Movement Disorders
Vol. 18, No. 11, 2003, pp. 1273–1279

Diagnostic Potential of Acoustic Startle Reflex, Acoustic Blink Reflex, and Electro-oculography in Progressive Supranuclear Palsy: A Prospective Study

Alexandre Gironell, MD,[1]* Jaime Kulisevsky, MD,[1] Carles Roig, MD,[1] Berta Pascual-Sedano, MD,[1] Antoni Rodríguez-Fornells, PhD,[2] and Pilar Otermin, MD[1]

[1]*Department of Neurology, Hospital de la Santa Creu i Sant Pau, Autonomous University of Barcelona, Catalonia, Spain*
[2]*Department of Neuropsychology, Otto-von-Guericke University, Magdeburg, Germany*

Abstract: We carried out a prospective study to analyze the diagnostic potential of acoustic startle reflex (ASR), acoustic blink reflex (ABR) and electro-oculography (EOG) in early stages of atypical parkinsonian syndrome. The study was carried out in a consecutive series of 41 patients clinically diagnosed as atypical parkinsonism (mean time from first symptoms of 38 months and follow-up of 26 months). The three procedures were carried out immediately after the first clinical evaluation. ASR and ABR were elicited by auditory stimuli while the patient was attending to a simple reaction time task. Outcome measures were: ASR (absence/presence, latency), ABR (absence/presence, latency) and EOG (suggestive/not suggestive of progressive supranuclear palsy [PSP]). Final clinical diagnosis was carried out by two neurologists blind to the neurophysiological results. A study of diagnostic sensitivity and odds ratio (OR) calculation for the PSP diagnosis was carried out. Neurophysiological examination showed the following sensitivity/specificity (%) for the diagnosis of PSP: ASR: 100/89; ABR 85/89; EOG 100/72. OR values were: ASR: 0.011; ABR: 0.037; EOG: 0.038. The three tests taken simultaneously showed a sensitivity of 100% and a specificity of 95%. The three neurophysiological tests investigated provided sensitive and specific measures with predictor value in early stages of atypical parkinsonian syndrome. © 2003 Movement Disorder Society

Key words: startle reflex; blink reflex; electro-oculography; progressive supranuclear palsy; parkinsonian syndromes; multiple system atrophy

Pre-mortem differential diagnosis of parkinsonian syndromes may be difficult, particularly in early disease stages, resulting in suboptimal diagnostic accuracy.[1,2] Early differentiation among parkinsonian disorders is important because prognosis, complications, and response to therapy vary according to the underlying pathology. Previous evidence from the literature suggests that some non-invasive neurophysiological investigations may add laboratory support to clinical differential diagnosis of patients presenting with a parkinsonian syndrome. Electro-oculographic (EOG) recording demonstrative of supranuclear gaze palsy represents neurophysiological evidence of a major diagnostic criterion for progressive supranuclear palsy (PSP). Although EOG has been suggested as useful in early diagnosis of the disease,[3,4] its sensitivity and specificity is not completely known. Few studies have reported on selective abnormalities of the auditory startle reaction (ASR), a brainstem reflex that originates in the nucleus reticularis pontis caudalis,[5–7] and abnormalities of the auditory blink reflex (ABR) in PSP.[8–10]

The aim of the present study was to investigate the diagnostic potential and the predictor value of the ASR, ABR, and the EOG when carried out in the early stages of atypical parkinsonian syndromes using a prospective design.

PATIENTS AND METHODS

The study included 41 consecutive outpatients (24 men, 17 women; mean age, 67.9 years; range, 57–77

*Correspondence to: Dr. A. Gironell, Department of Neurology, Hospital de la Santa Creu i Sant Pau, Av.S.A.M Claret, 167, 08025 Barcelona, Catalonia, Spain. E-mail: agironell@correu.vilaweb.com
Received 12 November 2002; Revised 5 February 2003, 16 April 2003; Accepted 9 May 2003

years; mean disease duration, 38.2 months; range, 6–45 months) attending for the first time the Movement Disorders Section of the Sant Pau Neurology Department, and suspected to suffer an atypical parkinsonism. Diagnosis of atypical parkinsonism was made if the patient presented a rigid-akinetic syndrome with unusual clinical findings such as poor response to levodopa, moderate or severe autonomic dysfunction, cerebellar disorder, supranuclear gaze palsy, dementia preceding or at the onset of parkinsonian symptoms, or alien arm. That is, the patients did not fulfill the diagnostic criteria for idiopathic Parkinson's disease (PD) according to the London Brain Bank.[1]

The study protocol was approved by the Hospital Ethics Committee and was carried out in accordance with international ethical regulations.[11] All subjects gave written informed consent to participate in the study, obtained after the nature of the procedure had been fully explained.

Electrophysiological study including ASR, ABR, and EOG was carried out between 1 to 4 weeks after clinical diagnosis of atypical parkinsonism. Patients were followed clinically for a mean of 26 ± 11 months. A final clinical diagnosis of the parkinsonian syndrome was then made by two neurologists blind to the neurophysiological results.

Patients were excluded from the study if severe hypoacusia (auditive threshold in one ear higher than 50 dB) was detected in a preliminary acoustic threshold study. None of the patients was taking alcohol, benzodiazepines, or dopaminergic drugs at the time of the neurophysiological study.

Acoustic Startle and Blink Responses

The experiment was conducted in a quiet laboratory with the patient seated 1 m in front of a computer screen at eye level, in a comfortable chair with arm- and backrests. The patient's arms were positioned on the padded armrest of the chair with a switch in the dominant hand. Surface silver-silver chloride electrodes were applied to the right orbicularis oculi, masseter, and sternomastoid muscles. Because the ABR response is not thought to be part of the true startle reflex,[2] we measured separately the ABR obtained at the orbicularis oculi and the startle reflex obtained at the masseter and sternomastoid muscles. For the orbicularis oculi, the two recording electrodes were placed 1 cm below and 1 cm medially from the external canthus. For the masseter, the recording electrode was placed over the midbelly of the muscle and the reference electrode was placed over the angle of the jaw. For the sternomastoid, the recording electrodes were placed 2 cm apart over the midbelly of the muscle. Electromyograph (EMG) activity was recorded in analog form using a electromyograph (Grass 8-plus EEG; Quincy, MA). The EMG signal was digitized with an A/D converter board and stored for off-line analysis using *Neuroscan 3.0* (Herndon, VA) software. Raw EMG from each muscle was rectified and sweeps were carried out after each stimulus. The 50-msec period before onset of the stimulus was used as the baseline value in each of these sweeps.

To obtain the ASR and ABR we used the start-react test method developed by Valls-Solé and colleagues.[12] This consists of delivering a startle stimulus when the subject's attention is focused on reacting to a visual "go" signal.[12] In healthy individuals, it has been found that the startle response elicited with this procedure shows larger EMG responses and less habituation, thus improving the performance of the startle reflex in the laboratory.[13,14]

Acoustic stimuli for ASR and ABR.

Acoustic startle stimuli consisted of 1-kHz square waves of 150 msec duration at 110 dB administered binaurally through air headphones. The choice of stimulus parameters was based on previous works.[14,15]

Reaction time paradigm.

A simple reaction time task without warning stimuli was executed. Each trial began with the presentation of a green square for 150 msec (vertical visual angle approximately 4°). Subject response was awaited until 1000 msec after the imperative stimulus onset. A fixed interstimulus interval of 4 seconds was used between trials. This fixed interval induced motor preparation as in the case of using warning stimuli.[16]

Subjects received two blocks of trials; each block consisting of 50 trials (40 non-startle trials and 10 startle trials). Startle trials were delivered randomly in each block with a 20% occurrence probability. Each block was followed by a short break. Subjects were tested after an initial practice period. Acoustic startle stimuli were presented unexpectedly at the same time as the imperative stimuli and for the same duration. Subjects were instructed to press the right button simultaneously upon presentation of the green square and to ignore the presence of auditory stimuli throughout the experiment. A fixation dot in the middle of the screen was visible throughout the experiment. Reaction time paradigm and acoustic startle stimuli were administered using *Neurostim* (Herndon) software. All ASR studies were carried out by the same examiner (A.G.). Reaction time and the start-react effect were not measured in this study because response speed was not emphasized.

Electro-oculographic Study

Eye movement recordings were carried out with an automated electronystagmography package (Nystar; Nicolet Audio Diagnostics, Madison, WI). With the patient seated and the head fixed, a visual stimulus appeared at visual height. The stimulus was an illuminated target 2.54 mm × 6.35 mm (Nicolet light bar visual stimulator), which appeared in an 80° curved field-shape screen that provides uniform viewing at 91 cm. Recording electrodes were placed in the outer canthus of both eyes and above and below the left eye. The ground electrode was placed on the forehead. Calibration response in the horizontal and vertical plane was evoked with 16° square wave stimulus around fixation point. Insufficient response (extremely hypometric saccades or slowness) did not permit calibration in some cases and consequently oculomotor data was not available.

Horizontal and vertical saccades.

In a random saccades test, patients were instructed to follow 28 target jumps of the visual stimuli (14 to the right, 14 to the left), which appeared randomly during 40 seconds with an amplitude range of 6–32° and a variable time interval. For fixed saccades, the patients were asked to follow 14 stimulus jumps (7 to the right and 7 to the left, alternating), which always appeared with a 20° amplitude and a fixed time interval of 2.5 seconds during 40 seconds. Peak velocity index (automated calculated ratio between obtained mean velocity and the expected normal mean velocity) in random and fixed vertical and horizontal saccades was considered.

Optokinetic nystagmus.

Patients were instructed to look at the midpoint of a row of lights and watch them moving across the screen. The fixed velocity of the row was 20 degrees per second in each direction for 20 seconds and with a target spacing of 10.24 degrees. The number of nystagmus evoked for horizontal and vertical stimulation was considered.

Square waves.

Presence of square waves was registered using a 40-second fixation of a (immobile) central point. Patients were instructed to fix their gaze on the stimulus. All EOG studies were carried out by the same examiner (C.R.).

Clinical Diagnostic Criteria

Clinical diagnosis of the parkinsonian syndromes after the follow-up period was carried out according to the following criteria: the London Brain Bank criteria for idiopathic PD[1]; criteria of Gilman and coworkers[17] for probable multiple system atrophy (MSA; MSA-P or MSA-C type); the National Institute of Neurological Disorders and Stroke and the Society for PSP diagnostic criteria for PSP[18]; and the research criteria for diagnosis of the clinical syndrome, usually accompanied by the pathology of cortical-basal ganglionic degeneration (CBD).[19]

The final clinical diagnosis was carried out separately by two neurologists experienced in movement disorders (J.K. and B.P.) who were blind to the neurophysiological test results. In cases of disagreement, a consensus was obtained after new analysis of the clinical data. A κ index was calculated for the first independent diagnosis.

Data Analysis

Acoustic startle and blink responses.

The presence of ASR in masseter or sternomastoid (or in both) muscles in the 20-trial average was examined. Absence of ASR in both the masseter and the sternomastoid muscles was considered if the amplitude (μV) of the EMG startle response recorded was inferior to 5 μV and was not evidenced in visual inspection of the average. Onset latency of the ASR was also examined. The time interval was measured between onset of acoustic stimulus and the onset (<2 SD difference from the baseline) of the averaged EMG response in the sternomastoid muscle. If there was no ASR in sternomastoid muscle, ASR latency of the masseter muscle was used.

Another variable of interest was the presence of ABR in the orbicularis occuli in the 20-trial average. Absence was considered if the amplitude (μV) of the EMG startle response recorded was inferior to 5 μV and was not evidenced in visual inspection of the average. Onset latency of the ABR was determined by measurement of the time interval between onset of acoustic stimulus and onset (<2 SD difference from the baseline) of the averaged EMG response.

Electro-oculographic study.

Results of the EOG study were reported as either suggestive (when the velocity of vertical saccades were <2 SD of normal velocities [<70% of velocity index]) or not suggestive of PSP. The diminution or absence of optokinetic response and the presence of square waves on fixation were considered additional data supporting a diagnosis of PSP.

Statistical analysis.

A study of diagnostic value for PSP (sensitivity, specificity, positive and negative predictive value, positive and negative probability ratio) was carried out for each neurophysiological test (ASR, ABR, and EOG). Sensi-

TABLE 1. *Clinical data in the present study*

Final diagnosis	Cases (n)	Gender	Age* (yr)	Time (mo)	
				Pre-tests*	Post-tests*
PD	6	4 M, 2 F	66.0 ± 6.6	21.4 ± 23.7	27.1 ± 18.6
PSP	14	9 M, 5 F	72.5 ± 5.3	46.5 ± 33.8	21.6 ± 14.8
MSA	12	7 M, 5 F	74.4 ± 3.3	42.1 ± 25.9	24.9 ± 22.5
CBD	6	4 M, 2 F	69.2 ± 3.3	25.2 ± 10.7	28.8 ± 10.7
VASC	3	2 M, 1 F	68.0 ± 1.4	40.5 ± 16.8	13.5 ± 14.8

*Values are means ± SD.

PD, Parkinson's disease; PSP, progressive supranuclear palsy; MSA, multi-system atrophy; CBD, cortico-basal degeneration; VASC, parkinsonism of vascular origin.

tivity and specificity of the three tests taken simultaneously was also calculated by a logistic regression analysis. In addition, we calculated the odds ratio (OR), applying Yates' correction for each test. Statistical comparative analysis of ASR and ABR onset latency between parkinsonian syndromes was carried out using a *t* test. An inter-rater agreement κ test for the final clinical diagnosis between the two neurologists was also carried out.

RESULTS

The final clinical diagnosis in the present series was: idiopathic PD (n = 6), PSP (n = 14), probable MSA-P (n = 9), probable MSA-C (n = 3), CBD (n = 6), and 3 patients diagnosed finally as vascular (multi-infarct) parkinsonism. A very high inter-rater agreement was obtained between the two neurologists for the final clinical diagnosis (κ index = 0.950). Clinical characteristics of the patients in this study are presented in Table 1.

ASR and ABR responses were obtained in all 41 patients. EOG recordings were carried out in 35 patients (in 4 patients, calibration was not possible due to extreme ocular slowness and in 2 patients, EOG was not carried out due to technical reasons). The results of the neurophysiological tests obtained are presented in Table 2, and examples of ASR, ABR, and EOG of the present series are presented in Figures 1 and 2.

The ASR was absent in all patients diagnosed as PSP (100%), in 1 patient diagnosed as MSA (8.3%), and in 2 patients diagnosed as (CBD) (33.3%). The diagnostic value of ASR absence for PSP diagnosis showed: sensitivity, 100%; specificity, 89%; positive predictive value, 82%, negative predictive value, 100%; positive probability ratio, 9.0; and negative probability ratio, 0.0 (OR = 0.011; 95% confidence interval [CI] = 0.001–0.105). Overall, this means that absence of ASR in an atypical parkinsonian patient increases 90-fold the probability for diagnosis of PSP.

The ABR was absent in 11 of 14 patients diagnosed as PSP (78.5%) and in 2 patients diagnosed as CBD (33.3%). The diagnostic value of ABR absence for PSP diagnosis showed: sensitivity, 85%; specificity, 89%; positive predictive value, 80%; negative predictive value, 92%; positive probability ratio, 7.8; and negative probability ratio, 0.1 (OR = 0.037; 95% CI = 0.07–0.190). Overall, this means that absence of ABR in an atypical parkinsonian patient increases 27-fold the probability of the diagnosis of PSP.

TABLE 2. *Neurophysiological data in the present study*

Final diagnosis	ASR absent	ASR Latency (msec)[a,b]	ABR absent	ABR latency (msec)[b]	EOG Sac.		EOG ON		EOG square waves
					Vertical*	Horizontal*	Vertical**	Horizontal**	
PD	0/6	65.8 ± 32.4	0/6	61.3 ± 35.6	0/6	0/6	1/6	0/6	0/6
PSP	14/14	58.4 ± 13.5	12/14	55.0 ± 3.6	10/10	7/10	9/10	6/10	7/10
MSA	1/12	56.3 ± 22.8	1/12	47.1 ± 11.6	2/7	0/7	4/7	1/7	3/7
CBD	2/6	53.3 ± 11.5	2/6	49.3 ± 8.1	2/6	2/6	1/6	0/6	2/6
VASC	0/3	66.0 ± 21.2	0/3	60.5 ± 19.0	0/3	1/3	1/3	1/3	0/3

*Decreased velocity.

**Diminution or absence.

[a]ASR latency is measured in the sternomastoid muscle.

[b]Values are means ± SD.

PD, Parkinson's disease; PSP, progressive supranuclear palsy; MSA, multi-system atrophy; CBD, cortico-basal degeneration; VASC, parkinsonism of vascular origin; ASR, acoustic startle reflex; ABR, acoustic blink reflex; EOG, electro-oculography; Sac, saccades; O.N, optokinetic nistagmus.

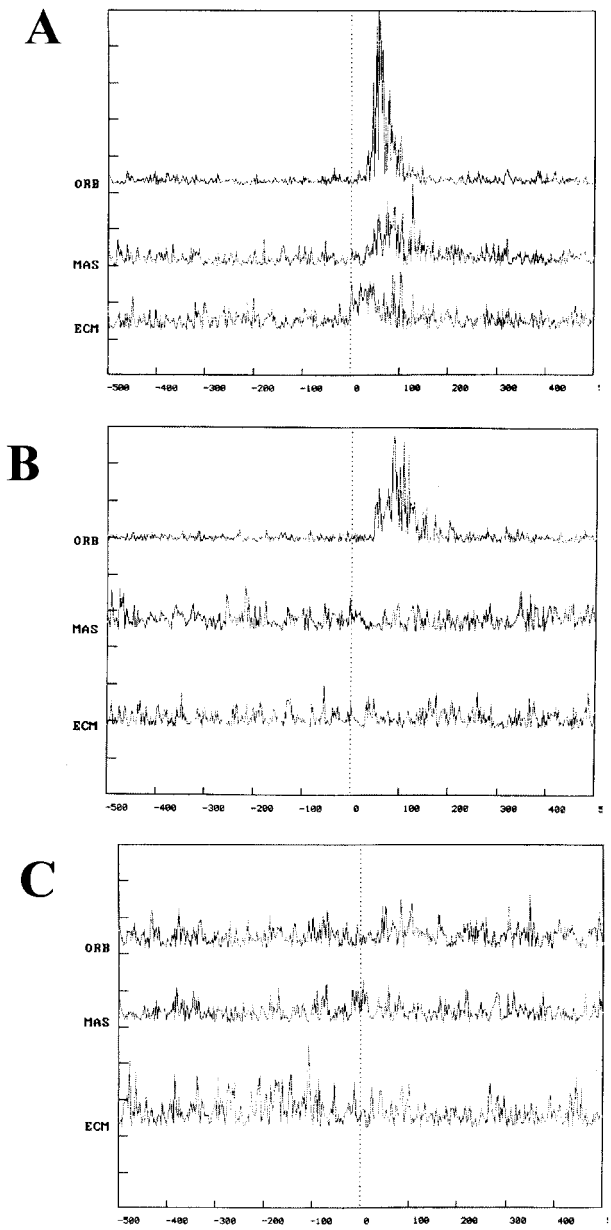

FIG. 1. Representative example of auditory startle and blink responses (rectified EMG average of 20 trials). **A:** Normal response. **B:** PSP patient. Note the presence of the blink response at the orbicularis oculi and the absence of muscular response in the masseter and the sternomastoid. **C:** PSP patient. Note the absence of muscular response in the muscles studied.

An EOG suggestive of PSP was observed in all patients diagnosed as PSP (100%). It was also found in 2 patients with CBD (35.5%) and in 2 patients with MSA (28.5%). EOG value for PSP diagnosis of showed: sensitivity, 100%; specificity, 72%; positive predictive value, 66%; negative predictive value, 100%; positive probability ratio, 3.5; and negative probability ratio, 0.0 (OR = 0.038; 95% CI = 0.004–0.373). This means that EOG suggestive of PSP in an atypical parkinsonian patient increases the probability of PSP diagnosis by 26-fold.

All three neurophysiological tests taken simultaneously showed sensitivity of 100% and specificity of 95%. No significant differences were evidenced in ASR and ABR latencies between the different clinical diagnosis of the parkinsonian syndromes (Table 1).

DISCUSSION

The main finding of our study is that the evaluated neurophysiological tests have a diagnostic usefulness in early stages of atypical parkinsonian syndromes. In particular, the absence of ASR has a great predictive value, increasing by 90-fold the probability for the diagnosis of PSP. The ABR was slightly less sensitive and the EOG recording slightly less specific. Combined use of the three tests facilitated diagnostic accuracy in earlier stages of atypical parkinsonian syndromes.

Besides the small number of patients included due to the exploratory nature of the study and the lack of pathological studies confirming the clinical diagnosis, two further limitations should be pointed out. The first is the intrinsic difficulty in clinical diagnosis of parkinsonian syndromes.[1,2] Nevertheless, the prospective design used increases the probability of a correct final clinical diagnosis due to the addition of new diagnostic clinical signs in the follow-up period in these progressive neurodegenerative diseases.[1,2,18] A second limitation refers to the comparison of ASR with other studies. ASR was elicited in our study while the patient was attending to a simple reaction time task, to avoid habituation phenomena.[12,13] This method differs from previous studies of Vidailhet and colleagues,[8] who obtained the ASR after three or four startle stimuli at random intervals of about 20 minutes. Kofler and associates[9] randomly applied varying interstimulus intervals between startle stimuli to avoid the habituation phenomena. Nevertheless, the method we applied has demonstrated in previous studies that startle and blink responses can be obtained easily, in less examination time, and can therefore be carried out routinely in any neurophysiological laboratory.[12–14]

In neurophysiological terms, results of the present study are consistent with abnormal function of the startle circuit in patients with PSP.[8–10] Few studies have addressed the probable diagnostic utility of ASR in parkinsonian disorders.[8,9] The first study of auditory startle response in atypical parkinsonism was carried out by Vidailhet and colleagues[8] in 1992, revealing that this brainstem reflex seems selectively poor and often absent in PSP patients, with the ASR in PD being similar to that

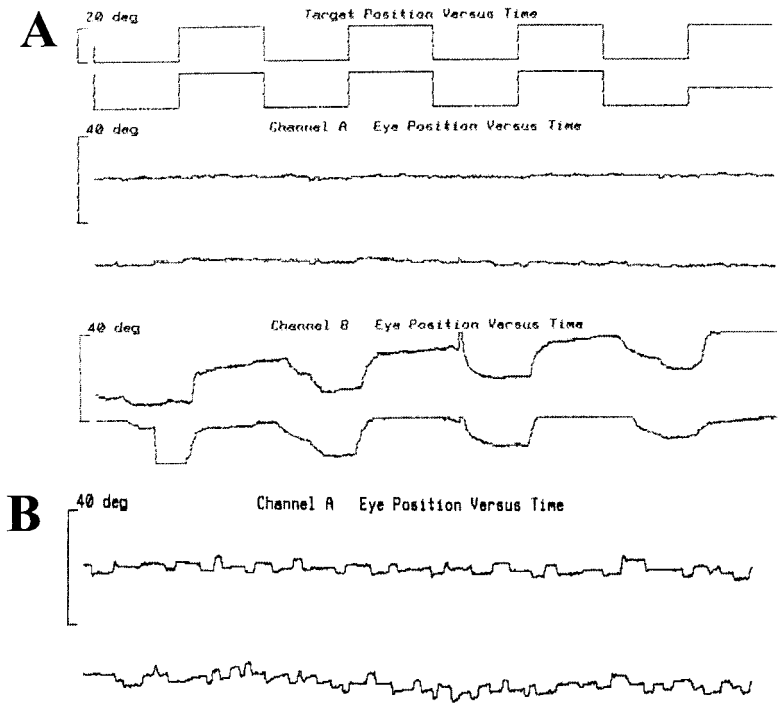

FIG. 2. Representative example of EOG recording in a PSP patient. Note the decreased vertical saccade velocity (**A**), and the presence of square-wave jerks (**B**).

in normal subjects. These authors related their results to the characteristic degeneration of the pontine reticular formation in PSP, mainly in the nucleus reticularis pontis caudalis, which is thought to be an important relay in the startle response.[8] Similar results were found in another recent study.[9] Moreover, it has been reported that ASR is normal in patients with MSA.[20] In our study, we found three false positive patients; two were diagnosed clinically as CBD and the third as MSA, without any diagnostic doubt, by the blinded neurologists. Our hypothesis is that although there is an early atrophy of the nucleus reticularis pontis caudalis in most PSP patients, this may be much less frequent in other parkinsonian syndromes.[21–23] The same reasoning may be applied to the ABR and EOG findings. In fact, atrophy of brainstem structures responsible for ABR and eye movements control may be found in several parkinsonian disorders, although not as selectively as in PSP patients.

In our study, the ASR and ABR were measured in the same paradigm. It is known that reflex EMG activity of ASR is first recorded in orbicularis oculi.[5,7] This is of similar latency to the normal ABR and, unlike the generalized startle response, it persists despite frequent presentation of the test stimulus. It has been argued that this early latency activity in orbicularis oculi represents an auditory blink reflex that is not part of the generalized auditory startle reflex.[5] For this reason, to reach the specificity of the ASR test, it is necessary to record the activity from the sternocleidomastoid or masseter muscles. In fact, the earliest recorded EMG activity in the "true" generalized startle response is seen in the sternocleidomastoid due to the caudal brainstem genesis of the reflex. Interestingly, we found 2 patients in whom ABR was present whereas ASR was absent. This finding was also described in the study by Kofler and associates.[9] Such observations support that the ABR and the ASR probably originate in different brainstem structures.

Electro-oculography recordings are helpful for the diagnosis of PSP. Vertical saccadic impairment and a decrease in horizontal saccade velocity are observed clinically in PSP patients and constitute a major criteria for the diagnosis.[3,18] Furthermore, in a recent study, consecutive EOG recordings helped to diagnose PSP earlier, and an EOG suggestive of PSP was observed throughout the disease course.[4] EOG characteristics of PSP were defined as an early decrease in saccade velocity and accuracy and the frequent presence of square-wave jerks.[4] In agreement, we found that the decrease of vertical saccade velocity in atypical parkinsonian syndrome is not only sensitive and specific but also has a predictor value for PSP diagnosis. Due to its low specificity, however, EOG should not be the only neurophysiological tests given to these patients. The combined use of the other two, ASR and ABR, may facilitate diagnostic accuracy.

In summary, to our knowledge, this is the first study that suggests a diagnostic and predictor value of noninvasive neurophysiological tests such as ASR, ABR, and EOG in atypical parkinsonian patients. Further studies with larger numbers of patients and pathological diagnoses are needed to extend our findings.

Acknowledgments: We thank I. Gich, MD, from the Epidemiology Department of Sant Pau Hospital for assistance with statistics.

REFERENCES

1. Hughes AJ, Daniel SE, Kilford L, Lees AJ. Accuracy of clinical diagnosis of idiopathic Parkinson's disease: a clinicopathological study of 100 cases. J Neurol Neurosurg Psychiatry 1992;55:181–184.
2. Hughes AJ, Daniel SE, Ben-Shlomo Y, Lees AJ. The accuracy of diagnosis of parkinsonian syndromes in a specialist movement disorder service. Brain 2002;125:861–870.
3. Santacruz P, Uttl B, Litvan I, Grafman J. Progressive supranuclear palsy: a survey of the disease course. Neurology 1998;50:1637–1647.
4. Rivaud-Péchoux S, Vidailhet M, Gallouedec G, Litvan I, Gaymard B, Pierrot-Deseilligny C. Longitudinal ocular motor study in corticobasal degeneration and progressive supranuclear palsy. Neurology 2000;54:1029–1032.
5. Brown P, Rothwell JC, Thompson PD, Britton TC, Day BL, Marsden CD. New observations on the normal auditory startle reflex in man. Brain 1991;114:1891–1902.
6. Davis M, Gendelman DS, Tischler MD, Gendelman PM. A primary acoustic startle circuit: lesion and stimulation studies. J Neurosci 1982;2:791–805.
7. Davis M. The mammalian startle response. In: Eaton RC, editor. Neural mechanisms of startle behavior. New York: Plenum Press; 1984. p 287–351.
8. Vidailhet M, Rothwell JC, Thompson PD, Lees AJ, Marsden CD. The auditory startle response in the Steele-Richarson-Olszewski syndrome and Parkinson's disease. Brain 1992;115:1181–1192.
9. Kofler M, Müller J, Wenning GK, et al. The auditory startle reaction in parkinsonian disorders. Mov Disord 2001;16:62–71.
10. Valldeoriola F, Valls-Solé J, Tolosa E, Nobbe FA, Muñoz JE, Martí J. Effects of a startling acoustic stimulus on reaction time in different parkinsonian syndromes. Neurology 1998;51:1315–1320.
11. World Medical Association Declaration of Helsinki. Recommendations guiding physicians in biomedical research involving human subjects. JAMA 1997;277:925–926.
12. Valls-Solé J, Solé A, Valldeoriola F, Muñoz E, Gonzalez LE, Tolosa ES. Reaction time and acoustic startle in normal human subjects. Neurosci Lett 1995;195:97–100.
13. Valls-Solé, Valldeoriola F, Tolosa E, Nobbe F. Habituation of the auditory startle reaction is reduced during preparation for execution of a motor task in normal human subjects. Brain Res 1997; 751:155–159.
14. Gironell A, Rodríguez-Fornells A, Kulisevsky J, Barbanoj M, Riba J, Pascual B. Abnormalities of the acoustic startle reflex and reaction time in gilles de la tourette syndrome. Clin Neurophysiol 2000;111:1366–1371.
15. Graham FK. Distinguishing among orienting, defense and startle reflexes. In: Kimmel HD, Van Olst EH, Orlebeke JF, editors. The orienting reflex in humans. Hillsdale, NJ: Erlbaum; 1979. p 137–167.
16. Klemmer ET. Time uncertainty in simple reaction time. J Exp Psychol 1956;51:179–184.
17. Gilman S, Low PA, Quinn N, et al. Consensus statement on the diagnosis of multiple system atrophy. J Neurol Sci 1999;163: 94–98
18. Litvan I, Agid Y, Calne D, et al. Clinical research criteria for the diagnosis of progressive supranuclear palsy (Steele-Richardson-Olszewski syndrome): report of the NINDS-SPSP international workshop. Neurology 1996;47:1–9.
19. Kumar R, Bergeron C, Pollanen MS, Lang AE. Cortical-basal ganglionic degeneration. In: Jankovic J, Tolosa E, editors. Parkinson's disease and movement disorders. London: Williams & Wilkins; 1998. p 297–316.
20. Valldeoriola F, Valls-Solé J, Tolosa E, Nobbe FA, Muñoz JE, Martí J. The acoustic startle response is normal in patients with multiple system atrophy. Mov Disord 1997;12:697–700.
21. Gibb WR, Luthert PJ, Marsden CD. Corticobasal degeneration. Brain 1989;112:1171–1192.
22. Daniel SE. The neuropathology and neurochemistry of multiple system atrophy. In: Bannister R, Mathias CJ, editors. Autonomic failure: a textbook of clinical disorders of the autonomic nervous system. Oxford: Oxford University Press; 1992. p 564–585.
23. Koeppen AH, Barron KD. The neuropathology of olivopontocerebellar atrophy. In: Duvoisin RC, Plaitakis A, editors. Olivopontocerebellar atrophies. New York: Raven Press; 1984. p 13–38.