Journal of Neurology, Neurosurgery, and Psychiatry 1989;**52**:656–658

Short report

Increased wave P 300 latency in progressive supranuclear palsy

C PIERROT-DESEILLIGNY, E TURELL, C PENET, D LEBRIGAND, B PILLON, F CHAIN, Y AGID

From the Clinique de Neurologie et de Neuropsychologie and Unité INSERM 289, Hôpital de la Salpêtrière, Paris (France)

SUMMARY The visually evoked P 300 wave and related reaction times (RTs) were studied in 25 patients with progressive supranuclear palsy (PSP). Both the P 300 wave latency and the RTs were significantly increased compared with 14 control subjects, and were correlated with an intellectual deterioration index calculated from neuropsychological scores. It is suggested that the study of wave P 300 may contribute to the diagnosis of cognitive disorders in PSP.

Wave P 300 is a long-latency, high amplitude positive component of "event-related potentials" (ERPs) occurring after a sequence of elementary cognitive processes.[1] It has already been shown that wave P 300 latency increased with age and in patients with dementia.[2-4] Cognitive disorders including frontal lobe like deficiency are always present in progressive supranuclear palsy (PSP) and may contribute to an early diagnosis of the disease.[5] Nevertheless, since these cognitive disorders may be difficult to detect because of the accompanying motor disturbances, possible anomalies in wave P 300 could facilitate this diagnosis. To test this hypothesis, a study of visually evoked P 300 wave, related reaction times (RTs) tasks and neuropsychological tests were carried out in 25 patients with PSP.

Patients and methods

Twenty-five patients with PSP were studied. The mean age was 68 years (range: 51–80) and mean duration of disease was 2·9 years (range: 1–6). The diagnosis of PSP was based on eight clinical criteria required for inclusion: (1) paralysis or significant slowness of vertical saccades (recorded with direct-current electro-oculography) always involving downward movement, with preservation of vertical oculocephalic movements; (2) extrapyramidal axial rigidity (with possible rigidity of the limbs), without tremor; (3) absence of, or poor response to levodopa treatment; (4) unsteady gait with falls; (5) dysarthria, occasionally associated with pseudobulbar palsy; (6) frontal lobe-like symptomatology; (7) gradual development of the disease; (8) normal CT scan, except for a slight or moderate diffuse atrophy.

Fourteen normal subjects were also studied as a control group (mean age: 66 years; range: 52–79). Their ages were not significantly different from those of patients.

To elicit wave P 300, the subjects were placed in a situation which both required their attention and prompted them to make a decision. They were instructed to respond to a particular type of visual stimulus, randomly interspersed with background visual stimuli which did not require a response, according to a previously described procedure.[6] The subjects faced a screen, in the centre of which an illuminated checkerboard, reversed every 600ms, formed the nontarget background stimulus. A laser beam fixed the subjects' attention to the centre. The target stimulus was the lighting of two groups of green diodes, each located laterally 20° off the centre. The left and right lightings (of 20 ms duration) were programmed to occur randomly both for the side stimulated and for the period between any two target stimuli in the set (2 to 5 s). The target stimuli had an intensity of 35 nits (lamberts), which was too weak to produce primary VEPs. This method was deliberately chosen to emphasise the task to be performed when confronted with visual stimuli that were difficult to detect.

A chloride silver-cup electrode was fixed with collodion to the midline site Pz and was referenced to similar electrodes on linked mastoids. Horizontal and vertical bipolar electro-oculograms were recorded during the task to ensure that ERPs would not be contaminated by eye movement artifacts. The recorded ERPs appeared on the visual display unit as averaged graphs. Only when the target stimulus gave rise to a motor response was a recording made. The record of the

Address for reprint requests: Dr C Pierrot-Deseilligny, Unité INSERM 289, Hôpital de la Salpêtrière, 47 bd de l'hôpital, 75651 Paris cédex 13, France.

Received 4 October 1988.
Accepted 28 November 1988

Table 1 *Wave P 300 latency and reaction times*

	Wave P 300 latency (mean, SD)	*Reaction times (mean, SD)*
Right		
Control	361, 38	363, 48
PSP	547, 128*	618, 182*†
Left		
Control	359, 41	359, 45
PSP	540, 127*	609, 174*†

* = Significant differences ($p < 0.001$) between the control group and the PSP group (analysis of variance). † = significant differences ($p < 0.01$) between wave P 300 latency and RTs (Student's paired t test).

evoked electrical activity was made during the 2 s following each of 60 left and 60 right stimulations. Monitoring allowed separation of left and right stimulations and discording of those trials were gaze movements crossed the threshold by more than 5° and those disturbed by EEG artifacts.

Reaction time was measured by the response interval from visual stimulus to the time the subject depresses a key with his thumb. Sixty stimulations were recorded on each side and appeared as histograms. An index of intellectual deterioration and of a global "frontal" score was also evaluated according to a previously described procedure.[7]

Results

Wave P 300 latency and RTs varied only slightly in the

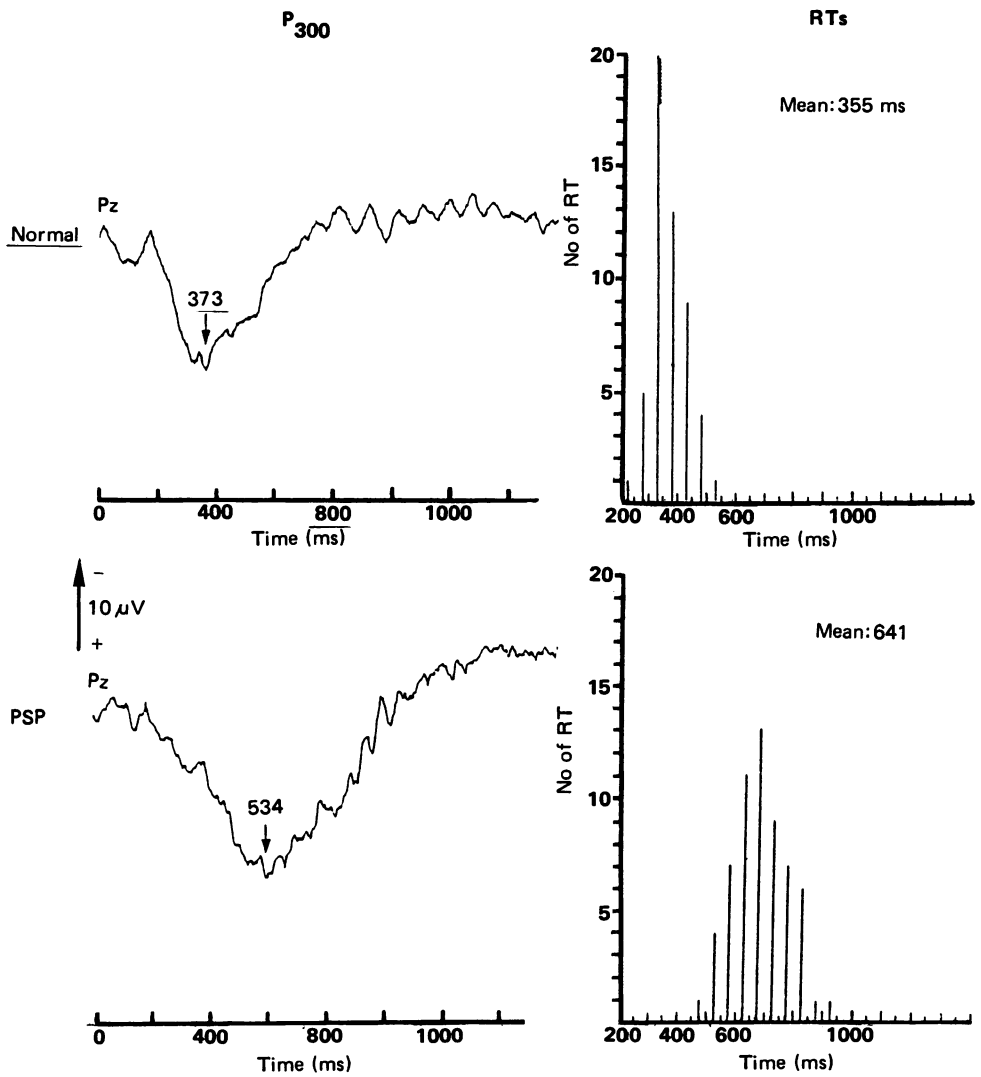

Fig 1 *Wave P 300 and histograms of reaction times (RTs) in one normal subject and in one patient with PSP (right stimulation only). Pz = parietal midline electrode.*

Table 2 *Relationships between wave P 300 latency, RTs and neuropsychological tests*

	Wave P 300 latency		*Reaction times*	
	Right	*Left*	*Right*	*Left*
Intellectual Deterioration Index	r = 0·562†	r = 0·567†	r = 0·678‡	r = 0·577†
Frontal Score	r = −0·274	r = −0·327	r = −0·373	r = −0·335

† and ‡ = significant correlations, with $p < 0.01$ and $p < 0.001$ respectively (Spearman rank correlation).

control group, as was reflected by relatively small standard deviations (table 1). Wave P 300 latency and RTs were significantly increased in the PSP group compared with the control group (analysis of variance) (table 1). The figure shows wave P 300 and histograms of related RTs in one normal subject and in one patient with PSP. In the control group, RTs were almost identical to wave P 300 latency. On the other hand, in the PSP group, RTs were significantly longer than wave P 300 latency (Student's paired *t* test) (table 1). The results of the P 300 wave and RTs did not differ significantly after right or left stimuli in either the control or the PSP group (Student's paired *t* test).

Significant correlations with the index of intellectual deterioration were observed for both the P 300 wave latency and the RTs (Spearman rank correlation) (table 2). No correlation was found between either parameter and the frontal score or the duration of the disease (results not shown).

Discussion

The latency of event-related potentials has been reported to increase in various dementing degenerative diseases such as Alzheimer's disease, Huntington's chorea and Parkinson's disease.[2-4 8 9] This study shows that such is also the case for PSP in which the increased latency appears to be even more marked than in other degenerative disorders. The anatomical damage in PSP is essentially subcortical,[10] but the increase in wave P 300 latency as well as the cognitive disorders could result from cortical deafferentation.[5]

Wave P 300 latency appears to be an interesting electrophysiological index of intellectual deterioration since a significant correlation was observed between these two factors. The absence of correlation between wave P 300 latency and the "frontal" score suggests that the frontal dysfunction, commonly found in PSP[5] and present in all our patients, was not the essential factor influencing the latency disturbance.

RTs were also found to be increased in patients. These times reflect both the duration of the decision process and that of execution mechanisms. Unlike the finding in normal subjects, RTs were significantly longer than wave P 300 latency. This suggests an impairment not only of the decision process but also of execution mechanisms.

Hence, the study of wave P 300 appears to be a promising electrophysiological method to test cognitive disorders of PSP.

The authors thank S Rivaud for technical assistance.

References

1 Donchin E, Ritter W, Cheyne-McCallum W. Cognitive Psychophysiology: the endogenous components of the ERP. In: Callaway E, Tueting P, Koslow SH, eds. *Events Related Potentials in Man*. New York: Academy Press, 1978:349–411.
2 Pfefferbaum A, Wenegrat BG, Ford JM, Roth WT, Kopell BS. Clinical application of the P3 component of event-related potentials. II. Dementia, depression and schizophrenia. *Electroencephalogr Clin Neurophysiol* 1984;**59**:104–24.
3 Syndulko K, Hansch EC, Cohen SN, *et al*. Long-latency event-related potentials in normal aging and dementia. *Adv Neurol* 1982;**32**:279–85.
4 Goodin DS, Aminoff MJ. Electrophysiological differences between subtypes of dementia. *Brain* 1986; **109**:1103–13.
5 Agid Y, Javoy-Agid F, Ruberg M, *et al*. Progressive supranuclear palsy: anatomoclinical and biochemical considerations. *Adv Neurol* 1986;**45**:191–206.
6 Lhermitte F, Turell E, Lebrigand D, Chain F. Unilateral visual neglect and wave P 300. A study of nine cases with unilateral lesions of the parietal lobes. *Arch Neurol* 1985;**42**:567–73.
7 Pillon B, Dubois B, Lhermitte F, Agid Y. Heterogeneity of cognitive impairment in progressive supranuclear palsy, Parkinson's disease and Alzheimer's disease. *Neurology* 1986;**36**:1179–85.
8 Hansch EC, Syndulko K, Cohen SN, Goldberg ZI, Potvin AR, Tourtellotte WW. Cognition in Parkinson's disease: an event-related perspective. *Ann Neurol* 1982;**11**:599–607.
9 Goodin DS, Aminoff JA. Electrophysiological differences between demented and non demented patients with Parkinson's disease. *Ann Neurol* 1987;**21**:90–4.
10 Steele JC, Richardson JC, Olszewski J. Progressive supranuclear palsy. *Arch Neurol* 1964;**10**:333–59.