Postreinforcement synchronization: Quantitative analysis of amphetamine effects¹

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Low doses of amphetamine (.25, .50, & 1.00 mg/kg i.p.) produced decrements in postreinforcement synchronization (PRS), but increased high voltage activity during nondrinking conditions. At 2.00 mg/kg the drug caused refusal to drink together with an increase in low-voltage activity during a nondrinking period. The complex array of amphetamine effects on ECG are discussed.

It has been noted by a number of investigators (e.g., Hess et al, 1953; Buchwald et al, 1964; Clemente et al, 1964; Rosen & Marczyński, 1967) that transient high-voltage slow-wave electrocortical activity (ECG) typically accompanies alimentary behavior in the cat. Clemente et al (1964) termed this effect post reinforcement synchronization (PRS). In an attempt to determine the underlying neurochemical substrates of this somewhat puzzling ECG phenomenon Rosen & Marczyński (1967) used alpha methyl meta tyrosine, a drug that produces a selective long-term depletion of brain norepinephrine, and reported an initial marked enhancement (10 min-1 h) followed by a rather long-term (48-h) diminution in the amplitude and duration of the PRS effect.

In none of the previous studies, however, was a digital analysis of the ECG data made. The ECG records are typically examined by eye and estimates of activity changes are analyzed. The present study reports a preliminary attempt to digitalize the PRS effect and to determine quantitatively, in line with the previous findings of Rosen & Marczyński (1967), if an adrenergic central nervous system stimulant (dextroamphetamine) would differentially affect the PRS and the normal resting ECG.

SUBJECT AND APPARATUS

A single adult male mongrel cat, weighing 4.3 kg, was used. Testing was conducted in a large EEG test chamber (LVE Model 1488) with a full-side one-way observation door. A Grass Model 7 polygraph recorded electrocortical activity via Microdot cables connected to the S through slip rings and Winchester plugs. BRS Digibit solid state modules were used to construct a digital EEG analyzer that counted spikes of different voltages. Schmitt triggers and emitter-followers were calibrated to pick up voltages of at least 10, 20, and 50 or more microvolts from Pin J7 of the polygraph driver amplifier and these voltages were

translated to digital counts recorded on mechanical counters. A series of solid state relays, multivibrators, and flip-flops provided precise control over the recording duration.

PROCEDURE

The S was surgically prepared, under pentobarbital anesthesia, with silver ball cortical recording electrodes embedded in the calvarium overlying the lateral (marginal) gyrus (AP 2.0, L 2.0), ectosylvian gyrus (AP 10.0, L 15.0) and posterior sigmoid gyrus (AP 23.0, L 4.0) of each hemisphere. The electrodes were soldered to a Winchester connector via copper wires and the entire assembly was cemented to the skull with dental acrylic.

Following a 2-week recovery period the S was given daily exposure periods to the test cage for another 2 weeks and was placed on a 23-h food and water deprivation schedule. During these daily periods the S was allowed access to 100 cc of milk ($\frac{1}{2}$ regular and $\frac{1}{2}$ condensed). Following this, it was placed back in its home cage and allowed 1 h of water and Teklad cat diet. Testing began once the S displayed no hesitation in consuming the milk when placed in the cage.

Daily testing consisted of three 100-sec recording periods. The first period occurred 15 min after the S was placed in the cage. Fifteen minutes later milk was introduced and a second recording was made. If the S stopped drinking for any reason the recording was stopped and continued again with the S's resumption of drinking. The milk dish was then removed and 15 min later another 100-sec record was sampled. Bipolar recordings from each cortical area were taken continuously. The 100-sec periods refer to the onset and offset of the counters which monitored only the lateral gyrus records since PRS was typically confined to this area.

On control days no injections were administered. On injection days the S, immediately prior to placement in the test cage, was injected with d-amphetamine (0.25, 0.50, 1.00 or 2.00 mg/kg i.p.)

dissolved in isotonic saline or a 2-cc saline placebo. The order of test days was randomized and the S received a total of 6 control days (saline or no injection) and 7 drug days (two at each dose except for 2.00 mg/kg at which only one test was run since the S refused to drink any milk). At least 2 days intervened between drug injections. On injection days a fourth recording period was added as a further control. This period preceded drug administration by 15 min providing a control on the drug day itself. Thus on drug days a predrug control record (15 min prior to injection), a postdrug control record (15 min following injection), a postdrug drinking record (30 min following injection) and a second postdrug control period (45 min following injection) was taken. In all cases, number of spikes at 10, 20, and 50 μ V or above were recorded for each 100-sec period.

RESULTS

The PRS phenomenon manifested itself very consistently with each milk consumption as an increase in the number of both 20- and 50- μ V spikes with a concomitant decrease in the number of 10- μ V spikes compared to both pre- and postdrinking periods (Table 1). T tests for correlated samples yielded significance in each case ($p < .01$). No differences were obtained ($p > .20$) between pre- and postcontrol nondrinking measures and the predrug nondrinking control measures.

Figure 1 presents the effects of the different doses of amphetamine on the 50- μ V activity for both drinking and nondrinking periods. In each case there is a dose-dependent decrease in number of 50- μ V spikes (high voltage slow). However, in the case of the drinking period, all doses lead to a reduction in activity as compared to control. There is no data point for the 2.00 dose since the S did not drink. In the case of the nondrinking activity, however, there is an increase in activity as compared with control for all but the 2.00 dose. Throughout, the amount of high voltage

Table 1
Mean No. of Spikes in 100 sec for Control and Amphetamine (.25, .50, and 1.00 mg/kg combined) Conditions

	10 microvolts	20 microvolts	50 microvolts
Control - N ^a	397.0	133.7	36.5
Control - D	298.8	202.0	187.8
Amphetamine - O	400.7	140.7	29.2
Amphetamine - N	343.2	132.0	58.8
Amphetamine - D	341.0	166.8	99.8

^a N = Nondrinking period (pre and post); D = drinking period; O = predrug nondrinking control period

Fig. 1. Mean number of 50- μ V spikes for drinking and nondrinking conditions during control (0) and amphetamine (.25, .50, 1.00, and 2.00 mg/kg) conditions.

activity is always greater during drinking than nondrinking periods.

The 10- μ V activity (low voltage fast) shows a concomitant decrease across the three low doses ($p < .01$). However, at 2.00 mg/kg, there is an increase in number of 10- μ V spikes. No significant changes in 20- μ V activity were observed for either drinking or nondrinking under the drug.

A comparison of drinking vs nondrinking activity within the drug days themselves across all three low doses revealed no change in 10- μ V activity and a significant increase in both 20- and 50- μ V activity for the drinking period ($p < .01$ in each case). These increases in the higher voltage activity under the drug were not as great as occurred under control conditions as is evident from Table 1. The differences between drug and control drinking conditions did not reach significance for either 10 or 20 μ V, but did for the 50- μ V condition ($p < .01$).

DISCUSSION

Amphetamine is generally classified as a stimulant that causes a desynchronized EEG characteristic of an arousal state (Goodman & Gilman, 1965). This represents a change in the resting electrocortical activity which is

typically in a high-voltage/slow-frequency (HVS) state to one of low voltage/fast frequency (LVF). In the present study no analysis of frequency changes was made and only voltage changes will be discussed.

The PRS in the present study was clearly reduced in magnitude by low doses of amphetamine which, however, did not cause its complete abolition, although an absence of drinking was noted at the highest dose used. These data are consonant with the author's previous suggestion (Rosen & Marczyński, 1967) that stimulation of the reticular formation, the structure upon which amphetamine is presumed to act to cause its arousal effects, will in turn antagonize those brain stem synchronizing mechanisms (Routtenberg, 1966) that presumably mediate the PRS. These data also lend support to the hypothesis that norepinephrine (NE) is involved in antagonizing PRS since amphetamine releases NE into the brain tissue (Glowinski & Axelrod, 1965).

The consistent yet complex array of data reported in the present study makes it difficult to describe in a simple and unitary fashion the effects of amphetamine on

electrocortical activity. Only at a dose of 2.00 mg/kg was there an increase in low-voltage spikes. At the lower doses there was a decrease. Additionally, in spite of the increase at low doses on nondrinking higher voltage ECG, there was a decrease in the higher voltage activity associated with drinking. Perhaps the approach of psychopharmacologists should be followed by analysts interested in EEG-drug effects. Dews & Morse (1961), for example, have noted that amphetamine has different effects on behavior depending on the control rate of responding, i.e., it increases low rates of responding while decreasing high rates of responding. Analyses of drug-EEG effects should consider control EEG activity as well as drug dose. It is clear from the present data that no general statement regarding the effect of amphetamine on the ECG can be made. Further experimentation is necessary to determine the generality of these results for other drugs.

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