Reflex myoclonus in olivopontocerebellar atrophy

M E Rodriguez, J Artieda, J L Zubieta, J A Obeso

Abstract
The presence of reflex myoclonus in response to touching and pinpricking the wrist or stretching the fingers and to photic stimulation was assessed in 24 patients with a presumed diagnosis of olivopontocerebellar atrophy (OPCA) and in 30 age-matched control subjects. Reflex myoclonus to somesthetic stimulation was found in 23 patients and in none of the controls. Photic myoclonus was present in 12 patients and in none of the controls. Electrophysiological study of the reflex myoclonus showed enhanced (> 10 μV) somatosensory evoked potentials and an associated reflex electromyographic discharge (C-wave) in 15 patients. These findings indicate that reflex myoclonus is common in OPCA and probably of cortical origin.

Methods
SUBJECTS
The study groups were made up of 24 patients (18 women and six men) with a clinical diagnosis of OPCA and a mean (SD) age of 62 (7) years and 30 age-matched (mean (SD) age 59 (10) years) normal volunteers (usually the patient’s spouse). A positive family history was present in two patients. All other patients were sporadic cases. The diagnosis of OPCA was established by the presence of a typical clinical picture (table 1); absence by history and laboratory tests of other causes of a cerebellar syndrome (trauma, anoxia, hypothyroidism; vitamin E deficiency; GM-2 gangliosidoses; adrenoleukodystrophy, etc); as well as a normal muscle biopsy in eight patients; and particularly by the presence on the CT brain scan of a pronounced and selective atrophy of the brainstem and cerebellum (fig 1). It must be taken into consideration that OPCA is actually a pathological diagnosis. In this sense, it would be most appropriate to consider our patients under the more general diagnostic category of multiple system atrophy, which comprises progressive autonomic failure (Shy-Drager syndrome), nigrostriatal degeneration, and OPCA. We prefer to continue using OPCA to refer to our patient population because all of them had clearcut signs of cerebellopontine damage at the time of study; this is not necessarily the case in patients with nigrostriatal degeneration and Shy-Drager’s disease.

CLINICAL ASSESSMENT
Two of us (MER, JAO) carried out a full neurological examination of all the patients. The presence of reflex myoclonus was investigated in the hands by stimulating with a light touch and by pin-pricking the palmar surface of the wrist and the metacarpal region of the index finger with a sharpened clip (not a thin needle such as the ones commonly used for parenteral drug administration). The effect of muscle stretching was studied by tapping the
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Figure 1  CT brain scans of a 62-year-old patient showing the typical brainstem and cerebellar atrophy (A,B,C) of OPCA but no supratentorial involvement (D).

CT BRAIN SCAN

The diagnosis of OPCA was mainly based on the findings by CT of the typical neuroradiological signs of cerebellar and brainstem atrophy. Atrophy of vermian structures was diagnosed when two or more sulci were clearly visible and by measuring the maximum width and surface of the superior cerebellar cistern. Atrophy of the cerebellar cortex was diagnosed when hemispheric sulci were seen. The median width of the sulci was also estimated. Measurements were made of the maximum width and surface area of the fourth ventricle. The relative size of the brainstem was determined. The cerebellar sulci were measured according to the method of Evans. The cerebellar sulci were studied in a series of patients with OPCA and control subjects. In the OPCA patients, the sulci were compared with the mean values of the control subjects.

Table 2  CT brain scan measurements in patients with OPCA and a control group

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Controls (n = 10)</th>
<th>Olivopontocerebellar atrophy (n = 24)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cerebellar sulci:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No in vermis (range)</td>
<td>0-2</td>
<td>2-6**</td>
</tr>
<tr>
<td>No in hemispheres (range)</td>
<td>0-2</td>
<td>2-10**</td>
</tr>
<tr>
<td>Width of vermis (mm)</td>
<td>1-7 (0-4)</td>
<td>2-8 (0-9)**</td>
</tr>
<tr>
<td>Width of hemispheres (mm)</td>
<td>2-5 (0-8)</td>
<td>3-7 (1)*</td>
</tr>
<tr>
<td>Superior cerebellar cistern:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diameter (mm)</td>
<td>14-5 (2-3)</td>
<td>20-4 (6)**</td>
</tr>
<tr>
<td>Surface area (mm²)</td>
<td>85-5 (31-5)</td>
<td>196-7 (78-6)**</td>
</tr>
<tr>
<td>Cerebellopontine angle cistern:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diameter (mm)</td>
<td>5 (1-3)</td>
<td>7-6 (1-5)**</td>
</tr>
<tr>
<td>Brainstem ratio</td>
<td>0-18 (0-05)</td>
<td>0-31 (0-05)**</td>
</tr>
<tr>
<td>Fourth ventricle:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Transverse diameter (mm)</td>
<td>10-9 (1-9)</td>
<td>12-1 (3-4)</td>
</tr>
<tr>
<td>Surface area (mm²)</td>
<td>73 (29-3)</td>
<td>104-3 (54-4)*</td>
</tr>
<tr>
<td>Evans' index</td>
<td>0-28 (0-03)</td>
<td>0-28 (0-04)</td>
</tr>
</tbody>
</table>

*P < 0.05; **P < 0.01.

Unless stated otherwise values are mean (SD).

wrist and fingers with a tendon hammer. The presence of reflex myoclonus was considered as definite when a visible muscle jerk was consecutively present after five identical stimuli in the same area of the hand.

ELECTROPHYSIOLOGICAL ASSESSMENT

The methods used have been described in detail. Reflex myoclonus was elicited by threshold electrical stimulation (0.1 ms duration, frequency <0.5 Hz) of the median nerve in the wrist, and recorded by bipolar surface electrodes placed on the forearm flexor and extensor muscles, simultaneously with the somatosensory evoked potentials recorded from the scalp. Subjects were comfortably seated on a couch with the limb totally at rest. A five channel Mystro (Medelec) machine was used.
stem was expressed as the width of the pre-
pointine cistern divided by the distance
between the posterior clinoid and the fourth
ventricle. The cerebellopontine angle cistern
was measured at its maximal width. The
presence of cortical atrophy was assessed by
the Evans’ index. All measures were esti-
mated directly from the films and converted
to actual values by means of the CT scale.
Table 2 summarises the CT findings. Severe
atrophy of the cerebellum and brainstem with
sparing of supratentorial structures (fig 1)
was present in the OPCA group but not in the
control group.

STATISTICS
Differences in the neuroradiological and
electrophysiological findings between the
groups were analysed by one-way ANOVA. A
χ² test was used for analysis of the presence or
absence of reflex myoclonus.

Results
Somaesthetic stimulation of the hand caused
reflex myoclonus in 23 of the 24 patients and
in none of the controls (p < 0.001). The jerks
were focal and therefore restricted to the
forearm muscles on the stimulated side in 18
patients. In these 18 patients, reflex
myoclonus was produced in either hand. Five
patients showed a generalised jerk after local
stimulation. Pin pricking provoked reflex
myoclonus in the 23 patients. Touching the
wrist or palmar surface of the hand elicited
myoclonus in 17 patients (75%) and stretch-
ing the finger flexors was accompanied by
myoclonus in three patients (18-7%). In most
patients the reflex myoclonus consisted of
several repetitive jerks produced by a single
stimulus. Such discharges could be seen by
visual inspection or felt by the examiner while
holding the hand of the patient.

Electrical stimulation of the wrist was
accompanied by a reflex muscle discharge (c-
wave) recorded from the relaxed forearm
muscles in 16 patients (fig 2). The mean
(SD) latency of this response was 39-9
(6-5) ms (range 30–50). In none of the
control subjects was a similar response obtained
during relaxation. The somatosensory evoked
potentials were of normal latency in the
OPCA group (table 3) but the mean ampli-
itude of the N20/P25 and P25/N33 waves was
significantly increased (fig 2) with respect to
the controls (table 3). The N20/P25 and the
P25/N33 waves were greater than 10 µV in
15 and 12 patients respectively. All patients
with a C-wave had a “giant” somatosensory
evoked potential.

Discussion
We found a high incidence of focal reflex
myoclonus to somatic stimuli in patients
with multiple system atrophy of the OPCA
type. This response was brisk, usually
localised to the forearm flexor and extensor
muscles, did not adapt to slow repetitive
stimulation (<1 stimulus per second), and
very often one single stimulus triggered sev-
eral muscle jerks. All these characteristics are
typical and compatible with a myoclonic
response and allow the differentiation of this
form of myoclonus from cutaneous reflexes.12
EMG recording corroborated the phasic and
short lasting character of the myoclonic dis-
charge. Photically induced myoclonus is also
fairly frequent in OPCA.13 14 By contrast,
spontaneous and action myoclonus were only
present in 12-5% of the patients. This figure
coincides with previous estimations of
myoclonus in OPCA.13 The existence of
reflex myoclonus has to be actively deter-
mined by the examiner, as this sign is often
free of symptoms.

Our finding indicates that reflex myoclonus
is common in OPCA and clearly a pathologi-
cal finding. We did not find this response in
the age-matched normal population. Further-
more, in a prospective study15 16 we found
reflex myoclonus (either somatic or
photic) in a very small proportion of patients
with typical signs and evolution of
Parkinson’s disease. Chen et al have also
reported a pathological exaggeration of the
long latency cutaneous reflex (E2) in patients
with multiple system atrophy,16 but less often
in patients with Parkinson’s disease. These
findings suggest that reflex myoclonus and
EMG responses evoked by electrical stimula-
tion may be useful signs in the differential
diagnosis of Parkinsonism.15 16

Electrical stimulation of the median nerve
evoked an EMG response (c-wave) in 16 of
the 23 patients with OPCA in whom there
was a reflex response clinically. This seem-
ingly lesser power of the electrical stimulus to
evoke reflex myoclonus in the hands may be

<table>
<thead>
<tr>
<th>Table 3 Summary of somatosensory evoked potentials in patients with OPCA and normal subjects</th>
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<tbody>
<tr>
<td>Somatosensory evoked potentials</td>
</tr>
<tr>
<td>--------------------------------</td>
</tr>
<tr>
<td>Latency N20 (ms)</td>
</tr>
<tr>
<td>N20-P25 (µV)</td>
</tr>
<tr>
<td>P25-N33 (µV)</td>
</tr>
<tr>
<td>2.6 (1.7)</td>
</tr>
</tbody>
</table>

**p < 0.01.
more apparent than real. It is possible that different stimulus characteristics, such as longer pulse duration and higher stimulation frequency, could increase the number of patients with a C-reflex. The latency of the C-reflex was around 40 ms in our patients. These data and the increased amplitude of the somatosensory evoked potentials in 15 patients strongly suggest a cortical origin\(^4\) for the focal reflex myoclonus detected in patients with OPCA. A detailed physiological study of the photomyoclonic response carried out in five of these patients also demonstrated a cortical origin for the visually evoked myoclonus.\(^4\) In cortical reflex myoclonus after electrical stimulation of a peripheral nerve the abnormal discharge arises in the sensorimotor cortex\(^9,17\) and in photic reflex myoclonus the paroxysmal discharge probably originates in the premotor areas.\(^14\)\(^,\)\(^18\) The finding of two types of cortical reflex myoclonus in patients with OPCA may suggest a generalised disorder of cortical excitability. The histological appearance of the cortex seemed totally normal in two of our patients\(^7\) as has been the case in other examples of cortical myoclonus.\(^19\)\(^-\)\(^21\) The pathophysiological basis of cortical myoclonus is not well understood. The cerebellum is the single CNS structure most often associated with myoclonus.\(^4\) It is tempting to suggest that cerebellar dysfunction could increase the gain of transcortical pathways leading to the pathological emergence of cortical reflex myoclonus.\(^4\) There are, however, several problems in concluding that cerebellar pathology is the only basis of cortical reflex myoclonus. Firstly, the same type of jerk can be recognised clinically in patients with cortical-basal ganglionic degeneration,\(^16\) Parkinsonism, and dementia,\(^16\) and progressive supranuclear palsy (personal observations), in whom the predominant pathology is not in the cerebellum. Secondly, and probably most important, the pathology in multiple system atrophy with OPCA predominance is by no means restricted to the cerebellum. Thirdly, in patients with a “pure” cerebellar degeneration, myoclonus is not necessarily present,\(^4\) and not even focal reflex myoclonus may be seen.\(^13\)

In summary, reflex myoclonus is a common finding in patients with presumed OPCA. This phenomenon has not been clearly recognised previously because of its scarce clinical impact but should be added to the phenomenology of multiple system atrophy with OPCA predominance.\(^3\)

Ms Maria del Mar López, Isabel Sánchez, and Carol Elden edited the article for publication.

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