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Antisocial personality disorder and cocaine dependence: their effects on behavioral and electroencephalographic measures of time estimation

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Abstract

The present study examined time estimation performance and concurrently-recorded electroencephalographic activity among 57 residential treatment program patients previously dependent on either cocaine or cocaine and alcohol. The patients were assigned to one of two subgroups based upon the presence ($n = 20$) versus absence ($n = 37$) of a comorbid diagnosis of Antisocial Personality Disorder (APD). Twenty-six subjects, who had no history of substance abuse and no diagnosis of APD, were also examined. All subjects performed a psychomotor task in which they were asked to press a response key exactly 2 s after the onset of a visual cue. Analyses revealed that cocaine-dependent patients with APD were often premature in their behavioral estimates of time passage. The analysis of a slow EEG potential, viz. the Contingent Negative Variation, recorded over the 2 s time estimation interval, also suggested premature response preparation in the cocaine-dependent, APD-positive group. Correlational analyses revealed that the number of conduct problems reported prior to age 15 was a better predictor of both premature responding and CNV amplitude than either severity of cocaine dependence, alcohol use, or anxious or depressed mood. The potential relevance of these findings for studies of future time orientation and delay discounting behavior are discussed. © 2001 Elsevier Science Ireland Ltd. All rights reserved.

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1. Introduction

A capacity for accurately estimating the passage of time is an important element of everyday life. Accurate time estimation is, for example, important for ensuring that activities, such as conversations, formal meetings, or solitary work, do not interfere with activities or events that follow. Accurate judgments about the duration of an activity are also important in planning and scheduling its reoccurrence. Obviously, external prompts, in the form of time-keeping devices and prompts by other persons, can serve to regulate behavior and inform us about time passage. An impairment in time sense can thereby be overcome, but only if the individual utilizes and responds to such prompts.

An impaired ability to estimate time has been anecdotally, and sometimes formally, linked to various forms of psychopathology. Both depression and anxiety have been related to distortions in time sense, in opposite directions (Hawkins et al., 1988; Meluzzi et al., 1991; von Kirchenheim and Persinger, 1991). Among individuals with psychoactive substance use disorders, an altered time sense has been formally demonstrated. For example, Smart (1968) found that alcoholics performed less well than social drinkers on Wallace's (1956) Future Time Perspective task, which measures the ability to conceptualize the future, in terms of the timing and ordering of future events. Manganiello (1978) described a similar finding from his comparison of 45 adult heroin addicts versus 50 high school students. In addition, Petry and colleagues (1998) compared 34 active heroin addicts to 59 non-drug-using controls. Heroin addicts scored lower than the control

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group on both the Future Time Perspective task and the future orientation subscale of the Stanford Time Perception Inventory (Zimbardo, 1992). In all three studies, substance-abusing patients reported shorter time horizons than the control group. Petry and colleagues (1998) have theorized that shortened time horizons contribute to the disadvantageous preference by substance abusers for smaller immediate rewards versus larger delayed rewards, as well as an underappreciation of the serious, and often delayed, negative consequences of substance abuse (Kirby and Herrnstein, 1995; Madden et al., 1997; Vuchinich and Simpson, 1998; Petry and Casarella, 1999).

To date, there are no studies which have examined the accuracy of time sense among substance-abusing patients who have verifiably discontinued active drug and medication use. Accordingly, it has been difficult to determine whether it originates from the acute effects of psychoactive drugs (Lapp et al., 1994). A disordered time sense may also be related to those personality disorders, including childhood Conduct Disorder and its continuance into adulthood as Antisocial Personality Disorder (APD), which are characterized by impulsivity and/or inattention. Interestingly, childhood Conduct Disorder and adult APD are significant risk factors for substance dependence (Hesselbrock et al., 1985; Malow et al., 1989; Yates et al., 1989; Kleinman et al., 1990; Rounsaville et al., 1991; Weiss et al., 1993) as well as many other forms of adult psychopathology (Robins, 1966; Robins and Price, 1991). Indeed, these premorbid personality factors might mediate the altered time sense that has been attributed to both substance abuse and mood disorders.

The present study is unique in examining the relative contributions of antisocial personality, depression, and anxiety level to altered time sense in a group of cocaine-dependent patients who had demonstrably remained abstinent from cocaine and other drugs for a 1–5 month period. The study also examined the relation between various measures of substance abuse severity and time estimation. None of the subjects enrolled in the present study were under the influence of psychoactive medications at the time of testing.

A second unique feature of the present study was the measurement of the ability to estimate the passage of a fixed interval of time via key press latency. Because of its relative simplicity, a manual key press response may be less dependent than are the aforementioned questionnaires upon group differences in reading skill, verbal comprehension, and motivation. It can also be hypothesized that response latency is a more valid estimate of time estimation ability for actual, discrete events than are perceptions regarding the duration and sequence of events embedded within fictional scenarios.

Yet another unique feature of the present study was the use of electroencephalographic activity recorded continuously throughout the time estimation interval. By constructing a time-point average of the electroencephalogram over trials, one can detect the emergence of a slowly developing negative voltage known as the Contingent Negative Variation (CNV; Rockstroh et al., 1982). The CNV is recordable during periods of time in which subjects are anticipating future events of personal or instructed significance (Ruchkin et al., 1977; Macar and Besson, 1985; Elbert et al., 1991; Hiraku and Sakuma, 1996). Normal subjects with accurate time estimation ability have been shown to exhibit CNVs of a smaller amplitude and slower rise time than normal subjects with poor time estimation ability (Ladanyi and Dubrovsky, 1985). The present study utilized the CNV as an objective marker of time estimation and response preparation.

2. Method

2.1. Subjects

Fifty-seven cocaine-dependent subjects were recruited from long-term residential treatment programs in Hartford, Connecticut. In addition, 26 non-drug-dependent subjects were recruited through newspaper advertisements. All of the subjects signed informed consent agreements approved by the University's Institutional Review Board. They were paid for their time.

Eligibility for the study was initially assessed through a brief interview. To be eligible, subjects were required to demonstrate adequate reading and comprehension skills for completing the informed consent agreement and demographic, drug use, and mood state questionnaires. Potential subjects were excluded if they possessed a lifetime history of a major medical disorder (neurological, hepatic, or cardiovascular); HIV infection; a head injury resulting in a loss of consciousness; seizures (including drug-related seizures); DSM-III-R defined opiate, sedative, or barbiturate abuse or dependence; a major psychiatric illness such as schizophrenia, or bipolar or depressive disorders; or a maternal history of substance abuse or dependence. Uncorrected visual or auditory deficits, and current psychoactive medication use, were also exclusionary.

After the screening interview, potential subjects were transported to the Health Center for a more detailed clinical evaluation and the laboratory study. The clinical evaluation involved two semi-structured psychiatric interviews: the Semi-Structured Assessment for the Genetics of Alcoholism (Bucholz et al., 1994; Hesselbrock et al., 1999) and the Addiction Severity Index (McLellan et al., 1980). The SSAGA permitted the assignment of Axis I and Axis II diagnoses according to DSM-III-R criteria. The ASI provided quantitative measures of alcohol and drug use. In addition, all subjects were

required to complete a number of questionnaires. These included the Michigan Alcoholism Screening Test (MAST; Selzer, 1971), Drug Abuse Screening Test (DAST-10; Skinner, 1982), Beck Depression Inventory (BDI; Beck et al., 1961), Spielberger State-Trait Anxiety Inventory (STAI; Spielberger, 1983), and the Hartford Shipley/Institute of Living Scale (Shipley, 1940).

Based on the results of the interview, the 83 eligible subjects were assigned to one of three groups. Group A was comprised of 20 subjects who met DSM-IIIR diagnostic criteria for both cocaine dependence and APD. Group C consisted of 37 cocaine-dependent subjects who did not meet the DSM-III-R diagnostic threshold for APD. The subjects assigned to Groups A and C were additionally required to have used at least six grams of cocaine per month during the year preceding treatment. They were evaluated after 1–5 months of verified abstinence. Abstinence was verified by urine toxicology and breath alcohol screens performed at frequent (1–2 × /week) and irregular intervals by research staff.

The control group — Group N — was comprised of 26 individuals with no history of substance abuse or dependence and no diagnosis of Antisocial Personality Disorder.

2.2. Procedures

The laboratory study was always scheduled to begin in the morning; the clinical evaluation and interviews followed. On arrival, the subject was asked to provide breath and urine samples for drug screening. If the samples tested positive for the presence of alcohol, cocaine, heroin, amphetamine, or marijuana, then the subject was immediately dismissed from the study.

The subject was escorted into the laboratory where electrodes for recording electroencephalographic and electro-oculographic activity were applied. Tin electrodes were applied to 15 scalp sites (FZ, CZ, PZ, F3, F4, C3, C4, P3, P4, T3, T4, T7, T8, O1, O2). Electrodes of the same type were applied to the tip of the subject's nose (non-cephalic reference), mid-forehead (ground), and in a diagonal orientation above and below the left eye (eye movement). Inter-electrode impedances were maintained below 5 KΩ.

Following the application of electrodes, the subject was escorted into an adjacent room and seated inside a soundproofed chamber. The EEG electrode cap (ECI, Eaton, Ohio) was connected to a bank of amplifiers. The quality of the recording was then verified.

The subject performed a number of cognitive and neurophysiological tests within this laboratory setting. The results of many of these tests have already been described in the literature (Bauer, 1996; Bauer and Easton, 1996; Bauer and Mott, 1996; Bauer, 1997a,b; Costa and Bauer 1997; Easton and Bauer, 1997; Bauer, 1998; Costa and Bauer, 1998). For the presently described test, the subject was instructed that he/she should press a response key to designate the passage of a 2 s interval following the onset of each of 50 cue stimuli. The cue stimulus was the letter 'X' presented in the middle of a computer display for 50 ms. A small fixation spot was presented in the center of the monitor at all other times.

The computer was programmed to present either a 500 or 2000 Hz tone 3 s after response execution. The 500 Hz tone was presented if response latency was within a 500 ms ($\pm$250 ms) window of the designated 2 s target. A 2000 Hz tone was presented if the response latency was outside of this range. The next trial commenced 5–10 s later. Subjects were allowed to practice the task for five to ten trials to verify their comprehension of the instructions.

2.3. Data reduction

Across 50 trials of the task, the number of key press responses were counted within each each half of the 2 s time estimation interval. Responses that occurred more than 2 s after the cue were not included in the analysis because such responses were rare. Expanding the frequency distribution so as to accomodate these rare, late responses would have been problematic for the assumptions of the analysis.

EEG and EOG signals were appropriately amplified (EEG gain = 20 K; EOG gain = 2 K) and filtered (bandpass = 0.01–12.5 Hz). The amplified signals were digitized at a rate of 200 Hz per channel. EEG activity recorded from each electrode site was tested offline for A-D converter saturation and eye movement (peak-to-peak EOG deviation > 50 microvolts) artifacts. A positive test for either condition resulted in the exclusion of both EEG and task performance data for that trial.

A minimum of 20 artifact-free epochs, commencing at stimulus onset and spanning the 2000 ms time estimation interval, were required for the data to be retained for further analysis. The epochs were averaged separately for each electrode site. The averages were then baseline-corrected relative to the average voltage during the initial 20 ms of the post-stimulus period.

CNV amplitude was measured in the averaged waveform within three time periods: 600–610 ms, 1200–1210 ms, and 1700–1710 ms post-stimulus onset. These three periods respectively estimated the amplitude of the early, middle, and late components of the CNV.

As an additional data reduction tool, a principal components analysis was applied to the amplitude of each CNV component. The PCA was used to reveal electrode sites that produced highly intercorrelated activity. As a result, CNV component amplitudes could be averaged across these intercorrelated sites yielding a more reliable estimate of the true amplitude as well as

a reduced likelihood of Type I error. A varimax-rotation of the principal components yielded two factors. The factor structure was the same for the early, middle, and late CNV components. The first factor was comprised of amplitudes measured at posterior electrode sites, viz. PZ, P3, P4, O1, O2, T3, T4, T7, and T8. The other factor was comprised of amplitudes measured at anterior or central sites, viz. FZ, CZ, F3, F4, C3, and C4. Amplitudes were averaged within each factor yielding a single amplitude measure for each combination of the two scalp regions (anterior/posterior) and three CNV components (early/middle/late).

3. Results

3.1. Demographic, psychological, and drug use characteristics

Table 1 summarizes the background characteristics of the three subject groups. One-way ANOVAs were used to evaluate group equivalence on continuous measures. Pearson's Chi-Square test was applied to categorical measures.

On average, the subjects were 33.8 years of age. Approximately 64% of the subjects were male. An identical percentage were members of a racial/ethnic minority. The subject groups did not differ in these demographic features.

The groups did differ significantly with respect to the number of self-rated alcohol [$F(2, 80) = 25.4$, $P < 0.001$] and drug abuse [$F(2, 80) = 229$, $P < 0.001$] problems, and the number of depression [$F(2, 80) = 8.3$, $P < 0.002$] and anxiety [trait: $F(2, 80) = 9.5$, $P < 0.001$; state: $F(2, 80) = 8.5$, $P < 0.002$] symptoms. Tukey *post hoc* tests revealed that the source of these significant main effects could be traced to a difference between the control group and the two cocaine-dependent groups. The cocaine-dependent groups collectively also differed from the control group with respect to the prevalence of paternal substance dependence [$\chi^2_{(2df)} = 10.6$, $P < 0.005$]. Cocaine-dependent groups with versus without APD did not differ on MAST, DAST-10, BDI, or STAI scores.

The cocaine-dependent patient groups did not differ in the percentage of their membership that was also alcohol-dependent or that possessed a paternal history

Table 1
Demographic, drug use, and psychological characteristics of study groups mean ± SD or percent

	Non-dependent APD-negative (Group N)	Coc-dependent APD-negative (Group C)	Coc-dependent APD-positive (Group A)	Test result	Significant pairwise comparisons
N	26	37	20		
Age	35.1 ± 6.2	33.8 ± 6.3	32.0 ± 5.1	$F = 1.4$	
Yrs. of education	14.1 ± 1.8	12.1 ± 1.6	11.1 ± 1.4	$F = 19.6$[a]	N>C, N>A
% Male	61.5	64.9	65	$\chi^2 = 0.1$	
% Caucasian	46.2	37.8	25.0	$\chi^2 = 7.7$	
IQ — Shipley scale	102.8 ± 12.6	92.4 ± 13.3	81.7 ± 10.9	$F = 15.0$[a]	N>C, N>A, C>A
% Paternal addiction	31.8	71.9	75.0	$\chi^2 = 10.6$[a]	N<C, N<A
% Alcohol dependent	NA	51.4	60	$\chi^2 = 0.1$	
Mos. of cocaine abstinence	NA	3.1 ± 1.5	2.8 ± 1.4	$F = 0.4$	
Yrs. of cocaine use	NA	11.9 ± 5.9	12.5 ± 5.2	$F = 0.1$	
# Alcohol problems — MAST	2.0 ± 1.7	12.3 ± 7.2	11.8 ± 7.0	$F = 25.4$[a]	N<C, N<A
# Drug problems — DAST-10	0.2 ± 0.5	7.4 ± 1.8	8.2 ± 1.4	$F = 229.1$[a]	N<C, N<A
Beck depression scale	4.4 ± 4.4	10.1 ± 6.2	9.8 ± 6.3	$F = 8.3$[a]	N<C, N<A
State anxiety — STAI	31.3 ± 8.7	41.1 ± 10.4	38.5 ± 7.7	$F = 8.5$[a]	N<C, N<A
Trait anxiety — STAI	35.9 ± 9.9	45.0 ± 8.3	45.3 ± 8.0	$F = 9.5$[a]	N<C, N<A

[a] $P < 0.05$.

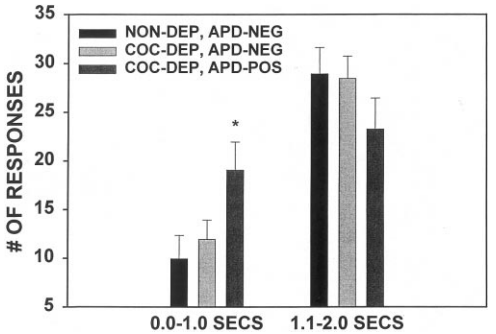

Fig. 1. Average (+1 SE) number of key press responses within each half of the 2 s time estimation interval as a function of Group. *$P < 0.05$.

of substance dependence. The patient groups were likewise similar in the number of years of cocaine use (minus years abstinent) and the number of months of cocaine abstinence. The only variable which differentiated among all three groups was the total IQ score from the Shipley Institute of Living Scale [$F(2, 80) = 15$, $P < 0.001$].

3.2. Task performance

A multivariate ANOVA, with age as a covariate, revealed a significant main effect of Group on reaction time and the number of responses executed within the 2 s time estimation interval [MANCOVA $F(2, 80) = 3.4$, $P < 0.05$]. Univariate ANCOVAs, accompanied by Tukey *post hoc* tests, revealed significantly [$F(2, 80) = 6.5$, $P < 0.005$] shorter reaction times among APD-positive cocaine-dependent subjects (1.09 ± 0.18 s) versus subjects enrolled in the APD-negative, cocaine-dependent (1.27 ± 0.24) and APD-negative, non-dependent (1.27 ± 0.20) groups.

These results were validated by the results of analyzing the number of responses emitted during each half of the time estimation interval. On average, members of the APD-positive, cocaine-dependent group executed significantly more responses during the first half of the time estimation interval in comparison to the members of the two other groups [$F(2, 80) = 2.98$, $P < 0.05$]. During the second half of the interval, the differences among the groups in response frequency were statistically nonsignificant. Fig. 1 illustrates these results.

3.3. CNV amplitude

CNV amplitudes were analyzed separately for the anterior and posterior regions. The analytic method was a 3 (Group) by 3 (CNV component) repeated-measures ANOVA with age as a covariate. The degrees of freedom were reduced by the Geisser-Greenhouse method so as to compensate for violations of the sphericity assumption that are inherent in time-series data. Corrected degrees of freedom are reported. Tukey *post hoc* tests were used to identify the source of significant main or interaction effects.

Analyses of anterior region CNV data revealed a significant interaction between Group and CNV component [$F(3, 30) = 2.75$, $P < 0.05$]. *Post hoc* analyses revealed that the early component of the CNV was significant larger in the cocaine-dependent, APD-positive group (-3.49 ± 6.74 μV) than in the cocaine-dependent, APD-negative (-0.76 ± 3.82 μV) or control (-0.58 ± 1.59 μV) groups. The main effects of Group and CNV component were not significant. Analyses of posterior region CNV data revealed no significant main or interaction effects.

Group-averaged CNV waveforms are presented for all 15 electrode sites in Fig. 2.

3.4. Correlational analyses

In an attempt to identify factors that might amplify or moderate the relationship between APD and impaired time estimation ability in cocaine-dependent patients, a small number of correlations were performed. The factors chosen for inclusion in the correlation matrix were justified on the basis of published speculation or clinical lore. More specifically, the following variables were chosen: depression, anxiety, severity of cocaine use, duration of cocaine abstinence, and the number of comorbid alcohol or drug use problems. In addition, the number of diagnostic criterion items for APD, reflecting both childhood and adult conduct problems, were examined.

Table 2 presents the results of these correlational analyses. As can be seen, only the number of conduct problems reported prior to age 15 (i.e. the number of Conduct Disorder criteria) correlated significantly with reaction time ($r_{\text{partial}} = -0.36$, $P < 0.05$) and early component CNV amplitude at anterior electrode sites ($r_{\text{partial}} = -0.41$, $P < 0.05$).

4. Discussion

The present study demonstrated that cocaine-dependent patients with APD executed more premature responses during a time estimation task than cocaine-dependent patients and non-drug abusing controls who did not meet APD diagnostic criteria. The electroencephalogram of the APD-positive, cocaine-dependent group was also characterized by the emergence of an early, frontally-dominant negativity (see Fig. 2) whose latency coincided with the time period (Fig. 1) containing this excessive number of responses. Cocaine-dependent patients and healthy controls who failed to meet APD diagnostic criteria exhibited a smaller electroencephalographic change of this type. The identical