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Electrophysiology of dementia

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Introduction

The recognition of moderate to severe dementia is not difficult for clinicians. It is in the earliest stages of dementia when the definition is most difficult. However, it is at this stage when the identification and therapeutic intervention can have the greatest benefit. The use of electrophysiological methods as objective measures of brain activity may provide a means for the early identification of impaired cognitive states. This paper reviews the use of conventional and quantitative electroencephalography (QEEG) and evoked potentials in dementia.

Conventional electroencephalography

Smith [1], in an excellent review of the age-related changes in electrophysiology, discusses the established criteria of EEG changes seen in dementia; for example, continuous θ and frontal intermittent rhythmic δ activity in toxic and metabolic encephalopathies, persistent δ foci in focal destructive processes, quasi-periodic sharp waves in Creutzfeldt–Jakob disease, and periodic triphasic waves in hepatic and renal encephalopathy.

Schlenska and Walter [2] examined the EEG changes in the early stages of Creutzfeldt–Jakob disease. The intermittent localized or lateralized δ activity that often precedes the typical periodic pattern comprises stereotyped waves of 500 ms duration with intermittent periodicity. A gradual alteration of the shape, duration, and periodicity of this waveform over a 3–9 week period results in the more characteristic pattern seen in the later stages.

The sensitivity of routine EEG is often insufficient to detect early cognitive changes in both degenerative dementias and encephalopathies. Weissenborn *et al.* [3] found normal EEGs in over 50% of patients with clinical signs of hepatic encephalopathy due to non-alcoholic cirrhosis. The authors did find that the P300 (see event-related potentials; ERPs) was significantly more sensitive than EEG.

Smith [1] also reviewed EEG studies, correlating diffuse slowing with intellectual deterioration in the elderly and

in patients with dementia of the Alzheimer type (DAT). Recently, Brenner *et al.* [4] found significant but mild generalized slowing in two groups of depressed patients, including 23 with no cognitive dysfunction and 10 with a non-progressive dementia. Generalized and focal EEG abnormalities were statistically more severe in the two groups of patients with probable DAT, including 23 patients with and 35 patients without depression. Focal abnormalities, mainly temporal slowing, were present in seven out of the 58 patients with probable DAT. The mean posterior α frequency was decreased in both demented groups, but was not significantly different between the demented and depressed patients. Approximately one third of the DAT group had normal EEGs. Similar changes in mean α frequency were described by Prinz and Vitiello [5] in 41 patients with possible or probable DAT, and in 22 patients with depression but no cognitive dysfunction. In this study, mean α frequency correlated with Mini-Mental Status scores, but not with age.

Ettlin *et al.* [6] prospectively used EEG, computerized tomography (CT), and clinical features as measured by the Hachinski score to differentiate autopsy-proven cases of DAT (15 subjects), multi-infarct dementia (MID; 11 subjects) and mixed dementia resulting from both DAT and MID (six subjects). All three methods were found to be equally accurate in diagnosing DAT, but clinical features were more sensitive than either CT or EEG in the diagnosis of MID. In mixed dementia cases, all three methods were equally poor. Combining the scores from all three techniques did not improve the accuracy of differentiating DAT from MID or mixed dementia, but did reach an 83% specificity when causes of dementia were included. The cases of DAT that were not diagnosed were missed because of misclassification into the mixed category, as focal findings suggested vascular lesions.

Devinsky *et al.* [7] compared EEG, CT, neuropsychological testing and 18-fluoro-deoxyglucose positron emission tomography in 28 patients with Down's syndrome. Four out of nine patients over the age of 40 years and six out of 19 patients under the age of 40 years had abnormal α rhythms. In the older Down's syndrome patients, this abnormality correlated with visuospatial and attention deficits, lateral and third ventricular enlargement, and

Abbreviations

CT—computerized tomography; DAT—dementia of the Alzheimer type; EEG—electroencephalography; ERP—event-related potential; HIV—human immunodeficiency virus; MID—multi-infarct dementia; QEEG—quantitative EEG.

diffusely decreased cerebral metabolism that was greatest in the parietal regions. These findings are largely consistent with those seen in DAT, and further suggest that the diffuse slowing seen with EEG reflects diffuse cerebral dysfunction. In the younger Down's syndrome patients, the abnormal α rhythm only correlated with increased metabolism in the calcarine and visual association cortices as well as with enlargement of the third ventricle, suggesting a different mechanism for EEG slowing in this age group.

Quantitative electroencephalography

The clinical application of QEEG with spectral analysis and topographic mapping is controversial. Fisch and Pedley [8] discuss the technical problems underlying this controversy; for example, errors in signal transformation, non-parametric analysis of stationary signals, the large numbers of variables analyzed retrospectively, and the intercorrelation of EEG features. Other factors cited include the variability in the environment and behavioral state as well as the lack of controlled, blinded experiments and corroborating studies. They recommend decreasing the number of variables analyzed and increasing the confidence interval and group size in order to minimize the statistical problems; however, they fall short of recommendations regarding the control of behavioral state during testing. Although Fisch and Pedley [8] disagree with the contention by John (*Science* 1988, 239:162–169) that QEEG provides objective validation of DSM-III diagnoses, they do cite work showing that QEEG abnormalities can be identified in patients who have normal conventional EEGs. Oken *et al.* [9] address some of the technical issues by examining the QEEG in patients with known cerebral lesions and abnormal EEGs. Using bipolar derivations and a natural log transformation, they found that absolute δ and θ , relative δ , θ , and α , and median frequency correlated best with conventional EEG. Z-scores (the number of standard deviations from the mean), when greater than three, resulted in no false-positives and identified 18 out of 20 patients as abnormal. When using Z-scores greater than two, 15 out of 69 'normals' were identified as abnormal, and only one patient was identified as normal. The criteria for 'normals' were not well characterized in this study.

Twenty-four patients with probable DAT were followed longitudinally for 1 year by Soininen *et al.* [10] who measured QEEG only from a T6–O2 derivation. Nine patients had normal QEEG at baseline. Half of these patients showed QEEG deterioration at 1 year, with all parameters changing except θ power. This group tended to be more severely demented and showed greater perseveration. At baseline, the unstable group showed more slowing in the θ range than the stable group; at 1 year, all parameters were significantly different between the groups. The stable group only differed from the controls in the θ power. The authors speculated that θ power may not appear to change in DAT, despite the overall slowing of EEG activity, because of the transitioning of power spectra from

α to θ to δ . The use of one bipolar electrode derivation severely limits the extrapolation of information obtained to the posterior regions of the head. This may explain why their results and sensitivities are nearly identical to the studies using conventional EEG.

We have recently reported focal left temporal QEEG abnormalities in patients with probable DAT. In our first study [11], eight right-handed patients, young controls and age-matched controls were examined with QEEG using a 32-electrode array with an averaged reference and square root transformation. On Z-score maps, we found significantly increased frontal and anterior temporal δ , with increased temporal asymmetry in the DAT group. However, age-matched controls also showed increased mid-parietal and left mid-temporal δ power in the absence of 'clinically significant' cognitive deficits (neuropsychological testing was not performed). We did not find any difference in α , θ , or β between the DAT and control groups, but we did find decreased α and β powers in the elderly controls. In our second study [12], we examined the QEEG in seven severely demented (Mini-Mental Status score < 8) and five moderately demented (Mini-Mental Status score = 16–25) patients with probable DAT. Age- and sex-matched controls scored between 25 and 30 on the Mini-Mental Status examination. δ and θ power was increased diffusely in the DAT groups, especially in left anterior temporal leads. There were significantly fewer leads showing abnormal δ power in the moderately demented group, with an average of four abnormal leads (T3, TT1, T5, FF), compared with 31 abnormal leads in the severely demented group. At least one anterior temporal lead was always abnormal for δ . The number of leads showing abnormal θ power was not significantly different between the patient groups. However, an average of nine leads were found to be abnormal for θ in the moderate group, and 24 leads were abnormal for θ in the severe group. Thus, the greatest effects were found in the left temporal areas, and abnormalities were more restricted to the left temporal region in the moderate cases. In fact, there was no overlap between the patients with probable DAT and the controls when using absolute δ power at T3. The Mini-Mental Status score correlated with δ power at all leads.

Ihl *et al.* (In *Topographic Brain Mapping of EEG and Evoked Potentials* edited by Maurer K. Springer-Verlag, 1989, pp 241–248) examined six patients with probable DAT and six age-matched controls with QEEG using linked mastoids as the reference. They found increased δ power in the DAT group, which was maximal at T3, P3, P4 and T6. θ power was maximally increased at Cz, and the mean α frequency was slower in the DAT group. Four hours after the administration of 600 mg pyritinol to DAT patients, the QEEG showed a significant decrease, compared with baseline, in δ and θ power, and an increase in α power; this was approaching the QEEG topographic pattern of the control group.

An 11-month longitudinal QEEG study of the incidence of dementia in 101 human immunodeficiency virus (HIV)-positive patients, with and without constitutional or neurological involvement, was performed by Parisi *et al.*

[13]. They found that 55% of neurologically asymptomatic individuals developed dementia if they had an abnormal QEEG. The earliest QEEG abnormalities usually included bilateral frontal θ of 6–7 Hz, with a normal background rhythm which preceded CT and neuropsychological changes. This progressed to frontal and temporal δ with generalized slowing in the range of 6–7 Hz and, finally, to generalized δ . Those asymptomatic subjects with a normal QEEG only had a 5% chance of developing neurological symptoms. These findings clearly warrant further investigation.

Sensory evoked potentials

Although most evoked potential research in dementia has focused on long-latency components, Buchwald *et al.* [14] recently demonstrated that middle latency components may also be useful in the diagnosis of dementia. They examined four males with biopsy-proven DAT, and two males with probable DAT. The P50 (or P1) amplitude significantly decreased in the DAT group at all stimulation rates; in some patients, they were virtually non-existent. The amplitude and latency of P30 (or Pa) were normal for both patient groups as well as for the control group. They postulate that this change in P50 in DAT reflects the loss of cholinergic input from the midbrain reticular formation to the intralaminar thalamic nuclei. They did not compare P50 amplitude with neuropsychological testing or EEG/QEEG.

Cognitive event-related potentials

The P300 component of the ERP may reflect the cognitive processes of stimulus recognition occurring in the hippocampus and amygdala (Smith and Halgren, *J Exp Psychol* 1989, 15:50–60). The P300 amplitude is known to increase with task relevance and the improbability of stimulus occurrence. Most investigators have found that the P300 latency increases by 1–2 ms/year when using a simple auditory target detection task. Age-related changes in the P300 amplitude remain controversial, largely because of its variability. A number of studies which were reviewed by Smith [1] demonstrated slowing and amplitude reduction of P300 in groups of demented patients. However, the variability of the P300 limits the clinical use of the ERP in diagnosing individual patients, at least when using non-specific cognitive tasks such as the target detection paradigm (Patterson *et al.*, *Electroencephalogr Clin Neurophysiol* 1988, 71:450–460). P300 variability may result from a number of factors: difficulty in peak selection; differences in experimental paradigms; differences in disease severity and subtypes of disease; or the inclusion of 'normal subjects' with subclinical cognitive dysfunction. The following studies use a target detection task and illustrate many of these problems.

In a recent study, Polich *et al.* [15] attempted to correct for a number of these factors by using control subjects

matched for age, sex, education and occupational level. ERPs were recorded from 16 patients in the early stages of DAT. Once again, significant differences were seen between the groups, but the overlap between the groups prevented the differentiation of individual subjects. Eighteen patients with possible or probable DAT (Mini-Mental Status score = 22–27) and 15 controls (Mini-Mental Status score = 28–30) were followed longitudinally by Ball *et al.* [16]. The rate of change in P300 latency was found to be significantly greater in the DAT group (23 ms/year) when compared with controls (3 ms/year). There was no significant difference in the rate of change between the questionable and mild DAT subgroups.

P300 abnormalities in myotonic dystrophy have been demonstrated. In Italy, Perini *et al.* [17] used ERPs to examine 27 patients with electromyographic and biopsy evidence of myotonic dystrophy. Fifteen of these patients had Wechsler Adult Intelligence Scale (WAIS) full-scale IQ scores of 71–84; six patients had scores less than 70. No P300 component could be identified in 13 patients, and the remaining 14 patients all had significantly lower P300 amplitudes when compared with 'sociodemographic-matched' controls. No difference in the P300 latency was observed. Patients with an absent P300 had significantly lower scores on the Mini-Mental Status examination; they also had low scores in digit symbol, arithmetic, information and digit span tests. In Japan, Hanafusa *et al.* [18] studied eight patients with myotonic dystrophy which had been diagnosed by electromyography and slit-lamp examination. The authors found prolonged P300 latencies in five patients at both Pz and Cz. P300 amplitude was only decreased at Pz in two patients.

Previous findings of P300 abnormalities in Parkinson's disease were confirmed by Gil *et al.* [19]. They studied 50 patients, comparing cognitive testing with ERP. Latencies of P160 (or P2), N240 (or N2), and P300 were prolonged in patients with Parkinson's disease. The N240 and P300 latencies correlated with age and cognitive test scores, such that demented Parkinson's patients had longer latencies than non-demented patients. There was no significant difference observed between the depressed and non-depressed patients. Starkstein *et al.* [20] also used ERPs and reaction times from seven non-demented Parkinson's disease patients during the 'on' and 'off' periods. Patients were also given a battery of neuropsychological tests, including the Wisconsin Card Sorting Test and the digit span test during the different periods. A significant decrement in P300 latency was observed during the 'on' periods, but reaction time and cognitive performance did not change. This suggests that dopaminergic contribution to the P300 involves mechanisms that are different to those involved in motor function and frontally-mediated cognitive tasks. These results contrast with the findings by Ito *et al.* [21], in which P300 latency in DAT correlated with the cerebrospinal fluid concentration of a serotonin metabolite, but not with a dopamine metabolite.

In hepatic encephalopathy due to non-alcoholic cirrhosis, the P300 was found to be much more sensitive than EEG and pattern reversal visual evoked potentials.

Weissenborn *et al.* [3] observed a prolongation of the P300 latency in 90% of patients with clinical signs of encephalopathy, and in 19% of those without encephalopathy. Both groups were significantly different from each other and from controls at the 1% level. P300 amplitudes were not significantly different between the groups.

Much of the P300 variability may result from the relatively non-specific nature of the target detection paradigm. These tasks should be designed to test specific cognitive deficits known to occur in a particular disease. An example of such a task is the Sternberg paradigm in which a memory set of increasing size allows the patient to be used as their own control. We have used this paradigm to study auditory short-term memory deficits in patients with conduction aphasia (Starr and Barrett, *Brain* 1987, 110:935-959). The mean amplitude of the patients' P450 component was less than half of that seen in controls, when using a one-item string in the auditory modality. When string length was increased from one to three items, the mean P450 latency of the patient group increased by 201 ms, compared with only a 64 ms increase in control subjects. ERPs using a memory task, such as the Sternberg paradigm, should allow electrophysiological measurement of relevant behavioral deficits in DAT.

Conclusion

As statistical techniques for QEEG have yet to be standardized, and the norms are not yet clearly established, it is prudent to follow the recommendations of the American EEG Society (*J Clin Neurophysiol* 1987, 4:75) and use QEEG as an extension of routine EEG in clinical applications. Unfortunately, we are now asking the same questions of QEEG that we ask of routine EEG, i.e. what changes occur in the distribution of various frequency bands in a particular disease? There are other questions that also need to be addressed. Evoked potentials analyze brain potentials in the millisecond range, underlying sensory, motor, or cognitive processes. Similar control of behavior during QEEG may enable preliminary analysis of longer-lasting cortical processes involved in learning, concept formation, and the planning and execution of behavioral responses. One example of this use of QEEG would involve recording between stimuli during ERP paradigms. Another example of such behavioral control would be the use of visual or verbal continuous performance tasks, such as those used in positron emission tomography, so that some measure of performance is available for the selection of QEEG epochs.

The concept that pathological processes cause abnormalities that were previously attributed to aging is gaining broad acceptance in many areas of science and medicine. This concept is particularly relevant as we attempt to understand the electrophysiological data that are accumulating with the newer computer-based systems. Smith [1] concludes by saying '... age-related changes in neurophysiological functions not attributable to pathological processes are probably minor.' Most of the recent studies

included in this review support such a concept. Thus, changes in the conventional EEG previously attributed to aging have now been found, in some instances using QEEG, to be markers of subclinical degenerative dementia or other encephalopathies; for example, asymmetrical temporal slowing may be an early marker of DAT, and background slowing can be correlated with cognitive dysfunction as opposed to age. The characterization of 'normal' is a critical issue.

Although the ERP does not appear to be a useful routine clinical test for the diagnosis of dementia, it does provide an extremely useful research tool. The ERP may be useful in following therapeutic effects and rate of disease progression in individual cases. The sensitivity and specificity of the ERP will probably improve as the specificity of the cognitive task increases.

Annotated references and recommended reading

- Of interest
 - Of outstanding interest
1. SMITH MC: Neurophysiology of aging. *Semin Neurol* 1989, ●● 9:68-81.
An excellent review of the reaction times, EEG, QEEG, evoked potentials, and ERPs in aging, with some discussion of the changes seen in dementia. 74 references.
 2. SCHLENSKA GK, WALTER GF: Temporal evolution of electroencephalographic abnormalities in Creutzfeldt-Jakob disease. *J Neurol* 1989, 236:456-460.
Periodic sharp waves may not appear early in the course of Creutzfeldt-Jakob disease. This paper demonstrates that these sharp waves evolve from long duration stereotyped waves, which comprise the intermittent localized δ activity seen during the first 3-9 weeks.
 3. WEISSENBORN K, SCHOLZ M, HINRICHS H, WILTFANG J, SCHMIDT ●● FW, KUNKEL H: Neurophysiological assessment of early hepatic encephalopathy. *Electroencephalogr Clin Neurophysiol* 1990, 75:289-295.
ERPs were found to be much more sensitive than EEG and visual evoked potentials in detecting hepatic encephalopathy due to non-alcoholic cirrhosis.
 4. BRENNER RP, REYNOLDS CF, ULRICH RF: EEG findings in depressive pseudodementia and dementia with secondary depression. *Electroencephalogr Clin Neurophysiol* 1989, 72:298-304.
Only 2 out of 10 patients with pseudodementia (depression with non-progressive cognitive dysfunction) showed mild generalized abnormalities, with significant slowing of the group mean posterior frequency. 15 out of 23 patients with probable DAT and depression had abnormal EEGs, with significantly more severe abnormalities, including focal temporal slowing and slower group mean posterior frequency.
 5. PRINZ PN, VITIELLO MV: Dominant occipital (alpha) rhythm frequency in early stage Alzheimer's disease and depression. *Electroencephalogr Clin Neurophysiol* 1989, 73:427-432.
The mean occipital frequency during wake on polysomnography was decreased in 22 depressed patients without cognitive dysfunction and, to a greater degree, in 41 patients with probable or possible DAT. Occipital frequency correlated with Mini-Mental Status scores, but not with age.
 6. ETTLIN TM, HANNES BS, KISCHKA U, ULRICH J, SCOLLO-LAVIZZARI ●● G, WIGGLI U, SEILER WO: Computed tomography, electroencephalography, and clinical features in the differential diagnosis of senile dementia. *Arch Neurol* 1989, 46:1217-1220.

EEG, CT and clinical features were compared in the diagnosis of autopsy-proven cases of DAT, MID, and mixed dementia. All 3 methods were equally sensitive in diagnosing DAT, but clinical features were more sensitive in MID. All 3 measures were ineffective in diagnosing the cases of mixed dementia.

7. DEVINSKY O, SATO S, CONWIT RA, SCHAPIRO MB: Relation of
 - EEG alpha background to cognitive function, brain atrophy, and cerebral metabolism in Down's syndrome. *Arch Neurol* 1990, 47:58-62.

These findings suggest that slowing of the α rhythm in older patients with Down's syndrome reflects diffuse cerebral dysfunction which is similar to that seen in DAT. α slowing in younger patients was associated with an increased metabolism in the visual cortex, suggesting a different mechanism than that seen in the older patients.

8. FISCH BJ, PEDLEY T: The role of quantitative topographic mapping or 'neurometrics' in the diagnosis of psychiatric and neurologic disorders: the cons. *Electroencephalogr Clin Neurophysiol* 1989, 73:5-9.

A brief review of the methodological problems of QEEG.

9. OKEN BS, CHIAPPA KH, SALINSKY M: Computerized EEG frequency analysis: sensitivity and specificity in patients with focal lesions. *Neurology* 1989, 39:1281-1287.

This study examines QEEG in patients with abnormal EEGs and focal lesions demonstrated on CT or magnetic resonance imaging. Parameters correlating best with EEG abnormalities were found to include absolute δ and θ power, relative δ , θ and α power, and mean frequency.

10. SOININEN H, PARTANEN J, LAULUMAA V, HEIKALA EL, LAAKSO M, REIKKINEN PJ: Longitudinal EEG spectral analysis in early stage of Alzheimer's disease. *Electroencephalogr Clin Neurophysiol* 1989, 72:290-297.

A 1-year longitudinal study of 24 patients with probable DAT which only uses one occipito-temporal derivation. The QEEG remained stable in 12 patients with less severe dementia and normal or mildly abnormal QEEG at baseline.

11. BRESLAU J, STARR A, SICOTTE N, HIGA J, BUCHSBAUM MS: Topographic EEG changes with normal aging and DAT. *Electroencephalogr Clin Neurophysiol* 1989, 72:281-289.

QEEG, using a 32-electrode array and averaged reference, revealed asymmetrical increases in anterior temporal δ power in 8 patients with probable DAT. Increased left parietal and temporal δ power of a lesser degree was also seen in age-matched controls, who had not been characterized neuropsychologically.

12. RICE DR, BUCHSBAUM MS, STARR A, AUSLANDER L, HAGMAN J, EVANS WJ: Abnormal slow activity in left temporal areas in senile dementia of the Alzheimer type. *J Gerontol: Med Sci* 1990, 45:145-151.

A QEEG study of 7 severely demented and 5 moderately demented right-handed patients with probable DAT suggested that increases in left temporal θ and δ power precede more diffuse changes. Using T3 absolute δ power, no age-matched controls scoring 25-30 on the Mini-Mental Status examination were identified as having DAT.

13. PARISI A, PERRI GD, STROSELLI M, NAPPI G, MINOLI L, RONDANELLI EG: Usefulness of computerized electroencephalography in diagnosing, staging, and monitoring AIDS-dementia complex. *AIDS* 1989, 3:209-213.

A 1-year longitudinal QEEG study of 101 HIV-positive patients in different stages of the disease. In neurologically asymptomatic individuals, 55% of those showing any QEEG abnormality developed dementia, as compared with 5% of those with normal QEEG.

14. BUCHWALD JS, ERWIN RJ, READ S, VAN LANCKER D, CUMMINGS JL: Midlatency auditory evoked responses: differential ab-

normality of P1 in Alzheimer's disease. *Electroencephalogr Clin Neurophysiol* 1989, 74:378-384.

The P50 (or P1) component of the auditory evoked potential was absent, or the amplitude reduced, in 4 biopsy-proven cases of DAT and 2 cases of probable DAT. This technique may provide an additional measure of decreased cholinergic activity in DAT.

15. POLUCH J, LADISH C, BLOOM FE: P300 assessment of early Alzheimer's disease. *Electroencephalogr Clin Neurophysiol* 1990, 77:179-189.

An ERP study of 16 patients with DAT in the 'early stages' and 16 controls matched for age, sex, education, and occupational level. Results show a prolonged P300 latency and reduced P300 amplitude in the DAT group, but overlap of distributions prevents the differentiation of individual subjects.

16. BALL SS, MARSH JT, SCHUBARTH G, BROWN WS, STRANDBURG R: Longitudinal P300 latency changes in Alzheimer's disease. *J Gerontol: Med Sci* 1989, 44:195-200.

18 patients with possible or probable DAT and 15 controls were followed for 20-40 months in a longitudinal target detection ERP study. The rate of change in the DAT group was 23 ms/year, and was significantly more than that in the control group. However, the rate of change could not be used to differentiate individual cases.

17. PERINI GI, COLOMBO G, ARMANI M, PELLEGRINI A, ERMANI M, MIOTTI M, ANGELINI C: Intellectual impairment and cognitive evoked potentials in myotonic dystrophy. *J Nerv Ment Dis* 1989, 177:750-754.

Decreased P300 amplitudes were observed in 27 patients with electromyographic and biopsy evidence of myotonic dystrophy. Patients in whom no P300 component could be identified tended to be more cognitively impaired. No differences were seen in P300 latency.

18. HANAFUSA H, MOTOMURA N, ASABA H, SAKAI T, KAWAMURA H: Event-related potentials (P300) in myotonic dystrophy. *Acta Neurol Scand* 1989, 80:111-113.

This study found prolonged P300 latencies in 5 out of 8 patients with electromyographic evidence of myotonic dystrophy, but decreased P300 amplitude in only 2 patients.

19. GIL R, NEAU JP, TOULLAT G, RIVASSEAU-JONVEAUX T, LEFEVRE JP: Maladie de Parkinson et potentiels évoqués cognitifs. *Rev Neurol (Paris)* 1989, 145:201-207.

An ERP and neuropsychological study of 50 patients with Parkinson's disease, demonstrating prolonged latencies of the P160, N240, and P300 components. Both N240 and P300 latencies correlated with cognitive test scores, but not with depression.

20. STARKSTEIN SE, ESTEGUY M, BERTHIER ML, GARCIA H, LEIGUARDA R: Evoked potentials, reaction time and cognitive performance in on and off phases of Parkinson's disease. *J Neurol Neurosurg Psychiatry* 1989, 52:338-340.

ERP, reaction time, and cognitive performance were measured in 7 non-demented patients with Parkinson's disease during the 'on' and 'off' periods. The P300 latency decreased during the 'on' periods, without associated changes in the reaction time and cognitive scores. This tends to support the theories regarding cholinergic contributions to the P300.

21. ITO J, YAMAO S, FUKUDA H, MIMORI Y, NAKAMURA S: The P300 event-related potentials in dementia of the Alzheimer type. Correlations between P300 and monoamine metabolites. *Electroencephalogr Clin Neurophysiol* 1990, 77:174-178.

Discusses ERP analysis in 40 patients with probable DAT. The P300 amplitude was found to correlate with cerebrospinal fluid levels of 5-hydroxyindoleacetic acid, but not with homovanillic acid. This suggests that serotonergic contributions to the P300 are more significant in DAT than are dopaminergic influences.