THE EFFECT OF AMPHETAMINE ON HIPPOCAMPAL EEG AND EOG ACTIVITY IN CATS

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Key words: amphetamine, hippocampal EEG, EOG, arousal, cat

Abstract. The effect of anorectic dose of amphetamine on some correlates of arousal (hippocampal EEG and EOG activity) was examined in cats. After injection of amphetamine the frequency of hippocampal rhythmic slow activity and EOG activity increased when preinjection value of rhythm slow activity was low, but decreased when it was high. Thus, amphetamine anorexia may be accompanied with an increase as well as with a decrease of arousal level.

INTRODUCTION

Amphetamine (AMPH) is generally assumed to act on brain monoaminergic mechanisms; anorexia, stereotypic behavior and other changes in motor activity are typically described after AMPH injections in rats and cats (1, 3, 4, 6, 7, 13, 14, 16, 17, 24, 26, 27). The above mentioned behavioral effects of administration of this drug may appear separately or simultaneously. The total pattern of the AMPH induced response seems to be dependent on the dose as well as on the experimental situation (6, 24).

The feeding-depressant effect of AMPH is explained, among others, on the basis of changes in arousal level: it is assumed that AMPH causes anorexia by increasing the level of arousal beyond the range which is optimal for alimentary behavior (23, 26). That explanation has been proposed in spite of the fact that the effect of AMPH on some behavioral
and electrophysiological correlates of arousal (10, 12) is still not well documented. To answer this question, in the present study we attempted to determine the effect of i.p. AMPH treatment on hippocampal EEG and oculomotor activity (EOG). According to some data (5, 10, 12, 18), hippocampal RSA frequency and EOG activity may be regarded as good indicators of the level of unspecific excitation in cats. Therefore we used these measures of arousal in our experiments.

MATERIAL AND METHODS

Subjects and surgery. The experiments were carried out on eight male, adult cats. Bipolar stainless steel teflon coated electrodes (250 μm in diam) were implanted into dorsal hippocampus (A = 4.5, L = 5.0, \( H = + 7.0 \)) according to Jasper and Ajmone-Marsan's stereotaxic atlas (11). Stainless steel ball electrodes (1.0 mm ball diam) were placed epidurally over frontal and occipital cortex. Additionally, one ball electrode, serving for recording the oculomotor activity was implanted under the orbital bone behind the eye ball. Some details of the surgery were described earlier (5, 8).

Apparatus and recording. The experiments were performed in 120 × 60 × 60 cm experimental cage with transparent front wall and ceiling, placed in semi-soundproof chamber. The behavior of the animals was observed on closed circuit TV. Hippocampal and cortical EEG, EOG, head movements and general motor activity were recorded on an 8-channel electroencephalograph (ORMED, Łódź, Poland). Motor activity was recorded with the electropneumographic method (8) and head movements were recorded with the use of the “free cable” technique (15). Spectral analysis of the hippocampal EEG was performed on line by means of an analyzer equipped with a series of nine filters (bandwidth of 1 Hz in the range from 1 to 8 Hz, and 2.0 Hz from 8 to 12 Hz). An integration unit was used for obtaining frequency histograms (power spectra). It was triggered automatically after each 30 s period of the analysis.

Procedure. Recordings started 2 weeks after the surgery. After 5 min of the control (preinjection) recording each animal was injected i.p. with 2 mg/kg of the DL-amphetamine sulphate (Psychedrinum, Polfa). AMPH was dissolved in a sterile 0.9% NaCl solution used as a vehicle. Only one dose of the drug was tested in each animal; we chose that dose as effective in evoking AMPH anorexia in the cat (13, 14, 26). Starting 5 min after the injection, 5 min periods of continuous recording were separated by 5 min intervals. Recordings were finished 90 min after the injection. The order of i.p. administration of the AMPH and vehicle was
as follows: 0.9% NaCl, AMPH, AMPH, 0.9% NaCl, AMPH, AMPH. The animals received not more than two injections a week.

The experiments were always performed on 23 h food deprived animals. After 90 min of recording each animal had free access to solid food (barley with boiled meat) and milk for 1 h. At this time only was the attitude of the animals to food and milk examined.

- Data analysis. The estimation of results was based on the behavioral and electrophysiological data obtained from four 5 min recording periods: 5 min before the injection (control), 10–15 min, 40–45 min, and 70–75 min after AMPH or vehicle solution administration. These periods were chosen as the most representative for evoked changes.

The following measures were used for the evaluation of AMPH effects: (i) APF — approximate peak frequency of the power spectra of the 5 min hippocampal EEG sample. This value was estimated with a method based on the interpolation procedure described by Arnolds et al. (2), (ii) EOG — summed duration of the oculomotor activity was obtained by measure of the number of eye movements per 5 min: each clear cut downward and upward deflection on EOG channel was regarded as one eye movement (Eμn). Some details concerning the estimation of rhythmic slow activity (RSA) of the hippocampus (APF) and EOG were described earlier (5, 9). As we have not found any significant changes in cortical EEG, and since the head movements were well correlated with EOG, those records were not analyzed quantitatively. The general motor activity was helpful in the qualitative analysis of the animal’s behavior, but was not statistically analyzed, either. Two way analysis of variance (21) was used for statistical evaluation of the data. Detailed comparisons were made with Wilcoxon and Mann-Whitney tests (21). A correlation between EOG and RSA frequency was examined with the use of the Kendal rank correlation coefficient (21).

RESULTS

Since behavioral and electrophysiological effects of the AMPH treatment were dependent on the animal and on the day of recording, at the beginning we described some differences in the animal's responding to the administration of the drug. A detailed analysis of results was based on the number of recording sessions with a similar pattern of changes after the injections.

RSA frequency, EOG and general behavior of cats after AMPH injection. Before the injection of AMPH (in the control period), the cats usually sat on hindlegs or lay on paws. From time to time they stood up and maintained a free-ranging exploratory behavior. The RSA fre-
frequency (expressed as APF value) from $3.41 \pm 0.27$ Hz to $4.02 \pm 0.20$ Hz. In the early postinjection period a gradual decrease in motor activity was observed in each animal. Ten to fifteen minutes after the injection, all animals decreased their free-ranging exploratory behavior and, typically, remained immobile sitting in the same place of the experimental cage. In four cats, after the first or first and second injection of AMPH, the total immobility was accompanied by a decrease in APF value, and by a drop in the number of head and eye movements (this pattern of behavior was observed in six recording sessions). In the other four cats after each injection of AMPH the frequency of RSA, the EOG activity and the number of head movements increased. The character of the observed head movements was earlier described in cats as "side to side looking stereotypy" (22). The same behavioral and electrophysiological

![Graph A](image1)

**Fig. 1.** RSA frequency (A) and EOG activity (B) in cats after ip amphetamine injections (2 mg/kg). 1, amphetamine injections when decrease in APF value and number of head and eye movements were observed ($n = 6$); 2, NaCl injections ($n = 10$); 3, amphetamine injections when increase in APF value and number of head and eye movements were observed ($n = 18$); *P* < 0.05; **P** < 0.01, vs. with preinjection level, Wilcoxon two-tailed test.
responses were also noticed after successive AMPH administrations in four earlier mentioned cats (totally, this pattern of behavior was observed in 18 recording sessions). It is necessary to emphasize that in all cases changes in RSA frequency were related to changes in EOG activity and to the number of head movements (Fig. 1). However, when a detailed analysis with the Kendall rank correlation coefficient was performed separately for the data obtained from successive recording sessions, a strong positive correlation \((r = +1, n = 4, P < 0.05)\) was found between the APF and EOG values in four out of eighteen cases, when the increase in recorded activities was noticed (Fig. 2).

In order to analyze the AMPH effects in greater detail, we grouped all obtained data according to the type of changes in behavior (increase vs. decrease in all measured activities) after AMPH injection. As it appeared, the type of drug effect on the investigated parameters was related to the preinjection value of RSA frequency and EOG activity (Fig. 1): the increase in APF, EOG activity and in the number of head movements were related to the preinjection RSA level and EOG activity; a decrease in both was associated with a decrease in these parameters. This indicates that AMPH is a potent agent capable of modifying the baseline activity of RSA and EOG, with the effect being related to the preinjection level of these parameters.
movements was typical when the preinjection RSA frequency was $3.41 \pm 0.24$ Hz and the number of eye movements was on an average $278 \pm 120$ Em) 5 min; the opposite pattern of changes occurred when the RSA frequency before the injection was $4.02 \pm 0.20$ Hz and number of eye movements on an average $497 \pm 160$ Em) 5 min. In the four earlier mentioned cats the first or the second injection evoked a permanent decrease in RSA frequency and EOG activity, but a successive administration of the drug produced an opposite effect. However, in spite of clear-cut differences in RSA frequency before the AMPH administration (Mann-Whitney test, $P < 0.02$, Fig. 1, curve 1 vs. 3), the values of APF observed in first hour after the injection of AMPH were almost the same in each case (Mann-Whitney test, Fig. 1A, $P > 0.05$, curve 1 vs. 3). A significant difference (Mann-Whitney test, $P < 0.05$, Fig. 1A, curve 1 vs. 3) was found in the second hour after the injection (70–75 min). All animals tested 90 min after the AMPH injection completely refused to ingest food. Hypervigilant and looking from side to side, they paid no attention to the food bowl in the experimental cage.

DISCUSSION

In the present experiments we confirmed the findings that RSA frequency correlates well with the changes in EOG activity (9) and the number of head movements (19). However, independently of the pattern of the electroencephalographic and EOG response, AMPH resulted in a total lack of locomotor activity, which is in contrast with some reports from rats (25).

The primary aim of the present study was to determine the effect of i.p. AMPH treatment on the level of arousal. Since some data (5, 10, 12, 18) justified the acceptance of the hippocampal RSA frequency and eye movements as good indicators of unspecific excitation in cats; we used these measures of arousal as well. It was rather surprising to find that AMPH injected in a dose that caused anorexia (i.e., the lack of spontaneous eating) in cats increased the RSA frequency and EOG activity when the preinjection APF value was low ($3.4 \pm 0.27$ Hz), but led to a decrease of these parameters when it was high ($4.02 \pm 0.20$ Hz). These results are interesting in light of other data obtained on rats (20), in which it was found that i.p. AMPH injections could evoke either motor hyper- or hypoactivity: the two opposing effects of the drug were dependent on the behavioral background (low vs. high level of motor activity) on which AMPH acted. Our results and those mentioned above indicate that the preinjection state determines the effect of AMPH on some be-
behavioral and electrophysiological responses of the animal; it may increase
the level of arousal when that observed before the injection is low, but
leads to a decrease when the level of unspecific excitation is already
high. It should be stressed, however, that in our experiments, indepen-
dently of the initial RSA frequency and EOG activity, the values of
these indices attained as soon as 10–15 min after AMPH treatment were
similar in all cases. Moreover, the mean level of arousal obtained after
AMPH administration did not exceed in 23 h food deprived animals the
preinjection maximal level which did not interfere with food intake.
Both the cause of the opposing AMPH action (increase or decrease of
arousal) and the relation between this phenomenon and related anorexia
remain an open question. In any case, if we assume that RSA frequency
and the number of eye movements are good indicators of unspecific ex-
citation, the obtained results give no reason for explaining the AMPH
induced anorexia in terms of increased or decreased level of arousal.

The results were presented at VII European Neuroscience Congress of European
Neuroscience Association (ENA), Hamburg, September, 1983.

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Accepted 1 October 1985