Journal of Neurology, Neurosurgery, and Psychiatry 1994;57:316–319

Reflex myoclonus in olivopontocerebellar atrophy

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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 somaesthetic 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.

(*J Neurol Neurosurg Psychiatry* 1994;57:316–319)

Myoclonus is a brief, shock-like muscle jerk arising in the CNS.[1] It can be classified according to its clinical presentation as spontaneous, action, or reflex.[2] Reflex is the term applied to muscle jerks produced by pin pricking, touching, or stretching a body part, or visual and auditory stimulation. Reflex myoclonus is usually focal or generalised.[2] The neuronal discharge responsible for reflex myoclonus most commonly lies in the sensorimotor cortex (cortical reflex myoclonus) or in the brainstem (reticular reflex myoclonus).[1 2]

Myclonus has rarely been reported in patients with olivopontocerebellar atrophy (OPCA).[3] In the few published instances, only severe action and spontaneous myoclonus were described.[4 5] We were impressed a few years ago by the unusually high frequency of cortical reflex myoclonus in patients with multiple system atrophy, particularly those with presumed OPCA.[6 7] We have therefore conducted a prospective study to assess the presence and clinical and electrophysiological features of reflex myoclonus in a large group of patients with OPCA and compared the findings with a control group.

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Received 11 March 1993 and in revised form 11 June 1993.
Accepted 21 June 1993

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)[3 8]; absence by history and laboratory tests of other causes of a cerebellar syndrome (trauma, anoxia, hypothyroidism; vitamin E deficiency; GM-2 gangliosidoses; adrenoleucodystrophy, etc)[8]; 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

Table 1 Clinical features in 24 patients with olivopontocerebellar atrophy

Feature	*No(%)*
Postural instability	24 (100)
Somaesthetic reflex myoclonus	23 (95)
Bradykinesia	22 (91·6)
Gait ataxia	16 (66·6)
Dysarthria	16 (66·6)
Dysmetria	15 (62·5)
Urinary incontinence	14 (58·3)
Photic reflex myoclonus	13 (54)
Rigidity	12 (50)
Dysphagia	10 (42·5)
Ocular square wave jerks	10 (42·5)
Focal dystonia	9 (37·5)
Hyperreflexia	8 (33·3)
Resting tremor	6 (25)
Spontaneous myoclonus	3 (12·5)
Action myoclonus	3 (12·5)
Orthostatic hypotension	3 (12·5)

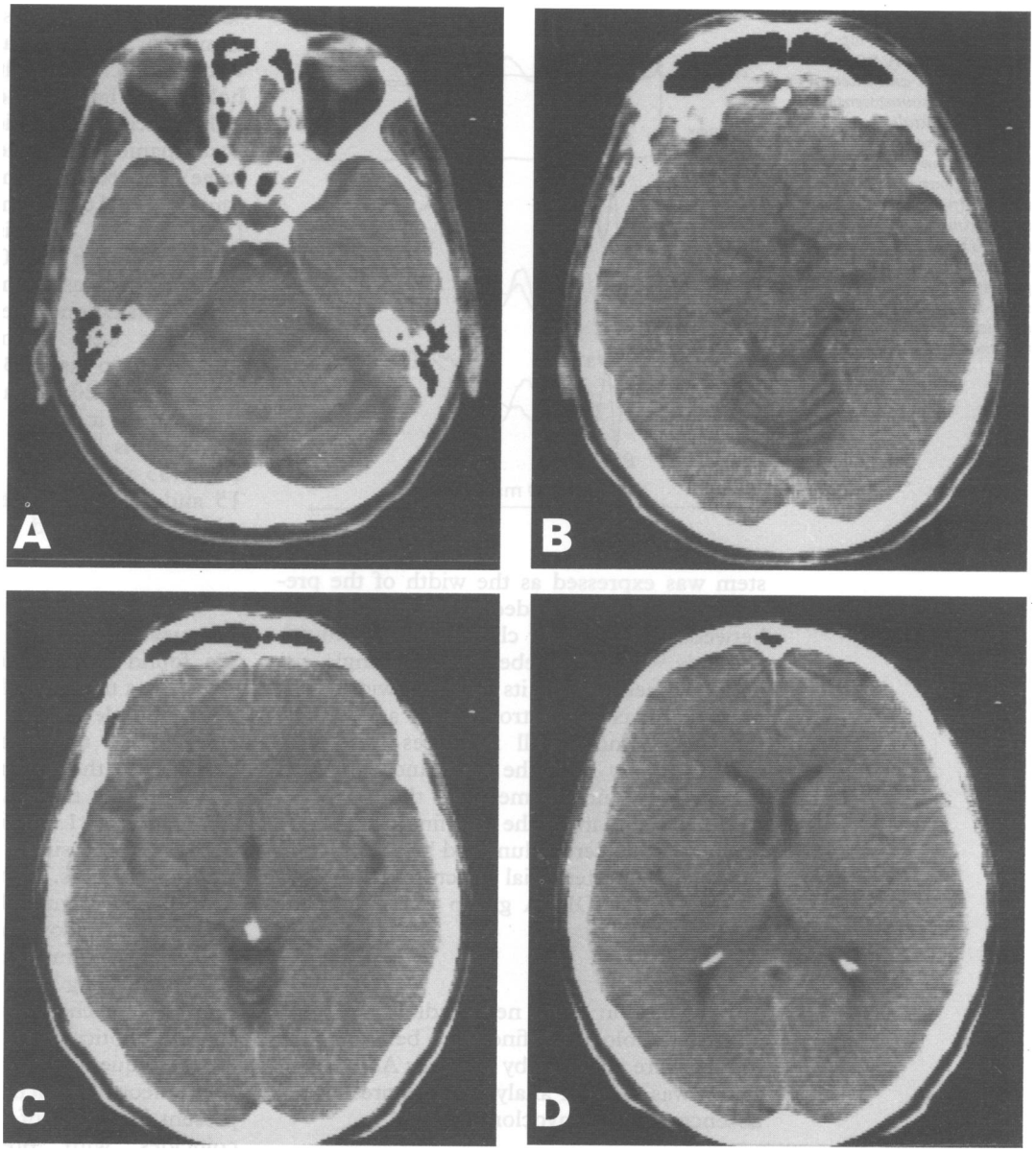

Figure 1 CT brain scans of a 62-year-old patient showing the typical brainstem and cerebellar atrophy (A,B,C) of OPCA but no supratentorial involvement (D).

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.[9] 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.

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

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

*p < 0·05; **p < 0·01.
Unless stated otherwise values are mean (SD).

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.[10] 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 brain-

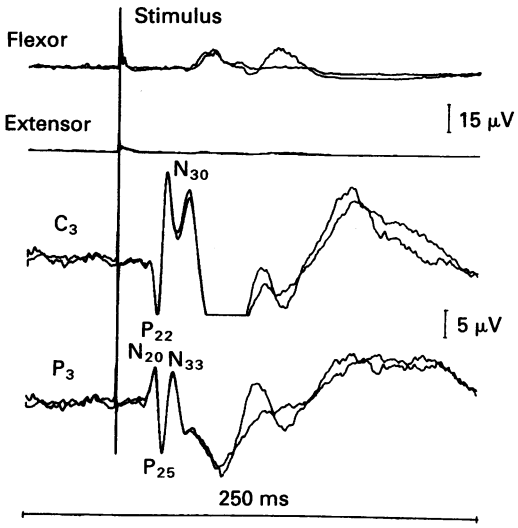

Figure 2 Electromyographic (top 2 channels) activity in forearm flexor and extensor muscles and somatosensory evoked potentials (2 bottom channels) recorded from rolandic (C_3) and parietal (P_3) regions after right median nerve stimulation in the wrist. The giant somatosensory evoked potential is accompanied some 18–20 ms later by a double myoclonic discharge in flexor muscles.

stem was expressed as the width of the prepontine cistern divided by the distance between the posterior clinoid and the fourth ventricle.[10 11] The cerebellopontine angle cistern was measured at its maximal width. The presence of cortical atrophy was assessed by the Evans' index. All measures were estimated directly from the films and converted into 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 χ^2 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 stretching 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 amplitude 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.

Table 3 Summary of somatosensory evoked potentials in patients with OPCA and normal subjects

	Controls (n = 30)		*OPCA (n = 24)*	
Somatosensory evoked potentials	*Mean (SD)*	*Range*	*Mean (SD)*	*Range*
Latency N20 (ms)	19·2 (1·1)	17·5–22	18·9 (1·3)	15·2–21·5
Amplitude N20–P25 (μV)	5·1 (1·9)	2·4–8·8	11·9 (5·9)**	3–25
Amplitude P25–N33 (μV)	2·8 (1·7)	1·0–8·2	10·3 (7·4)**	1·2–31·2

**$p < 0.01$.

Discussion

We found a high incidence of focal reflex myoclonus to somaesthetic 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 several 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 discharge. 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.[3 5] The existence of reflex myoclonus has to be actively determined by the examiner, as this sign is often free of symptoms.

Our finding indicates that reflex myoclonus is common in OPCA and clearly a pathological finding. We did not find this response in the age-matched normal population. Furthermore, in a prospective study[13 15] we found reflex myoclonus (either somaesthetic 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 stimulation 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 seemingly lesser power of the electrical stimulus to evoke reflex myoclonus in the hands may be

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[1 6] 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.[14] In cortical reflex myoclonus after electrical stimulation of a peripheral nerve the abnormal discharge arises in the sensorimotor cortex[6 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 6] It is tempting to suggest that cerebellar dysfunction could increase the gain of transcortical pathways leading to the pathological emergence of cortical reflex myoclonus.[6] 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,[8] 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 Elsden edited the article for publication.

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