Differential Associations of P300 Amplitude and Latency With Cognitive and Psychiatric Function in Solvent-Exposed Adults

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Cognitive and mood changes are central components of solvent encephalopathy. This study examined event-related potentials in relation to neuropsychological and psychiatric function in solvent-exposed adults. Results revealed that longer P300 latency was associated with poorer cognitive test scores, whereas reduced P300 amplitude was related to increased psychiatric symptomatology. The findings suggest that the cognitive deficits and the psychiatric disturbance following solvent exposure may have different neurophysiological bases.

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Both neuropsychological deficits and altered mood have been documented in numerous studies comparing solvent-exposed adults with healthy nonexposed control subjects. The most common impairments are seen on tests measuring learning and memory, motor speed, and mental flexibility. Self-report psychiatric inventories reveal more depression, anxiety, and somatic distress. Frequently, cognitive and mood changes appear together, although the World Health Organization (WHO) has distinguished between mood alteration (Type Ila) and cognitive impairment (Type IIb) in its classification of solvent encephalopathy.

In an effort to better quantify the alteration of central nervous system function in solvent-exposed patients, we have looked at event-related potentials (ERPs). ERPs provide a time-dependent measure for assessing the efficiency of information processing. The P300 component of the ERP is hypothesized to be a good indica-

tor of overall cognitive capacity and stimulus evaluation or decision. Increased latency of the P300 has been shown in persons with acquired brain damage (as in head injury and dementia), and several reports have shown correlations between learning, memory, and attentional tests and P300 latency. A decrease in amplitude of the P300 component has frequently been associated with mood and psychiatric symptomatology, and improvement in amplitude has been shown to parallel recovery of mood. Thus, latency has been associated strongly with temporal aspects of decision making, and it has been observed to be prolonged in persons with organic brain disorders. Amplitude has been related most strongly with evaluation of event significance and arousal, and it is reduced in persons with psychiatric symptomatology. When we compared solvent-exposed patients, nonexposed control subjects, and psychiatric control subjects, we found that exposed persons had significantly increased P300 latency compared with the control subjects, but no significant group reduction in amplitude, suggesting a greater role of CNS impairment for the group as a whole.

The present study examined the relationship between neuropsychological function, psychiatric state, and ERPs in persons with a history of organic solvent exposure. The hypothesis to be tested was that P300 latency would be associated with neuropsychological measures and P300 amplitude would be associated with psychiatric symptomatology. Confirmation of this hypothesis would suggest that cognitive and psychiatric components may have different underlying mechanisms.

METHODS

Subjects
Subjects were 30 persons who were referred to our clinic with a history of organic solvent exposure. No person had alcohol consumption exceeding two drinks per day, neurological or psychiatric history preceding the exposure, or a history of current or past alcohol or drug

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abuse. A semistructured occupational and environmental exposures questionnaire was administered to each person. All persons met WHO criteria for mild toxic encephalopathy, Type IIa/IIb. The average length of exposure was 5.7 years (range < 1 day–30 years), and the average number of weeks from the last exposure to the testing was 105 weeks (range 1 week–10 years). All persons were exposed to mixtures of aliphatic and aromatic organic solvents (for example, toluene and trichloroethylene). One person had an additional exposure to pesticides and another to inorganic mercury. The mean age and education of the group was 41.2 and 13.3 years, respectively (SD = 8.4 and 2.2). No person failed an auditory screen at 40 dB. All provided informed consent.

Evaluation of Neuropsychological Function and Mood
Subjects completed the Pittsburgh Occupational Exposures Test (POET) battery, a compilation of well-known neuropsychological measures including subtests from the Wechsler Adult Intelligence Scale–Revised (WAIS-R) and Wechsler Memory Scale, as well as tests assessing learning and memory, spatial ability, motor speed, and general intelligence. Results from a previous study of 182 healthy nonexposed blue-collar workers showed that the 21 tests in the POET battery form five discrete factors: general intelligence, learning and memory, visuospatial skills, psychomotor speed and manual dexterity, and attention and mental flexibility. A more specific description of the tests, the administration procedures, and the factor analysis is provided in that study.

Subjects also completed the Symptom Checklist-90-Revised (SCL-90-R), a self-report measure that asks respondents to rate how much they were distressed by 90 different problems (for example, "feeling blue") over the past month. This questionnaire provides a score for nine symptom areas (such as depression) as well as a Global Severity Index.

Evaluation of Event-Related Potentials
Event-related potentials were recorded during two "oddball" paradigms: Counting and Choice Reaction Time (RT). Auditory stimuli were tones either high (1,500 Hz) or low (800 Hz) in pitch (40 ms duration, ~65 dB, 3-s interstimulus interval) presented through a speaker in front of the subject. The high-pitched tone was presented with an overall probability of 0.25, and subjects were informed that two high tones could not occur in succession.

First, for the Counting task (two blocks, 80 trials per block), subjects silently counted the number of high-pitched, infrequent tones. This was followed by two additional blocks of the Choice RT task: subjects responded with a separate key press for each tone. ERPs (bandpass 0.01–30 Hz; digitization at 125 Hz beginning 200 ms before stimulus onset) were recorded from midline scalp locations (Fz, Cz, Pz, Oz; international 10/20 system) with an eye artifact channel (EOG), and average ERPs were computed from artifact-free trials. For the present analysis, P300 at the midline parietal electrode (Pz) was determined for the infrequent (high tone) condition for each task. P300 latency and amplitude (minus 200-ms prestimulus baseline) were recorded for the most positive peak in the 280–500-ms time window.

RESULTS
A summary z-score for each of the five neuropsychological domains (for example, Memory and Learning, Visuospatial) was computed for each subject. Separate multiple regression analyses were conducted with P300 latency and amplitude at Pz to infrequent tones for the Counting and Choice RT tasks as dependent variables. Independent variables were age, the z-scores for the five neuropsychological domains, and the SCL-90-R Global Severity Index. Age was forced into the equation and the remaining variables were entered in a stepwise fashion.

The average P300 amplitude and latency for the group (across tasks) were 9.55 µV and 389 ms, respectively. These are virtually identical to the values reported in our earlier study based on 12 of these exposed subjects.

For P300 amplitude, smaller amplitude was associated with heightened psychiatric symptomatology, as measured by the Global Severity Index, as well as slower times on the motor tests. The Global Severity Index accounted for 24% of the variance of the amplitude on the Counting task ($F = 8.9, P = 0.006$) and 35% of the variance of the Choice RT task ($F = 15.1, P = 0.006$). Scores on the motor tests accounted for 17% of the variance of the amplitude on the Counting task ($F = 8.2, P = 0.007$) and 16% of the variance on the Choice RT task ($F = 8.7, P = 0.006$). The Global Severity Index and motor tests together accounted for 43% and 47% of the variance on the Counting and Choice RT, respectively.

Age was not significantly associated with amplitude for either the Counting or Choice RT task ($F < 1.0$).

For P300 latency, a somewhat different pattern was noted. On the Counting task, the attentional factor accounted for 30% of the variance ($F = 11.9, P = 0.002$). That is, longer P300 latency was associated with poorer performance on measures of attention and mental flexibility. For the Choice RT measure, age, attention, and
general intelligence were significantly related to latency. On this task, longer latency was associated with increased age (16% of the variance, $F = 5.6, P = 0.02$) and lower scores on tests of intelligence (30% of the variance, $F = 15.4, P = 0.0005$) and tests of attention (8% of the variance, $F = 5.1, P = 0.03$).

Figure 1 provides illustrative data for ERP grand means from the midline parietal electrode in the Counting task. Data for the 5 subjects with the lowest and highest Global Severity Index score are superimposed. Note that the entire late positive complex, including P300, shows reductions in amplitude for persons with more psychiatric symptomatology (higher scores). A similar presentation for the 5 subjects who scored poorest on an attention test (Part B of the Trail Making) is presented on the right side. In addition to differences in amplitude, what is especially notable is that the peak latency for the largest positivity in the P300 region is seen later for those subjects with poor attention scores.

DISCUSSION

A marked difference was noted between P300 amplitude and latency and neurobehavioral results for this group of solvent-exposed subjects. Specifically, decreased amplitude was strongly associated with higher levels of psychiatric symptomatology, as measured by the Global Severity Index on the SCL-90-R. Decreased amplitude was also significantly related to slower times on measures of motor speed. P300 latency, however, was not associated with the psychiatric index, but was associated with performance on measures of cognitive function. Particularly noteworthy is that increased P300 latency, on both the Counting and Choice RT tasks, was related to poorer performance on measures of attention.

For the Choice RT task, longer latency was also associated with older age and lower general intelligence test scores.

The results agree with the assumption that amplitude is associated with mood state and arousal, but which are likely also to be affected by motor speed, and latency is associated with efficiency of cognitive processing, evidenced by the large amount of variance accounted for by the attention factor and general intelligence factor. Although our data show differential correlations between psychiatric symptoms and cognition and P300 amplitude and latency, we cannot say unequivocally that psychiatric and cognitive state are independent in exposed persons. However, when we went back and looked at the relationship between amplitude and latency we found no significant correlation for either the Counting or Choice RT conditions ($r = -0.09$ and $-0.19$, respectively, $P > 0.15$). Likewise, correlations between the five cognitive domains (z-scores) and the Global Severity Index were not significant (range 0.01 to 0.32, $P > 0.05$).

Several studies have reported correlations between P300 latency and neuropsychological tests scores, but few have looked at both psychiatric symptoms and cognitive performance simultaneously in association with ERP variables in the same individuals. No previous studies have explored these variables in persons with chemical exposure. Our results suggest that the psychiatric disturbance and the cognitive disturbance following solvent exposure are differentially associated with P300 amplitude and latency and may have different underlying mechanisms. Further research seems warranted to explore the use of P300—a brief, noninvasive physiological measure—in other patient populations.
who present with both cognitive and mood changes (as occurs in head injury). Furthermore, it may be worthwhile to investigate whether changes in psychiatric or cognitive function over time can be reflected in changes in P300 amplitude and latency; if so, these measures may aid in monitoring therapeutic intervention.

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