-tests were used to compare the motor and sensory excitability studies of the patients with 15 age-matched controls (mean age 57 years, 10 men and 5 women). $P < 0.05$ was considered significant.

RESULTS

The duration from acute infection was 25–76.5 (mean 53.9) years. Five patients had weakness in the median distribution, and 2 patients had low-amplitude median CMAPs. These patients and another had maximal weakness involving the median territories either on the side tested or in the contralateral limb (which could not be tested due to a confounding carpal tunnel lesion or a too-small CMAP for threshold tracking). None had sensory involvement. One patient had a thenar tremor, with frequent myokymic discharges noted in the abductor pollicis brevis muscle on needle EMG.

Abbreviations: ALS, amyotrophic lateral sclerosis; CMAP, compound motor action potential; EMG, electromyography; MUNIX, motor unit number index; PPS, post-polio syndrome; SMA, spinal muscular atrophy; τ_{SD}, strength–duration time constant

Key words: amyotrophic lateral sclerosis; motor neuron disorders; nerve excitability; past polio; poliomyelitis

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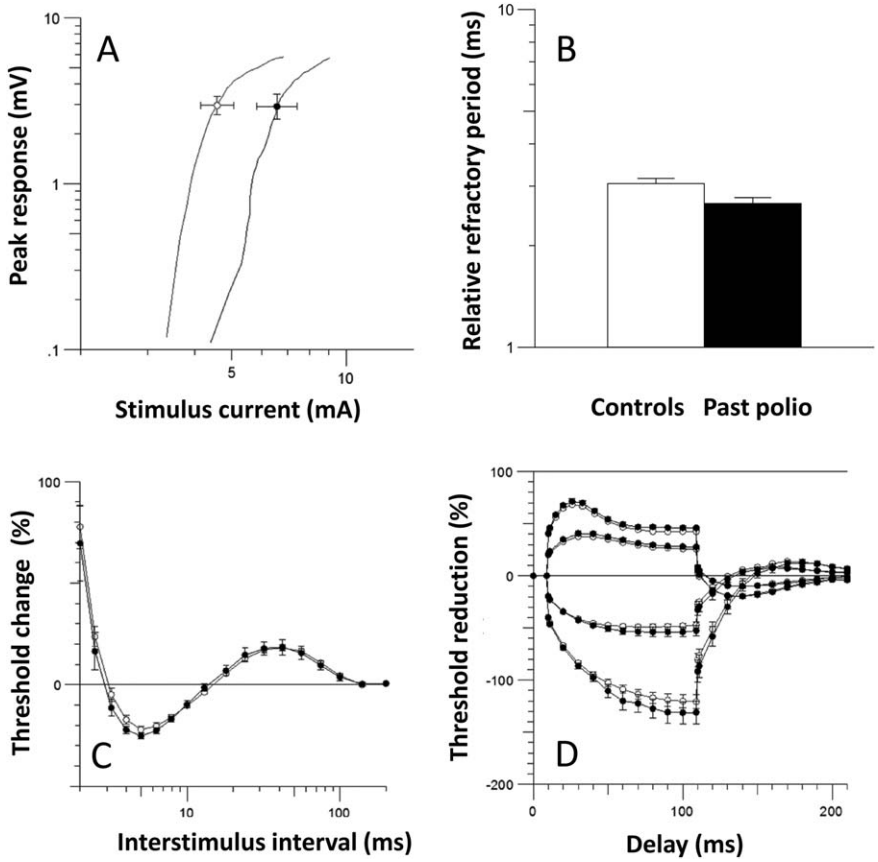

FIGURE 1. Median motor excitability (filled circles = patients, empty circles = controls; error bars = SEM). **(A)** Stimulus–response curves. Peak responses are not significantly different, but there is a shift of the stimulus–response curve to the right with a concomitant increase in rheobase. **(B)** The relative refractory period is shortened in patients, possibly because of their warmer temperature. **(C)** The recovery cycle shows no significant change in either the super- or subexcitability. **(D)** Non-significant "fanned-out" appearance in threshold electrotonus.

For the motor studies, an increased stimulus was required for a 50% CMAP response (6.6 vs. 4.6 mA; $P = 0.03$; Fig. 1A). There was a corresponding increase in the rheobase (4.3 vs. 3.0 mA; $P = 0.047$). These 2 changes were more marked when comparing the 5 subjects with weakness to controls (8.2 mA; $P = 0.01$; and 5.5 mA; $P = 0.02$, respectively). A reduction in the relative refractory period (RRP) (2.7 vs. 3.1 ms; $P = 0.02$; Fig. 1B) was explained in part by an increase in temperature (34.0 vs. 33.1°C; $P = 0.04$). The τ_{SD} was increased, but not significantly (0.55 vs. 0.46; $P = 0.11$). The only significant correlation of the individual excitability parameters with the CMAP amplitude was in the stimulus required for 50% CMAP ($r = -0.65$; $P = 0.04$) and the stimulus–response slope ($r = -0.76$; $P = 0.02$).

Eight patients had median sensory excitability studies. There was a significant increase in threshold change to hyperpolarizing conditioning current after 10–20 ms (−92.4% vs. −83.0%; $P = 0.003$). In addition, latencies to sensory nerve action potentials appeared to be increased (4.0 vs. 3.3 ms; $P < 0.001$), despite a warmer temperature for these subjects (34.5 vs 33.6°C; $P = 0.06$).

The excitability characteristics of 1 subject in this cohort with evidence of nerve hyperexcitability showed increased motor subexcitability in the recovery cycle outside the 95% confidence interval for control subjects, which differs from previous group observations in ALS.

DISCUSSION

The changes seen in patients with past polio bear some similarities to the changes seen by others in ALS,[9,10,15] but to a lesser extent. This suggests that there may be excitability changes inherent in past poliomyelitis similar to other motor neuron disorders. These could be generic and accompany the metabolic stress placed on surviving axons with enlarged motor units, but possibly to a lesser degree in stable past polio. Although not to a significant extent, the motor τ_{SD} and the threshold change to depolarizing conditioning current in threshold electrotonus (Fig. 1D) appeared to be increased marginally in our patients, most of whom

had normal CMAP amplitudes. It is unclear why there was a mean latency prolongation for the sensory studies despite their warmer temperatures, but excitability differences can be responsible for changes in conduction velocity.

We did not necessarily study the most affected limb but relied on the premise that poliomyelitis often affects all lower motor neuron segments, albeit in a subclinical fashion, which may only be detected with needle EMG.[16] Nevertheless, even in weak muscles, it was not possible to detect motor excitability changes except in the absolute measures, and relative excitability measures were not significantly different. It is possible that the changes observed in motor excitability would have been more marked in an advanced or progressive phase of the disease, such as in PPS. However, a subject with myokymic discharges had changes in subexcitability that were not seen in advanced ALS, and the changes may be secondary to compensatory ectopic activity rather than implying another mechanism for the excitability differences in surviving motor neurons.

In conclusion, our findings are not suggestive of significant change in axonal membrane properties in patients with past polio. It is possible that, in ALS and SMA, the surviving motor neurons are more diseased than what we observed in this cohort. The process of axonal attrition with regeneration and sprouting may not manifest marked changes in excitability even in the context of significant clinical and standard nerve conduction abnormalities, and our study underscores the complementary nature of the 2 electrophysiological techniques.

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