Alterations in Heart Rate and Pupillary Response in Persons with Organic Solvent Exposure

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Cardiac and pupillary reactivity were examined in 25 persons with a history of exposure to organic solvents and 19 nonexposed controls during performance of a counting and a choice reaction task. The solvent-exposed group demonstrated an atypical pattern of responding across tasks. While control subjects showed a decline in heart rate across the two conditions (e.g., habituation), exposed persons had an increase in heart rate. Initial pupil diameter was similar for both groups, but only the control subjects exhibited habituation across the two tasks. In the exposed group, higher heart rate was not associated with higher levels of self-reported anxiety. Anticipatory cardiac deceleration preceding unpredictable events was significantly less in the exposed group, but there were no significant group differences on poststimulus acceleration. The results suggest that persons with solvent exposure have a deficiency in the allocation of attention (reduced anticipatory deceleration and decreased pupillary dilation). It is further suggested that difficulty in the allocation of attention produces an increase in tonic sympathetic levels when confronted with a cognitively challenging task. In this experiment, in which the choice reaction task was purposely presented last, and was apparently more challenging for exposed persons, a failure to exhibit autonomic habituation over the course of the session characterized the solvent-exposed group.

Key Words: Heart rate, pupillary response, organic solvents, choice reaction task, counting task, autonomic responsiveness

Introduction

Clinical disease states associated with organic solvent exposure are well documented (Spencer and Schaumberg 1980). Both clinical and epidemiological studies have demonstrated decreases in cognitive function (e.g., decreased attention and memory, psychomotor slowing) and alterations in personality (e.g., increased anxiety, irritability, and depression) in persons with a history of exposure to solvents (Baker et al 1988; Linz et al 1986; Morrow et al 1989, 1990, 1991, 1993; Parkinson et al 1990; Struwe and Wennberg 1983). The pattern of cognitive impairment in solvent-exposed persons suggests particular difficulty in dividing and/or sustaining attention. A recent study found that, in comparison to demographically matched controls, solvent-exposed persons adequately recalled previously learned information from long-term memory, but their performance was impaired when they were required to sustain speed and maintain alertness (Morrow et al 1992). The findings were considered evidence of a limitation in the allocation of attentional resources; however, because arousal must be maintained in order to perform well, an alternative explanation was a generalized decrease in arousal.
Variations in autonomic nervous system function, such as alterations in respiration, heart rate, skin conductance, and pupil size, provide an objective marker of emotional and mental activity, as well as overall arousal. Cardiac changes in normal subjects, particularly phasic changes, are sensitive to shifts in attention; that is, heart rate decelerates in response to an anticipated stimuli and then accelerates after stimulus delivery (Lacey and Lacey 1974). Likewise, pupillary behavior is highly correlated with the initiation and maintenance of attention: When subjects are asked to perform simple or complex mental tasks (e.g., recalling a string of numbers) there is a corresponding dilation of the pupil (for review see Loewenfeld 1993; Steinhauser and Hakerem 1992). The present study was designed to address the hypothesis that persons with a history of organic solvent exposure have a deficiency in attentional processing independent of reductions in arousal. Heart rate and pupillary response changes to predictable and unpredictable events were assessed in solvent-exposed persons and normal controls. Two attentional tasks—modifications of an oddball paradigm—were employed. In this case, high- and low-pitched tones were presented with the stipulation that the high tones occurred much less frequently and never occurred twice in succession. Informing the subject of these stipulations allows for the evaluation of predictive (attentive) and unpredictable (nonattentive) events on cardiovascular and pupillary reactivity. Previous studies of event-related potentials have demonstrated a prominent distinction between these conditional events (Steinhauser and Zubin 1982; Steinhauser et al 1992).

The measurement of heart and pupil responsiveness provides a noninvasive, objective assessment of physiological activities that is sensitive to changes in information processing. Recording physiological responses to demands on attentional processing may further clarify the nature of the cognitive deficits often described in persons with organic solvent exposure and address possible decreases in arousal.

**Methods**

**Subjects**

Twenty men and five women with neurasthenic symptoms (e.g., headaches, dizziness, fatigue) following exposure to organic solvents were evaluated. No person had a history of past loss of consciousness, hearing loss, or alcohol consumption exceeding two drinks per day. Psychiatric history was obtained via self-report and survey of medical records. No patient had a history of psychiatric assessment or treatment prior to their exposure. A semistructured occupational and environmental exposures questionnaire was administered to each person. All persons met criteria for mild toxic encephalopathy, Type 2A/2B (cognitive and personality changes) (Baker and Fine 1986). The mean duration of exposure was 4.7 years (median, 1 year; range, <1 day to 30 years), and the mean amount of time from the last exposure to the assessment was 2.5 years (median, 1.2 years; range, 2 weeks to 10 years). All persons were occupationally exposed, and the primary exposures consisted of mixtures of aliphatic and aromatic organic solvents (e.g., toluene and trichloroethylene). One person had an additional exposure to pesticides and another to inorganic mercury. Three of the exposed subjects were taking high blood pressure medication (nifedipine 30 mg; verapamil HCl 240 mg; verapamil HCl 250 mg), one patient was being treated with an antidepressant (amitriptyline 75 mg), and one patient was prescribed antiepileptic medication (divalprox 250 mg). The mean age for the exposed group was 43.2 years (SD = 7.9).

The normal control group consisted of 19 male volunteers recruited for the Pittsburgh Vulnerability Study of schizophrenia (Steinhauser et al 1991) who were screened for medical and psychiatric disorders using a semi-structured interview to assess DSM-III-R Axis I and Axis II disorders (APA 1987; Spitzer and Endicott 1979; Pfohl et al 1983). The mean age of the control group was 34.8 years (SD = 7.8). All subjects were given a detailed description of the study and informed consent obtained. All subjects passed an auditory screen at 40 dB.

**Heart Rate and Pupil Recording**

Heart rate was recorded via placement of large Ag/AgCl electrodes under the left ribcage and on the right shoulder. A small electrode was placed on the forehead to serve as ground. A Grass Model 12 polygraph amplified the signal, and a Schmitt trigger was used to detect the R-wave. The time of each R-wave, to the nearest msec, was recorded by computer.

Pupillary diameter was measured from the analog output of a Gulf & Western Applied Science Lab pupillometer. The digitization rate was 60 samples/sec with an accuracy of 0.025 mm. Individual trials were viewed on a monitor placed outside the testing suite and rejected by the experimenter online if a lid closure, eyeblink, or major artifact was present. All data were stored on magnetic media by a PDP-11/73 (MINC) laboratory minicomputer. Offline, the computer also checked for possible blinks or artifacts that had been undetected during the experiment.

Event-related potentials were recorded from six scalp locations. Analysis of these data, including the P300 component, have been reported elsewhere (Morrow et al 1992).

**Procedure**

The subject sat upright in a darkened room, and resting the chin and forehead in a head rest. Positioned directly in front of the subject (57 cm) was an arrangement of four red light-emitting diodes to serve as fixation. The subject was
asked to blink as infrequently as possible and to maintain fixation on the lights during the testing. Communication between the experimenter and subject was via intercom. Subjects completed a modified auditory “oddball” paradigm in both Counting and Choice Reaction conditions. In both tasks subjects were presented with high-pitched tones (1500 Hz) and low-pitched tones (800 Hz) at 65 dB A for 40 msec through a speaker placed in front of the subject. Tones were presented at an interstimulus interval of 3 seconds, with 80 trials/block. Subjects were informed of two restrictions. First, the high-pitched target tone would not occur as often as the low-pitched tone. Second, the high-pitched tone would never occur twice in a row. Prior to the first block of testing, subjects were asked to predict what tone would occur after a “high;” all subjects correctly answered that a “low” tone would be heard next. A computer randomly generated the sequence of tones such that high tones were presented 25% of the time. Thus, there were three conditional probabilities. When a target tone (high pitch) was present, there was a 100% probability that the next tone would be a nontarget (low pitch). If a nontarget tone was presented, the subsequent tone could be either a nontarget (67% probability) or a target (33% probability). For the counting task, subjects were told to count the occurrence of the high-pitched tones (targets) silently and to report the number of high tones (but not low tones) at the end of each block. In the choice reaction task, subjects pressed a button following each high tone, and a different button following each low tone, with responding hands switched between the two blocks and counterbalanced between subjects. For all subjects, the same order of tasks was purposely employed: counting first, choice reaction second. This was done because it emphasized that only high tones would be overtly task relevant for the initial counting task, while all tones then became relevant for the choice reaction task. Two blocks of trials were collected for each task.

A reward of 25 cents was given to subjects if they counted all targets. Ten cents was given if they made only one or two errors. No monetary reward was provided if they made three or more errors. In the counting task, only four exposed subjects had more than one error/block. In the choice reaction task, three exposed subjects had between two and 10 errors on a block, and five subjects had more than 10 errors on one of two successive blocks. All incorrect trials were excluded from the analysis. In those subjects with more than 10 errors, additional blocks of trials were collected for that condition.

Data Reduction and Analysis

For heart rate, time between successive R-waves (interbeat interval, IBI) was computed in msec. If several R-waves were detected within 400 msec, or if changes in IBI were greater than 200 msec from one interval to the next, then these were interpreted as artifacts. Cardiac changes preceding and following stimulus presentation were included only if that trial and the preceding and subsequent trials were free of artifacts. This provided an overall time window of 9 sec for examining cardiac changes. Average IBI was determined from the eight R-waves calculated for each of the three probability conditions, starting at two beats prior to stimulus delivery (IBI = 2), during delivery of the stimulus (IBI = 0) and four beats following stimulus delivery (IBI = 4).

Heart rate in beats per minute (bpm) was also obtained by converting the IBI for individual trials for each subject. This was computed by calculating the average heart rate every 0.5 sec for 14 periods, beginning 2.5 seconds prior to stimulus onset.

Trials in which there was overt movement or excessive blinking were deleted from the pupillary analysis. For each subject, separately by task and by probability across artifact-free trials, an average pupil diameter was computed at successive 16 msec time points, beginning 200 msec prestimulus and continuing up to 2200 msec poststimulus. The initial diameter was computed as the average prestimulus diameter.

When subjects are required to process relevant information, their maximum pupillary dilation (in darkness) occurs with a peak latency of approximately 1200 msec after stimulus onset (Friedman et al 1973; Steinhauer and Hakern 1992). The diameter of the pupil at 1200 msec was automatically extracted from each wave form, and the difference from initial diameter calculated. A second dilation amplitude measure was obtained at the true peak diameter occurring in the 900–1800 msec range, and the amplitude and latency of this peak was stored.

To summarize, pupillary variables extracted from the average wave form across artifact-free trials included mean prestimulus pupil diameter, extent of dilation at 1200 msec, extent of dilation at peak diameter, and latency to peak diameter.

The primary analyses employed were repeated measures ANOVA, with degrees of freedom reduced according to the Greenhouse-Geisser correction (Jennings and Wood 1976). Age was entered as a covariate in the analyses. For the cardiac analysis, Group differences (solvent vs. control) were compared by task (counting vs. choice reaction) × probability (0.33, 0.67, 1.0) × IBI (7 intervals). Group differences for pupillary measures were compared by task × probability.

Results

Cardiac Activity

Figures 1 and 2 present the average cardiac data for each group by task (counting and choice reaction), at the three probability conditions, across successive IBIs. The stimulus
The pattern of heart rate activity is clearly different when the stimulus is predictable (1.0 condition). In this condition, heart rate accelerated prior to the stimulus and then decelerated following the stimulus event. This acceleration is likely due to a continuation of the poststimulus acceleration from the preceding trial in which the target tone was presented. These patterns replicate previous findings for this task (Hill et al. 1992; Steinhauser et al. 1992).

The pattern for the choice reaction task (see Figure 1, bottom) is similar to the counting task, except that there is now an anticipatory deceleration in the 1.00 condition. This is thought to be due to the subject’s preparation for an overt motor response (Jennings et al. 1990). In addition, as the choice reaction task always carried out after the counting task, the typical finding of decreased overall heart rate representing habituation as well as the task specific pattern (Hill et al. 1992) was observed for controls.

Interbeat interval was shorter for exposed subjects (758 msec, equal to a heart rate of 79.16 bpm) as compared to controls (858 msec; 69.93 bpm). Though age was not a significant covariate, it did reduce the significance of the difference between groups ($F(1,42) = 3.04$, $p = .088$). A significant main effect of Probability ($F(2,84) = 3.60$, $p = .03$) and IBI ($F(6,252) = 8.77$, $p = .0001$) was observed. Also found were significant interactions of Task by Group ($F(1,42) = 9.08$, $p = .004$), task by probability ($F(2,84) = 7.11$, $p = .001$), and probability by IBI ($F(12,504) = 4.53$, $p = .0001$). A three-way task by probability by IBI ($F(12,504) = 1.91$, $p = .03$) interaction was also obtained. The interaction of group by task reflects the fact that exposed subjects show an increase in heart rate going from the counting to the choice reaction task, while the heart rate for control subjects decreased across tasks (see Figure 3). That is, exposed subjects show an atypical pattern of increasing heart rate rather than the typical habituation.

Further analyses were done to compare differences in anticipatory deceleration and poststimulus acceleration (see Figures 4 and 5). Anticipatory deceleration was calculated as the change in heart rate from IBI:−1 to IBI:1. A significant main effect of group ($F(1,42) = 10.43$, $p = .002$) reflects the fact that exposed subjects show less anticipatory deceleration than controls. Main effects of task ($F(1,42) = 7.42$, $p = .009$) and probability ($F(2,84) = 5.03$, $p = .009$) indicate larger deceleration in the choice reaction task and larger decelerations in the unpredictable conditions (0.33 and 0.67), respectively. A three-way group by task by probability interaction ($F(2,84) = 4.04$, $p = .021$) reflects less anticipatory deceleration in the exposed subjects when they were performing the choice reaction task and the stimulus was predictable.

A more restricted analysis of anticipatory deceleration was performed using only the two unpredictable conditions (0.33 and 0.67 probability). Significantly greater deceler-
Table 1. Mean (SD) Cardiac and Pupillary Values for Rare Tones, 0.33 Condition

<table>
<thead>
<tr>
<th></th>
<th>Controls</th>
<th>Solvent-exposed</th>
<th>Controls</th>
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<tbody>
<tr>
<td>Cardiac measures</td>
<td></td>
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<tr>
<td>Prestimulus interbeat interval (msec)</td>
<td>853.1 (158.6)</td>
<td>761.7 (134.7)</td>
<td>864.4 (164.1)</td>
<td>752.9 (140.5)</td>
</tr>
<tr>
<td>Deceleration (msec)</td>
<td>7.2 (12.0)</td>
<td>3.9 (6.2)</td>
<td>9.9 (14.6)</td>
<td>6.1 (6.4)</td>
</tr>
<tr>
<td>Acceleration (msec)</td>
<td>-17.4 (14.7)</td>
<td>-9.6 (15.9)</td>
<td>-19.1 (48.3)</td>
<td>-6.6 (13.9)</td>
</tr>
<tr>
<td>Pupillary measures</td>
<td></td>
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<tr>
<td>Prestimulus diameter (mm)</td>
<td>6.92 (0.69)</td>
<td>6.81 (1.01)</td>
<td>4.82 (1.18)</td>
<td>6.90 (0.86)</td>
</tr>
<tr>
<td>Peak dilation (mm)</td>
<td>0.16 (0.08)</td>
<td>0.11 (0.08)</td>
<td>0.16 (0.10)</td>
<td>0.08 (0.09)</td>
</tr>
<tr>
<td>Latency to peak dilation (msec)</td>
<td>1392.9 (137.0)</td>
<td>1351.4 (108.0)</td>
<td>1484.4 (171.2)</td>
<td>1376.0 (236.4)</td>
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RT = reaction time.

ition was seen for controls as compared to exposed subjects ($F(1,42) = 5.68$, $p = .022$). A lack of condition effects implies that both unpredictable events resulted in anticipatory deceleration.

Analysis of poststimulus acceleration (IBI:0 to IBI:3) revealed no difference between the groups ($p = .17$). Acceleration was greater in the choice reaction task (task: $F(1,42) = 3.91$, $p = .05$), reflecting the initiation of a motor response, and there was a greater acceleration for unpredictable events (probability: $F(2,84) = 5.71$, $p = .006$).

Pupillary Activity

Pupillary measures of prestimulus diameter were available for 14 exposed subjects and 18 controls (mean age = 39.5, SD = 7.9, and 33.8, SD = 7.3, respectively) (the pupil-meter was unavailable during a period of testing due to repairs). The grand mean pupillographic record across subjects for the 0.33 condition in the counting task is shown in Figure 6 for control and exposed subjects. Note that for these data averaged across all subjects in each group, the observed peak diameter occurs somewhat later than the standard 1200 msec latency that was also evaluated. Values for prestimulus diameter, extent of peak dilation, and latency to peak dilation in the 0.33 condition are shown in Table 1.

Across tasks and conditions, initial pupillary diameter (covarying for age, which was a significant covariate, $p =$

Figure 3. Average prestimulus heart rate and pupil diameter, each corrected for age, are shown for both tasks. Note the decrease in both heart rate and pupil diameter for controls (circles) as contrasted with the stability or increase of these measures during the session for exposed subjects (*) when presented with the choice reaction task.

Figure 4. Anticipatory deceleration as a function of event probability, calculated as the increase in interbeat interval from IBI:=1–IBI:1.
was significantly larger for the solvent-exposed patients (6.87 mm) than for controls (5.90 mm) \(F(1,29) = 26.49, p = .0001\). Age-corrected means are shown in Figure 3. There was a significant group \(\times\) task interaction \(F(1,30) = 63.11, p = .0001\), which demonstrates a much more complex situation: controls exhibited decreasing pupil diameter from counting (6.95 mm) to choice reaction (4.86 mm), while exposed subjects showed a similar counting diameter (6.82) to controls, but slightly increased average choice reaction diameter (6.93 mm) (Figure 3). That is, overall pupillary diameter failed to exhibit habituation across tasks for the solvent-exposed subjects. Given the large decrease in pupil diameter across tasks for controls as compared to exposed subjects, we examined individual data for the controls more closely. The mean change accurately reflected the group as a whole: 15 subjects showed a decrease of more than 2 mm, one showed a decrease of 0.7 mm, and only two controls showed a lack of habituation, with an increase of 0.12 mm between tasks. A main effect for probability across groups reflected a larger average diameter for the 1.00 condition \(F(2,45) = 3.73, p = .043\) than for the other conditions.

Pupil dilation at 1200 msec after stimulus onset (relative to the prestimulus diameter) was also compared for each of the probability conditions and tasks. There was a main effect of probability \(F(2,58) = 23.02, p = .0001\) as well as a probability \(\times\) group interaction \(F(2,58) = 4.76, p = .012\) (see Figure 7). Controls showed a consistent pattern of increasing dilations with decreasing event probability, as has been reported previously (Steinhauer and Zubin 1982). The interaction reflects a significantly greater difference between probability conditions for controls than for exposed subjects. Essentially the same results were obtained...
when these analyses were repeated using the maximally observed peak dilation amplitude rather than the amplitude at 1200 msec.

The apparently larger dilation for controls than exposed subjects was examined further using only the data for the infrequent 0.33 conditions in both tasks, which yielded the largest dilations for both groups. There was a marginally significant finding of greater dilation for the control than exposed subjects at 1200 msec ($F(1,29) = 4.12, p = .052$), with a stronger effect observed when extent of maximum peak dilation was compared between controls (0.160 mm) and exposed (0.093 mm) persons ($F(1,29) = 5.45, p = .026$).

Although there was a pattern for longer latencies to the peak of dilation for controls (mean 1350 msec) than for the exposed group (1301 msec), this represents only about three sampling points, and there was no significant difference in latency between subject groups. Peak latency tended to be longer for the choice reaction task than for counting ($F(1,30) = 13.13, p = .0011$). Lower event probabilities, associated with higher amplitude dilations, were also observed to have longer peak latencies ($F(2,58) = 11.82, p = .0001$).

The correlation was computed between change scores (difference between counting and choice reaction) for both heart rate and pupil response. The positive correlation ($r = 0.43, p = .015$) demonstrates that similar patterns of habituation, or its absence, characterized subjects across autonomic measures.

**Assessment of Mood and Exposure-Related Variables**

As part of an ongoing study, all of the exposed subjects had completed the Symptom Checklist 90-R (SCL-90-R, Derogatis 1975) in order to obtain a measure of psychological symptomatology (e.g., depression, anxiety). For the most part, subjects had completed the questionnaires within several weeks of the psychophysiological assessment. In order to look at self-reported distress and performance on cardiac activity, correlations between the anxiety subscale from the SCL-90-R and average heart rate for the counting and choice reaction tasks were computed. Self-reported anxiety was negatively correlated with heart rate (counting $r = -0.46, p = .02$; choice reaction $r = -0.48, p = .01$). Thus, higher heart rate was associated with less anxiety. Correlations were unchanged after deleting those five people whose questionnaires were completed more than six weeks prior to the psychophysiological testing ($r = -0.43$ and $-0.44$, respectively). There was no significant relationship between duration of exposure, episodes of peak exposure, or weeks since exposure with heart rate change scores on either counting or choice reaction tasks.

**Discussion**

These results suggest that workers with a history of exposure to organic solvents have alterations in autonomic responsivity when confronted with a task requiring mobilization of attention. The most surprising finding was that exposed subjects failed to habituate across tasks. This was apparent for both cardiac and pupillary reactivity. Heart rate increased in the exposed group as subjects went from the counting to the choice reaction task. Nineteen of the 25 exposed subjects had a heart rate change score that demonstrated a failure to habituate. Pupil diameter, which declined by 2 mm in the control group across the two tasks, increased slightly for the exposed group. In addition, exposed subjects showed less cardiac anticipatory deceleration prior to certain and uncertain events in both counting and choice reaction tasks.

Although overall heart rate was higher for exposed subjects, suggesting increased autonomic arousal, covarying age resulted in a nonsignificant group difference. However, the increase in heart rate across tasks does suggest increased sympathetic arousal, possibly in response to a cognitively challenging event. The choice reaction task, which always followed the counting task, has higher task demands. That is, for this task the subject must attend to each stimulus, determine if it is high or low, select the appropriate hand for a motor response, and then execute the response. The counting task is less demanding, requiring the subject only to count infrequent tones and to ignore the rest. Many of the exposed subjects reported that the choice reaction task was much more difficult for them than the counting task. Indeed, the average errors were greater for the choice reaction task as compared to the counting task (10.5 and 2.9, respectively). In normal controls, varying task difficulty has been shown to alter heart rate. When subjects are given cognitive tests (mental arithmetic, abstract reasoning) that are easy, hard, or impossible, there is an increase in heart rate from the easy to the more difficult tasks, even after controlling for energy expenditure (Carroll et al 1986). In marked contrast, controls in this and other studies (Hill et al 1992), schizophrenic outpatients and their brothers (Steinhauer et al 1990), and alcoholics and their brothers (Hill et al 1992) all exhibited decreased heart rate across these tasks as the sessions progressed. We would suggest that exposed subjects are utilizing more effort, as reflected in increasing heart rate, to deal with a more cognitively effortful task.

In order to ascertain that the changes noted in the exposed group were not due to gender or medication status, we went back and compared cardiac levels among the five female subjects, five males who were on medication, and 15 males not receiving medication. Premstimulus pupil diameter was compared among four of these women and 10 of the unmedicated males (pupil data were unavailable for one woman and the five medicated males). There were no significant
differences among groups on either measure, although it was noted that female subjects tended to have higher heart rates and smaller pupil diameters than males. Regardless of gender for both measures, and for medication status assessed for heart rate, a lack of habituation was observed across tasks in each of the subgroups.

Exposed subjects exhibited smaller anticipatory deceleration in comparison to control subjects. Cardiac deceleration prior to stimulus delivery is taken as preparation for an imperative stimulus or preparation to make a response, while poststimulus acceleration reflects the psychological significance of the information received (Lacey and Lacey 1974; Coles and Duncan-Johnson 1975). Another way of describing this bidirectional change, as formulated by Jennings (Jennings et al. 1978; Jennings and Hall 1980), is that deceleration is coincidental with holding available processing capacity for the intake of information (i.e., allocating attention), while acceleration is contingent on ongoing processing of the information for its psychological relevance. The decreased anticipatory deceleration found for the exposed subjects suggests a deficiency in the allocation of attention. Similarly, the smaller differences in pupillary dilation among conditions for the exposed subjects reinforces the notion that decreased resources are being utilized in the processing of information during these tasks.

In a prior study (Morrow et al. 1992), we measured the ability of exposed patients to focus and maintain attention by asking them to perform a continuous performance test employing degraded visual stimuli over successive blocks, in which reaction time was recorded to target stimuli. False positive and false negative errors were also recorded. Over the six blocks of trials, reaction time increased by approximately 50 msec for both exposed and control subjects. However, while controls were able to improve performance on this vigilance test (i.e., d' increased on this version), exposed persons became less accurate. We hypothesized that exposed subjects had fewer attentional resources to devote to information processing; however, an alternative explanation was that a reduction in arousal was responsible for the exposed subjects’ vigilance decrements. Vigilance tasks require continued alertness to a monotonous task, and decrements in vigilance could occur to declines in arousal. Results from the present study lend support to our first hypothesis: that efficiency of attentional allocation is reduced in exposed subjects. This is reflected in their attenuated anticipatory deceleration. Arousal is actually heightened, as indicated by their increase in heart rate across tasks. Previous studies of persons with right hemisphere lesions, who have impairments in the orientation of attention (Morrow and Ratcliff 1988), have also been found to have reductions in anticipatory deceleration (Yokoyama et al. 1987).

Poststimulus acceleration was similar for both exposed and control subjects. Cognitive operations have been linked to acceleration (e.g., encoding, memory maintenance, and rehearsal of information) (Jennings and Hall 1980, Jennings et al. 1990). During this phase of cardiac activity, subjects are thought to be actively processing information concerning stimulus delivery (e.g., probability and relevance). The lack of accelerative differences between the two groups suggests that both groups adequately processed the salience of the information. We reported that exposed subjects could recall previously learned information as well as controls (Morrow et al. 1992). The present findings, in conjunction with our previous work, support the notion that exposed persons have reductions in allocating attentional resources, but the information that is processed can be adequately perceived and maintained.

It is unlikely that the alteration in psychophysiological responses exhibited by exposed persons is attributable solely to increased psychological distress. In fact, we noted the opposite. We were surprised to find that self-reported anxiety was actually less in those persons whose heart rate was highest. Although overall anxiety is high in the exposed group (average SCL-90-R Anxiety subscale T-score = 79), it was not the case that those with higher anxiety also had higher heart rates. Higher heart rates are reported for a number of patient populations, including persons with chronic stress (Davidson and Baum 1986), posttraumatic stress disorder (Blanchard et al. 1986), panic disorder (Roth et al. 1992), and schizophrenia (Zahn et al. 1991). It is not clear why those exposed subjects with higher heart rates report less anxiety. One reason may be that our measure of anxiety, the SCL-90-R, asks persons to rate anxiety over the past several weeks. Anxiety in relation to the testing per se (state anxiety), which was not assessed, may be unrelated to reports of generalized anxiety (trait anxiety). Alternatively, those who report the least anxiety, and have the highest heart rate, may have a defensive personality style which has been shown to increase autonomic responsivity (Weinberger et al. 1979).

Jennings (1992) has postulated a midbrain inhibitory circuit, consisting of limbic structures (amygdala, hippocampus), which regulates intended actions and autonomic requirements (e.g., slowing of heart rate via vagal inhibition). Recently, Bell and colleagues (1992) hypothesized that changes in neurophysiology, cognition, and affect following chemical exposure may result from kindling of limbic structures. Neuronal excitability in the limbic system, particularly to olfactory pathways, which are the primary route for solvents to enter the brain (Ghantous et al. 1990), may be altered as a result of an initial exposure such that thresholds are lowered to subsequent low-level exposures. Autonomic pathways, which are regulated by limbic structures, would thus be altered. If this inhibitory system were altered via limbic changes, there would be a state of decreased attention, which would be reflected in less anticipatory deceleration.
tion, and disruptions to the inhibition of arousal that are consistent with the present data. We have follow-up data on three of our exposed subjects, showing altered cardiac and pupil reactivity, over time. For this purpose, we report illustrative values for the 0.33 rare stimulus condition.

The first subject, who initially showed a normal cardiac habituation response, failed to show habituation on a subsequent evaluation. The initial heart rate averaged 77 bpm on the counting task and 76 bpm on the choice reaction task—demonstrating a normal decline in heart rate across tasks. Pupil diameter, however, failed to habituate (7.09 cm to 7.16 cm). The first testing was completed 2 weeks following an acute exposure to aromatic solvents. At the second evaluation, 33 months after the exposure, both pupil and heart rate failed to show habituation: the average heart rate for the counting and choice reaction tasks was 83 and 86 bpm, and pupil diameter increased from 7.10 cm to 7.65 cm, respectively. The second subject had worked with mixtures of organic solvents for over 2.5 years. At the initial assessment, conducted 66 weeks after the last exposure, there was a normal habituation in pupil responding (9.03–8.11 cm) but a mild increase in heart rate across the two tasks (84.4–84.8 bpm). At the follow-up evaluation, 9 months after the first testing, habituation was absent going from the counting to the choice reaction task for both pupil (9.11–9.45 cm) and heart rate (85–90 bpm). The third subject had an acute, peak exposure to mixtures of aromatic solvents. The first assessment was completed 100 weeks after the exposure and showed habituation of the pupil (6.12–5.71 cm) and very mild habituation of heart rate (55.4–55.2 bpm). A follow-up testing was done 2 years after the initial testing, and both pupil and heart rate failed to habituate (7.50–7.80 cm and 68–69 bpm, respectively).

Applying a model of kindling would suggest that the exposure altered limbic nuclei and subsequent stressors (intermittent over time), modified neuronal sensitization, increased susceptibility to a cognitive challenging event, and altered arousal. The nature of the subsequent stressors cannot be ascertained, whether low-level environmental exposures or persistent psychological stressors. The lack of correlation between weeks postexposure and atypical responding may not be inconsistent with such a model. That is, the change in responsibility over time may depend on the intensity of the original stressor (e.g., exposure) as well as how reactive the individual is and not directly on the passage of time (Antelman et al 1991). Future longitudinal studies are warranted to address possible intervening stressors that may affect changes in autonomic reactivity.

To our knowledge, this is the first study that has examined cognitively elicited autonomic responsiveness in persons with organic solvent exposure. The findings suggest that the allocation of attention is disrupted in these individuals. As a consequence of deficient allocation of attention, relatively benign tasks (e.g., a discriminative response task) are cognitively challenging for exposed persons and thus elicit sympathetic arousal. The intriguing changes in three of the exposed subjects—an enhancement of atypical responding over time—is suggestive of intervening factors that may modulate information processing and autonomic reactivity. Whether this is a result of limbic kindling is speculative; however, further explorations of cardiac and pupillary reactivity following chemical exposure should be undertaken, with particular attention to changes in autonomic responses over time.

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References


