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Correlation between Cognitive Capacity Screening Examination and Cognitive Evoked Potential in Alcohol-Dependent Patients

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The aim of this study was to verify the significance of cognitive evoked potentials and the correlation between the auditory event-related potential and the Cognitive Capacity Screening Examination (CCSE) in alcohol dependent patients. The P300 studies using an auditory paradigm were performed on 25 alcohol dependent patients, and then the results were compared with score of the CCSE.

1) The latencies of the P300 were significantly prolonged in the patient group compared with the control group, and the scores of CCSE were significantly reduced in the patient group compared with the control group ($p<0.05$).
2) There were significant negative correlation between P300 latency and scores of the CCSE ($p<0.05$, r= -0.774).
3) There were no significant correlation between P300 latency and the total amount of ethanol ingestion ($p>0.05$).
4) There was significant reliability in P300 latency study (alpha=0.9771).

These findings suggest that the latency of P300 may be useful as a clinical electrodiagnostic measurement that can objectively reflect cognitive dysfunction in alcohol dependent patients, and it can be used as a quantitative analysis of cognitive dysfunction even for early asymptomatic alcohol dependent patients.

Key Words: Event related potential, alcohol dependence

INTRODUCTION

Cognitive function refers the function of cerebral cortex in which the subjects of thought or perception are thought, felt and remembered, and the function is decreased by various diseases inducing brain damage or aging. For the treatment of general encephalopathy, cognitive function is significantly correlated with the prognosis, it serves as an important factor for the prediction of functional recovery,[1,2] and it may play an important role in the prognosis of alcohol-dependent patients whose central nervous system (CNS) is damaged. This is why studies to develop a precise, convenient test for cognitive function are necessary and so many types of tests with different testing methodologies have been designed. For the assessments for cognitive disorder, the Event-Related Potential is recorded from the electrical actions occurring in cerebrum due to such stimulation as visual, hearing and somatic sensations, and it is considered useful for assessing the sensory & cognitive processes.[3] Cognitive evoked potential reflecting cognitive function is classified into intrinsic and extrinsic evoked potentials, but the former is not proper to reflect concentration because it is affected by external factors including the intensity and frequency of different kinds of stimuli; the latter is also called the Event-Related Potential or Cognitive Evoked Potential and it reflects the high-level cognitive processes because it is affected by intrinsic factors including the psychic state. This is due to its close association with the cognitive processes of the subject rather than with the physical characteristics of the stimulation.[4] Cognitive Evoked Potential forms waves such as N100, P200, N200, P300, and slow waves, based on the order of

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stimuli, and the P300 wave (300 msec on mean latency) is known to be associated with cognitive function. The latency of P300 reflects the time requiring for categorizing an event and deciding, while its amplitude reflects the association with the recall in the secondary memory.[5]

Cognitive Evoked Potential testing is not clinically common, but this test has recently been widely studied by researchers in the fields of psychiatry and neuroscience, and it can be clinically applied for depression,[6] dementia,[7] schizophrenia,[3,8] parkinsonism,[9] stroke,[10] closed head injury,[11-13] and for the degree of recovery from a comatous state.[14] However few studies have reported on applying the test to alcohol-dependency. In order to assess the cognitive function that may affect the prognosis of alcohol-dependency treatment, the authors in this study performed Cognitive Evoked Potential testing and the Cognitive Capacity Screening Examination (CCSE) to identify the correlation between the two and their clinical efficiency. We analyzed the results with the clinical indicators related with alcohol dependency to investigate whether Cognitive Evoked Potential testing with the neurobehavioral CCSE can serve as objective, quantitative tools for examining the cognitive function of alcohol-dependent patients to aid in the assessment and treatment of cognitive disorder caused by alcohol dependence.

MATERIALS AND METHODS

Subjects

The subjects of this study were 25 alcohol-dependent patients who had no medical history of dementia or auditory abnormality. Meanwhile, 25 persons whose past history did not include alcohol dependence and who were approximately the same age as the patients were selected as the control group. All the alcohol-dependent patients satisfied at least three of the following diagnostic criteria within the previous two months. 1) Tolerance; when the same amount of alcohol showed a considerably decreased effect or when the an increased amount was required for intoxication or to achieve the desired effect; 2) characteristic withdrawal symptoms; 3) when the patient drinks more than or longer than what he/she had intended to; 4) when a continuous desire for alcohol intake occurs or when the effort to control alcohol intake is not successful; 5) when the patient spends a lot of time for drinking or for doing something to avoid drinking; 6) when the social or vocational activities or the spare time of the patient is given up or reduced; and 7) when the patient knows he/she has permanent or repetitive problems socially, psychologically or physically, but they cannot stop drinking.

Methods

A Nicolet Viking IV (was used for recording the event related potential, and an oddball paradigm was selected to be the stimulus. The intensity of the stimulus was 70 dB, and the frequent stimuli were of a high frequency (2 KHz), while the rare stimuli were of a low frequency (1 KHz). The sensitivity was 20 uV/division and the sweep speed was 75 msec/division, and the recording was done with an averaging technique. The CCSE was a questionnaire that was given as a screening test for cognitive function.

Process

The subjects were placed in a supine position in a quiet room at room temperature, and the authors attached active electrode to the skin of the scalp, reference electrode to both mastoid processes and a ground electrode to the center of the chin. An oddball paradigm was selected to be the stimuli and it was presented 100 times, while the rare stimuli were presented as 20% (20 times) of the stimuli.

Cognitive evoked potential

The room for the test was quiet, dark and devoid of outside noise to avoid external stimulation, and the room was at room temperature. The subjects were placed in a supine position and allowed to relax without sleeping. The oddball paradigm was presented to the subjects without any previous information. The latency was measured at the peak of P300.

Statistical analysis

The Student t-test was used in order to identify the difference of P300 latency and CCSE between the control group and the patient group, while Pearson's correlation was used in the analysis for investigating the association between the CCSE, the neurologic symptoms and alcohol drinking of the subjects, and the P300. The reliability was obtained from four repeated tests for the P300 latency.

RESULTS

General & Medical Characteristics of Subjects

The mean age of the two groups was 41.68 ± 8.02 years for the patient group and 42.60 ± 8.92 years for the control group, and no significant difference was found between the two. The ratio of males and females was 24 : 1 for both groups. The years of education were 9.7 ± 3.4 years for the patient group and 10.1 ± 3.9 years for the control group, and no significant difference was observed between the two (Table 1). The mean drinking amount of the patient group was 931.91 ± 855.65 kgm, and 13 patients showed peripheral neuropathies such as limb numbness, six patients had depression and one had a history of suicide. Six cases of diabetes, four cases of hypertension, and ten cases of other diseases were observed as accompanying disorders (Table 2). The diagnostic evaluation of peripheral neuropathy included a history of symptom, and a motor and sensory conduction study. The decreased amplitude of nerve action potentials, the slowed conduction velocities and prolonged distal latencies were used as the diagnostic parameters of the nerve conduction study. A diagnostic evaluation of depression included a complete history of symptoms, i.e., when the depression started, how long it lasted and how severe the symptoms were. Last,

Table 1. General Characteristics of Subjects

		Group 1 (N=25)	Group 2 (N=25)	*p*-value
Age (years) (mean ± SD)		41.68 ± 8.02	42.60 ± 8.92	NS
Sex	male (%)	24 (96)	24 (96)	NS
	Female (%)	1 (4)	1 (4)	NS
Education (years) (mean ± SD)		9.7 ± 3.4	10.1 ± 3.9	NS

Group 1, patients group; Group 2, control group; NS, not significant.

Table 2. Medical Characteristics of the Subject in the Patient Group (N=25)

		Number (%)
Total ethanol intake (kg) (mean ± SD)		931.91 ± 855.65
Complication	Parethesia[1]	13 (52.0)
	Depression	6 (24.0)
	Hallucination	3 (12.0)
	Sucidality	1 (4.0)
Accompanied disorder	Diabetic mellitus	6 (24.0)
	Hypertension	4 (16.0)
	Others[2]	10 (40.0)

[1]Parethesia means peripheral neuropathy.
[2]Others are spinal stenosis (N=4), thyroid disease (N=1), prostate hypertrophy (N=2), and gastric ulcer (N=3).

diagnostic evaluation based on the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR) was done, by referral to a psychiatrist.

Comparison of cognitive evoked potential and CCSE

The latency of Cognitive Evoked Potential was 354.76 ± 27.92 msec for the patient group and 325.40 ± 14.92 msec for the control group, while the CCSE was 27.76 ± 1.85 and 29.24 ± 0.97 for the patient group and the control group, respectively. The latency of the patient group was significantly increased and CCSE were significantly decreased when compared to that of the control group ($p<0.05$, Fig. 1).

Correlation between cognitive evoked potential and CCSE in the patient group

The changes in the P300 latency for the CCSE were more decreased as the values of CCSE were increased, and the correlation coefficient between the CCSE and P300 latency was -0.774, which showed a significant inverse correlation ($p<0.05$, Fig. 2).

Correlation between alcohol amount and cognitive evoked potential

There was no significant correlation in the changes in latency for the alcohol amount ($p>0.05$).

Cognitive evoked potential and CCSE according to complications

The Cognitive Evoked Potential for the group having a medical history of complications was 371.69 ± 29.81 msec for the peripheral neuropathy patients, 366.33 ± 43.72 msec for the depressed

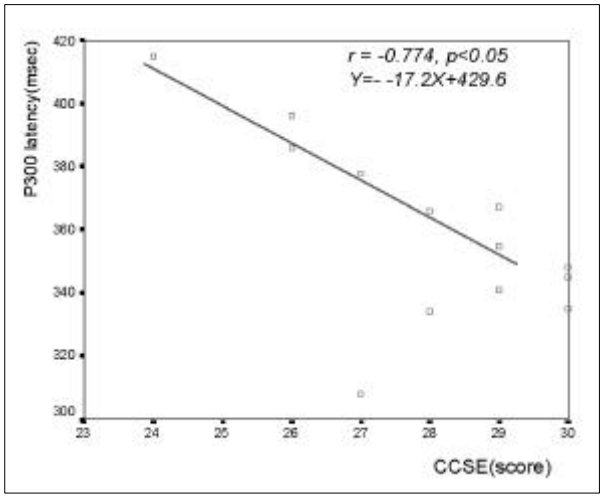

Fig. 2. Correlation between Cognitive Evoked Potential and the CCSE in the patient group. The changes in P300 latency for CCSE were more decreased as the values of CCSE were increased, and the correlation coefficient between the CCSE and P300 latency was -0.774, which showed significant inverse correlation.

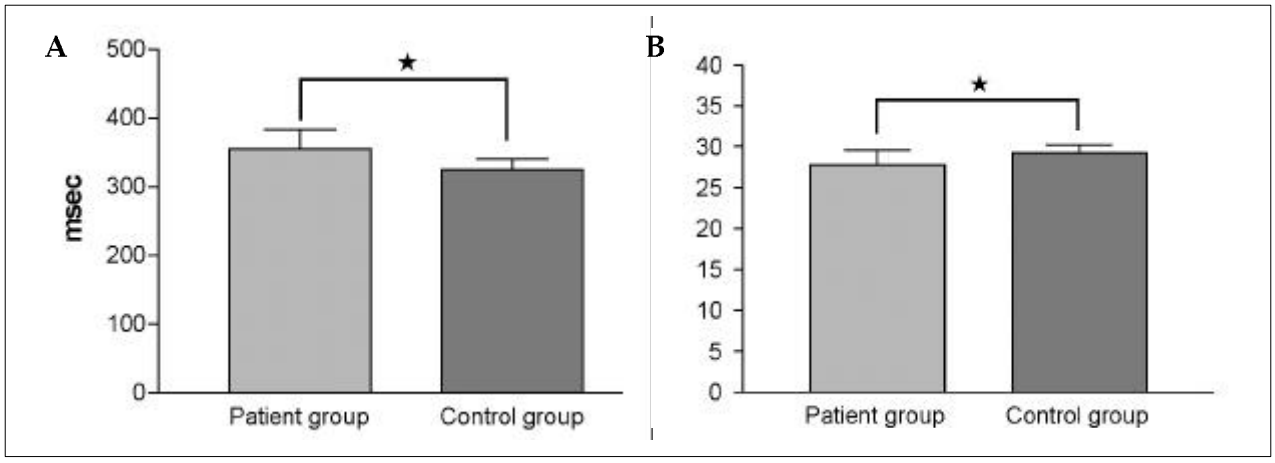

Fig. 1. Comparison of Cognitive Evoked Potential (A) and CCSE (B). The latency of the Cognitive Evoked Potential was 354.76 ± 27.92 msec (the patient group) and 325.40 ± 14.92 msec (the control group), while the CCSE was 27.76 ± 1.85 and 29.24 ± 0.97 for the patient group and control group, respectively. The latency of the patient group was significantly increased and CCSE was significantly decreased, when compared to that of the control group. *$p<0.05$.

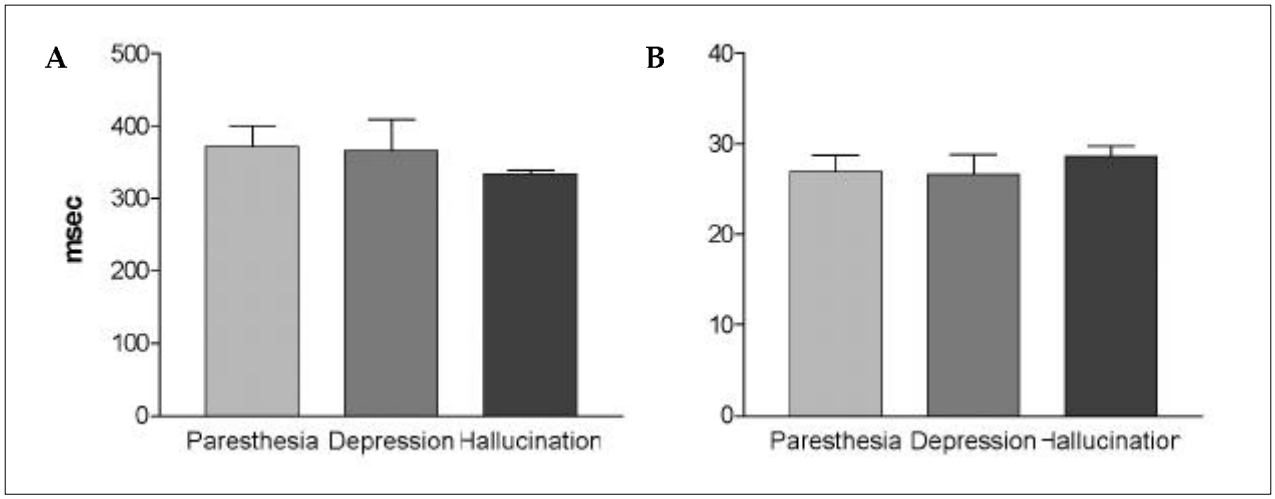

Fig. 3. Comparison of Cognitive Evoked Potential (A) and CCSE (B) according to complications. The Cognitive Evoked Potential for the group having medical history of complications was 371.69 ± 29.81 msec (peripheral neuropathy), 366.33 ± 43.72 msec (depression), and 334.33 ± 0.58 msec (hallucination), while the CCSE for the groups were 27.00 ± 1.83, 26.67 ± 2.25, and 28.67 ± 1.15 respectively, and there were no significant difference between the group having a medical history of complications in the P300 latency and CCSE. $^{*}p<0.05$.

patients, 334.33 ± 0.58 msec for the hallucinating patients, and 378.00 msec for the suicidal patients, while the CCSE for these group was 27.00 ± 1.83, 26.67 ± 2.25, 28.67 ± 1.15, and 27.00, respectively; there were no significant differences between the group with a medical history of complications for the P300 latency and CCSE ($p>0.05$, Fig. 3).

Reliability for P300 latency

In the four repeated tests for P300 latency, the alpha value showed high reliability (0.9771).

DISCUSSION

Since Goodin et al.[7] reported for the first time that the latency of the P300 wave could be used as a susceptible indicator for the changes in the cognitive function related with ageing, many researchers have supported Goodin's report. According to the literatures, the latency of P300 is generally increased by 1 - 2 msec per year for a normal person, and Polich[15] proved that there was linear relationship between the P300 latency and a person's age. However, many researchers agreed that the amplitude of the P300 is rarely affected by age. The reason for the increase in P300 latency according to age is usually considered to be the general decline of the neurotransmitters in the CNS and the delay in the transmission due to the changes in myelin degeneration.[16] Lee et al.[17] reported that the P300 latency of the patients with a decline in memory was significantly increased when compared to that of the control group, but no correlation was found between the memory test and P300 among the patient group. Therefore, they suggested that P300 was appropriate in the assessment for more wide-ranging disorders of cognitive function such as dementia than for localized functional disorders. According to Mun and Kim,[18] in a study in which 93 normal persons were selected as the subjects for the estimation of the regression line of P300 based on age, an increase of 1.2 msec per year was observed when the subjects were at least 19 years old. In the study with normal subjects whose mean age was 21.2, Polich[19] reported that the amplitude of the P300 was lower and its latency was longer when the subjects did a difficult work rather than an easy work, and the amplitude was higher and the latency was longer when the subjects did a work requiring counting numbers rather than when they did a work requiring the pushing of buttons. Although studies on the cognitive evoked potential of the patients with

encephalopathy are not common, Goodin et al.[20] in 1978 reported that the P300 latency of the patients with cerebral apoplexy was similar to that of normal people unless the patients were accompanied with dementia. Lee et al.[21] in 1986 reported on the cognitive evoked potential in psychiatry, Chae et al.[8] in 1990 reported that the P300 of patients with depression was delayed for a while, and Chung et al.[22] in 1996 reported that the latency of the cognitive evoked potential of patients with traumatic brain injury was significantly delayed when compared to that of the control group.

Cognition is best defined as the acquiring, storing, retrieving and using knowledge. Cognitive impairment has long been linked with the chronic abuse of alcohol, because alcoholics express many types and degrees of cognitive deficits.[3,5] A small amount of alcohol induces excitation in CNS, and in general, alcohol, as a nonspecific suppressor, exhibits a sensitive inhibitory action on the reticular formation, which has compound functions, and alcohol has an action on the cerebral cortex to induce excitation and disorders in thinking faculties such as memory, cognition, judgement, attention, information processing, response time, coordination and language. In addition, the continuous intake of alcohol induces Korsakoff's psychosis whose cardinal symptoms are amnesia, disorientation, confabulation, peripheral neuropathy and dementia associated with alcoholism. Therefore, alcohol drinking plays an important role in the prognosis of patients, and so these patients require early diagnosis and treatment. However, the existing tests such as Mini Mental State Examination (MMSE) that defines a deficit pattern, is a complex and inexact task, and the other existing tests for cognitive function such as the Loewenstein Occupational Therapy Cognitive Assessment (LOTCA) or the Motor free Visual Perception Test (MVPT) requires many hours to examine subjective information and the general cognitive function of the subject, and these tests also have a difficulty for quantification and continuous follow-up observation.[1,2] Other studies have reported on using the CCSE for alcohol depend patients as a method reflecting the general cognitive function, but the results were various based on the studies.[5] In this study, in which the CCSE as a common method for selectively examining the cognitive function of alcohol dependent patients and P300 latency were used, the P300 latency of the patients was significantly delayed when compared to that of the control group, and there was a difference on the CCSE between the two groups. Significant correlation was found between the CCSE and P300 latency. Such results indicate that the cognitive evoked potential is significantly delayed in alcohol dependent patients, and so it can be applied as a objective screening method to assess cognitive function. However, clinicians should consider that alcohol dependent patients who show no clinical abnormality of the CNS or on the diagnostic imagings may have a decline in cognitive function when the physician is observing the patients. Further studies are needed to focus on the influence of complications such as depression, peripheral neuropathy and other accompanying diseases that can occur in alcohol dependent patients on the cognitive function and the Cognitive Evoked Potential. The combination of continuous follow-up and clinical studies is necessary for investigating the cognitive-related complications on the abnormalities seen on the early cognitive evoked potential.

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