Event-Related Potentials in Workers with Ongoing Occupational Exposure

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Introduction
The cognitive impact of occupational exposure to organic solvents has primarily been studied with neuropsychologic and behavioral measures (Hartman 1995). A small literature has addressed aberrations in event-related potentials (ERPs) in persons with clinical complaints associated with neurotoxic chemical exposure (El Massiou et al 1986; Morrow et al 1992, 1996; Teo and Ferguson 1985; Wasch et al 1989). For these exposed individuals, prolongation of the P300 component of the ERP is the most consistently reported finding. Prolongation of P300 latency also has been associated with acquired brain damage such as dementia (Goodin et al 1978) and posttraumatic amnesia (Onofri et al 1991). ERP data are presented from painters with ongoing workplace exposures who had not previously presented with occupationally-related impairments.

Methods
Journcymen painters (n = 35, mean = 16.7 years work experience) were recruited from the union roster. Exclusion criteria included reports of voluntary solvent use or documented neurologic disorder. Painters were tested either free of exposure to paints and solvents for at least 4 days (free, n = 18), or had been acutely exposed (acute, n = 17) within the last 1–66 (mean = 24.6) hours. Controls with no history of solvent exposure or neurologic disorder (n = 41) were recruited from other unions and the community. Demographically (Table 1), controls differed only on a younger mean age (F2,73 = 3.86, p < 0.03) and by participation of women. All three groups differed from each other for blood lead levels (µg/dL) obtained at the time of testing (data were unavailable for three controls) (F2,70 = 19.7, p < 0.0001). Career and past year exposure indices could be evaluated for the painters (Fidler et al 1987). DSM-III-R Axis I and Axis II symptomatology was assessed using the Structured Clinical Interview for DSM-III-R (SCID) (Spitzer et al 1989) and Personality Disorder Examination (Loranger 1988). Painters and controls did not differ for rates of substance use diagnoses, or Axis II personality disorders prior to early adulthood, but painters had a higher rate of Axis I mood disorders. Details are available for diagnostic findings (Condray et al submitted) and neuropsychologic performance (Morrow et al 1997).

Auditory ERPs were evaluated during two tasks. Infrequent (25%) 1500 Hz or frequent (75%) 800 Hz tones (40 minutes duration, 65 dBA SL, 4 minutes rise/fall) were presented at 3 second intervals, 80 trials/block. Subjects were informed that high-pitched tones could not occur in succession. In the counting task, the subject counted the number of high tones, reporting his/her count after each of two blocks (160 trials). In the subsequent choice reaction task, subjects pressed different buttons to high or low
tones on each of two blocks. The electroencephalogram (EEG) (bandpass .01–30 Hz) from Fz, Cz, Pz, P3, P4, and Oz, referred to linked ears, was digitized at 8 msec intervals for 1200 msec, beginning 200 msec prior to stimulus onset. Vertical EOG was employed to detect ocular artifacts; trials exceeding an EOG range of 75 μV were excluded during off-line analysis. Data were digitized by a Digital Equipment Corp. PDP-11/73 system and analyzed by FORTRAN and Macro-11 software developed in the laboratory (additional procedural details are given in Morrow et al 1992). This report is based on artifact-free ERPs to infrequent tones. There were no significant differences among groups in the mean number of individual trials (30.8) contributing to the ERP average to rare tones in each task. Component peaks were identified by computer algorithm and verified or modified by two raters blind to group status. Latencies (at Pz for P300, at Cz for N100, P200, and N250) and peak amplitude measures at all electrodes (minus a 200 msec prestimulus baseline) were stored automatically. Latencies were analyzed using a 2 (task) × 3 (group) factor analysis of variance (ANOVA) with an additional factor of electrode (six sites) for amplitudes. As appropriate, degrees of freedom were adjusted (Greenhouse-Geisser). Main effects of task, electrode, and task × electrode interactions have been omitted.

**Results**

**ERP Latencies**

Grand average ERPs to rare tones are presented for the choice reaction task (Figure 1). The waveforms appear similar across groups, although a later P300 component is visible for acute painters at Pz. Across tasks, P300 latency to target stimuli (Figure 2) was significantly longer for acute painters (380.5 msec) than for either controls (354.1 msec) or free painters (352 msec) (main effect for group: $F_{2,73} = 4.4, p = 0.016$, post hoc Newman-Keuls $p < 0.05$). No other ERP components showed latency effects associated with group.

**ERP Amplitudes**

P300 amplitude (maximum at Pz) to rare stimuli did not differ significantly among groups ($p = 0.66$) or between tasks (Figure 3). No group effects were associated with N100 or P200 amplitude.

N250 (Fz-Cz maximum) was characterized by an electrode × group interaction ($F_{4,151} = 2.6, p = 0.03$). After N250 data were normalized (Hill et al 1995; McCarthy and Wood 1985), a task × electrode × group interaction was observed ($F_{4,162} = 4.2, p = 0.002$). Normalized amplitudes indicated enhancement of vertex negativity (or relative decreased frontal negativity) in the choice reaction task for painters, but not for controls. Restricting the analysis to the difference between normalized Fz and Cz amplitudes continued to show a task × group interaction ($F_{2,73} = 4.91, p = 0.01$). Increased frontal-to-vertex negativity between tasks was greater for free painters than for controls (simple effects, $p < 0.05$); acute painters scored in between. N250 amplitudes are plotted for each group at Fz and Cz as a function of task in Figure 4.

Further analyses of P300 latency, and N250 amplitude differences (Fz–Cz) examined age as a covariate, used a trimmed control group not differing in age from the painters, or excluded all subjects with any history of major depressive disorder. P300 latency and N250 amplitude
effects (normalized or unscaled) remained significant in all comparisons. Given the large size of the control group with respect to each of the painter groups after acute or free status was determined, subanalyses using a comparably-sized group of controls (n = 18) were conducted. P300 latency effects (mean for the reduced control group = 355.1 msec), and N250 amplitude effects were still significant and similar to those observed using the entire control subject group.

The associations among electrophysiologic responding, career solvent exposure, and blood lead were examined using multiple regression analysis. The predictor variables were the career exposure index and blood lead level. The dependent variables were the ERP measures (P300 latency, N250 amplitude at Fz and at Cz) in each task. The model was tested separately for the free and acute painter groups. The model did not predict P300 latency in either task for either group. In contrast, the amplitude of N250 at Fz during the choice reaction task was predicted by blood lead level in the free group ($R = 0.52$, $F_{1,16} = 5.89$, $p < 0.05$). The model was not successful in predicting the following: N250 amplitude at Fz in the acute group, N250 at Cz for choice reaction, and either Fz or Cz during the counting task for either group.

**Discussion**

Prolongation of P300 latency was observed in painters acutely exposed to solvents, and N250 amplitude negativ-
The fact that N250 negativity occurred less in acute than free painters suggests that frontocentral N250 amplitude may be a long-term indicator of chemical exposure that is masked or normalized following acute exposures. There have been no previous reports of similar clinically-related effects of N250 amplitude. Note that there were higher measures of career exposure as well as higher blood lead levels in the free than in the acute painters. This suggests that lifetime exposures are currently confounded in these groups. Future analyses where the same painters are examined at both acute and free periods are underway, and should help to clarify these questions.

P300 latency was significantly prolonged only in painters with recent occupational exposures. A similar effect was observed in patients with clinical impairment following exposure to organic solvents even after several years (Morrow et al 1992). In that case, however, and in other clinical populations, a persistent finding of prolonged P300 latency appears to be associated with significant chronic clinical impairment. The normal latencies of free painters in the present study implies that delay in P300 latency is a reversible phenomenon at this stage of their careers. What is not known is whether elderly workers with similar solvent exposure reach a phase at which P300 latency no longer recovers, and is associated with enduring impairment in such individuals; this is a critical clinical question that needs to be examined in the future. P300 latency may be an optimal indicator for the effectiveness of protective equipment for blocking the deleterious effects of hazardous chemicals on brain function.

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References


