Short report

Spinal somatosensory evoked potentials in hereditary spastic paraplegia*

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SUMMARY Cervical somatosensory evoked potentials elicited by median nerve stimulation were recorded from 18 cases of hereditary spastic paraplegia. Motor and sensory nerve conduction in the median nerve was normal in each. In one third of the patients no spinal evoked potential was detectable. In the remainder the amplitude of the evoked potential was reduced in comparison with a control series; the latency was not significantly different. These changes suggest that a selective degeneration of the centrally directed axons derived from the dorsal root ganglion cells occurs in this disorder. The findings are discussed in relation to previous reports on the pathological appearances.

This study was prompted by the observation that in patients with hereditary spastic paraplegia with associated sensory loss, usually of posterior column type, sensory nerve action potentials are normal (Thomas, unpublished). This suggested that the site of the lesion responsible for the sensory changes lies within the central nervous system. Fibre degeneration is known to be present within the posterior columns in hereditary spastic paraplegia. In order to explore the integrity of the centrally directed axons of the primary sensory neurons, it was therefore decided to examine spinal somatosensory evoked responses in patients with this condition. The present report records the results of a study on 18 patients.

Material

The observations were made on 12 male and six female patients with hereditary spastic paraplegia. They were derived from 12 families in which the inheritance was autosomal dominant in seven and of probable autosomal recessive pattern in four. In one of the latter families there were four affected siblings born to unaffected first cousin parents. Only one of the affected individuals in this family consented to evoked potential recordings. There were no other instances of consanguinity. One single case lacking a family history was included (case 2), but the diagnosis seemed probable on clinical grounds.

Recordings were also made on 10 healthy subjects who ranged in age from 22 to 53 years. Seven were male and three female.

Methods

The technique described by Matthews et al was adopted. The right median nerve was stimulated at the wrist through bipolar electrodes with 200 μs square wave pulses at four times the threshold for sensation at a rate of 3 per second, using a Devices isolated stimulator. Recordings were made from the midline of the neck posteriorly with disc electrodes just rostral to the spine of the seventh cervical vertebra (Cv7 electrode) and at the skull base (Cv2 electrode). A reference electrode was placed in the midline over the anterior part of the scalp (FZ site in 10–20 system) and an earth in the midline just posterior to the vertex. Skin resistance was less than 5 kΩ, usually 1–2 kΩ. The potentials were amplified by a Devices amplifier with filters set to 2.5 kHz low pass, 0.16 Hz

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high pass. 256 sweeps were averaged by a Datalab DL4000 averager and the measurements made from photographs. The observations were obtained from at least three runs to ensure that any response was consistent.

Results

Motor and sensory nerve condition was examined in the right median nerve at the time of the recording. Motor conduction velocity over the forearm, recording from abductor pollicis brevis, was within normal limits in all the patients (55.5±5.3 m s⁻¹, range 49–66 m s⁻¹) as was the distal motor latency (3.7±0.38 ms, 3.2–4.0 ms). Sensory conduction was also normal in all instances when assessed by stimulation of the digital nerves of the index finger through ring electrodes and percutaneous recording over the median nerve at the wrist (amplitude 13.9±3.2 µV, 10–21 µV; latency to negative peak 3.1±0.5 ms, 2.9–4.0 ms).

For the spinal somatosensory evoked potentials, the amplitude measured to the nearest 0.5 µV, and latency of the main negative (N13) peak obtained from the Cv7 electrode are shown in the table. No potential was detectable in six patients. In the remainder, the mean amplitude was 1.25±0.69 µV. This was significantly less (p<0.001) than the mean value for the control subjects, which was 3.0±0.83 µV. The latency of the N13 peak, which was (13.2±0.94 ms) in the control subjects, was the same 13.2±0.81 ms in those patients in whom the potential was obtained.

Table  Clinical details, and amplitudes and latencies of cervical (Cv7 recording) somatosensory evoked responses in 18 patients with hereditary spastic paraplegia

<table>
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<tr>
<th>Case no</th>
<th>Family no</th>
<th>Age (yr)</th>
<th>Sex</th>
<th>Age of onset</th>
<th>Inheritance*</th>
<th>Sensory loss</th>
<th>Spinal evoked potential amplitude (µV)</th>
<th>Spinal evoked potential latency (ms)</th>
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*AD autosomal dominant; AR autosomal recessive; S single case.

Discussion

Hereditary spastic paraplegia was first clearly delineated by Strümpell. Subsequent studies have demonstrated that the disorder is genetically heterogeneous: there exist cases in which the condition is present in a relatively "pure" form and others where there is a variety of other coexistent features. Holmes and Shaywitz reviewed the world literature and, employing strict diagnostic criteria, accepted 104 reported families with the "pure" form of the disease. Of these, inheritance was autosomal dominant in 70%. It is possible that early and late onset forms exist in both the autosomal dominant and recessive groups. X-linked inheritance is extremely rare. The present cases were all examples of the pure form of the
Spinal somatosensory evoked potentials in hereditary spastic paraplegia

245
disease, apart from cases 11 and 12 who displayed
disordered eye movements and Case 18 who
developed some distal amyotrophy in the limbs
later in the course of his illness.

A previous study by McLeod\(^7\) has documented
preservation of sensory nerve action potentials
and this was confirmed here for the upper limbs.
The new observation in the present study is that
despite preserved sensory nerve conduction, the
spinal somatosensory evoked responses in heredi-
tary spastic paraplegia may be undetectable and
that when they are obtainable, they tend to be of
reduced amplitude. The N13 somatosensory spinal
evoked potentials are usually considered to reflect
presynaptic and postsynaptic potentials arising in
the dorsal horn.\(^10\) A neuropathological basis for
this is suggested by the report by Behan and
Maia\(^4\) who recorded fibre degeneration in the
posterior columns in patients with the pure form
of hereditary spastic paraplegia but showed pres-
servation of the posterior spinal roots. Degenera-
tion in the posterior columns has also been noted
by Strümpell,\(^5\) Schwarz and Liu\(^2\) and Schwartz.\(^3\)
It is not yet established whether the intramedullary
portion of the fibres of the spinal roots that reach
the posterior horns, and which are likely to be
involved in the generation of the spinal somato-
sensory evoked responses, are also implicated in
the degenerative process.

These observations suggest that degeneration of
the centrally directed processes of the primary
sensory neurons may occur within the posterior
columns, but that the posterior roots outside the
cord and the peripherally directed axons in the
peripheral nerves remain intact.

The concept of a selective distal degeneration
of axons had its origins in the neuropathological
studies of Mott\(^13\) at the end of the last century on
Friedreich's ataxia and other disorders and by
Greenfield\(^12\) in his monograph on the spinocer-
bellar degenerations. Cavanagh\(^13\) formulated the
notion of a "dying back" of axons towards the
cell body more precisely. Subsequently Spencer
and Schaumburg\(^15\) pointed out that the changes
represented a multifocal distal but preterminal
degeneration of axons that often simultaneously
involved the peripheral and central nervous
system. In particular, both the centrally and
peripherally directed axons from the primary
sensory neurons were affected, so that the term
centralperipheral distal axonopathy was intro-
duced.\(^15\) In subacute myelo-optic neuropathy re-
lated to cloquinol intoxication, it is known that
degeneration occurs in the rostral portions of the
posterior columns and the caudal portion of the
corticospinal pathways in the spinal cord,\(^15\) suggest-
ing a "dying-back" process. Despite the fact that
patients have symptoms suggestive of a peripheral
neuropathy, the evidence for the occurrence of
degeneration in the peripheral nerves is slender.
The suggestion was therefore made (Thomas, un-
published) that there was a selective distal
axonopathy affecting only the central processes
of the primary sensory neurons, together with
other CNS pathways such as the corticospinal
tracts and the visual pathways. This was later
shown to be the case for experimental cloquinol
neurotoxicity in the dog.\(^17\) It seems likely that
hereditary spastic paraplegia provides a further
instance of this type of effect.

The reason for the distal situation of the lesion
in the "dying-back" neuropathies is uncertain, but
in toxic and deficiency neuropathies Schoental
and Cavanagh\(^18\) proposed that cofactor inactiva-
tion in the axon may be responsible. From
observations on certain toxic neuropathies Spencer
et al\(^19\) suggested that glycolytic enzyme inactiva-
tion may be involved. Enzyme synthesis takes
place in the cell body and therefore replenishment
will be least effective distally. The structural
differences between the various instances of dying-
back neuropathy that have been described, and
their different behaviour in relation to super-
imposed experimental nerve injury,\(^20\) suggest that
the target system within the axons is likely to be
different in those conditions that are structurally
dissimilar. Isoniazid gives rise to a distal axon-
opathy that particularly affects the peripheral
nervous system. The explanation may be that this
substance crosses the blood-brain barrier rather
poorly.\(^18\) The mechanism for a selective CNS
distal axonopathy is at present obscure. If dis'al
axonopathies result from a depletion or inherited
deficiency of enzymes involved in the mainte-
ance of structural integrity, it is conceivable that
different enzyme systems are present in axons within
the central and peripheral nervous systems.

In contrast to hereditary spastic paraplegia,
Friedreich's ataxia gives rise to degeneration of
both the centrally and peripherally directed axons
of the larger dorsal root ganglion cells.\(^5\) The
peripheral sensory nerve action potentials are
therefore diminished or lost\(^22\) and spinal somato-
sensory evoked potentials are reduced in amplitude
or undetectable.\(^10\) Parietal somatosensory evoked
potentials in this condition are delayed.\(^10\) In sub-
acute combined degeneration of the cord from
vitamin B\(_{12}\) deficiency, there is some evidence,
derived from evoked potential recording, that the
centrally directed axons of the dorsal root ganglion
cells are affected earlier than the peripheral axons.  

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References


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