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Effect of Acute Alcohol Treatment on Dopamine Concentration in Corpus Striatum of Rats: a Voltammetric Study

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Summary

A voltammetry technique has been used to determine changes in dopamine release in the rat corpus striatum after two doses of ethanol administration. The dopamine oxidation current reached a maximal value at 30 min after the first alcohol dose with a subsequent decrease towards the initial level at 60 min and kept to the basal level with a statistically insignificant oscillation. When a second dose of alcohol was applied at 60 min, it was followed by a decrease of the dopamine oxidation current peak to 50 % of the initial value after another 60 min observation. The results resemble the known effect of alcohol on human behaviour (excitation followed by depression).

Key words

Rats – Alcohol treatment – Dopamine in Striatum – Voltammetric determination

Introduction

Statistical data have suggested that consumption of alcohol as a drug represents a grave world-wide health care problem (Davis *et al.* 1987); at the same time, it is one of the most frequent psychiatric disturbances occurring in both males and females in several geographical regions (Mayers *et al.* 1984).

Although the effect of acute and chronic alcohol consumption on a number of physiological functions, including biochemical changes (Tremoliers *et al.* 1973) and behaviour (Liljequist and Engel 1977), has been described in detail and the clinical manifestation of alcoholism are well known, the pathophysiological mechanisms have not been exactly defined in many cases, as yet. Several experimental animal studies (Begleiter 1975, Wise 1975) have suggested that the mechanism underlying the alcohol effects in the central nervous system might also be associated with the influence on the concentration, release and/or metabolism of biogenic amines in the cerebral tissue (e.g. Ylikahri *et al.* 1978).

The present paper deals with the effect of acute alcohol administration to rats on changes in extracellular dopamine concentration in the corpus striatum as detected by voltammetry.

Material and Methods

Eight SPF male Wistar rats weighing 300 g, fasting 12 hours before the experiment, were used. The animals were anaesthetized with chloral hydrate (400 mg/kg b.w.) and 30 min later they were mounted in a stereotaxic apparatus. A hole was drilled into the skull, the dura and the pia mater were pierced and an electrochemically prepared working microelectrode (Gonon *et al.* 1981) was stereotaxically inserted (Fifkova and Marsala 1957) into the corpus striatum (AP-1.0 mm, L 2.3 mm, V 4.0 mm). The working carbon microelectrode was made of pyrolitic carbon fibre (7 μm in diameter) insulated in a glass micropipette with a length of the exposed tip of 200 μm. The additional and reference Ag/AgCl electrodes were in contact with the dura, and were attached to the bone with minute inox steel screws.

A differential pulse voltammetry technique was used for electrochemical analyses (PA4, LP Praha) – with the following parameters: linear potential sweep from -100 mV to 500 mV, scan rate 50 mV/s, pulse amplitude 50 mV, pulse duration 60 ms, pulse period 0.2 s. Measurements were repeated in 10 minute intervals.

The oxidation potential peak values obtained during the first 40 min were taken as 100 % initial value. Subsequently, the animal received, *via* gastric tube, ethanol diluted with physiological saline (0.15 g/kg b.w. in total volume of 2 ml/ and voltammogrammes were recorded over the next 60 min. After this interval, the animals received a repeated ethanol dose (the same concentration and volume as previously) and voltammogrammes were taken over additional 60 min.

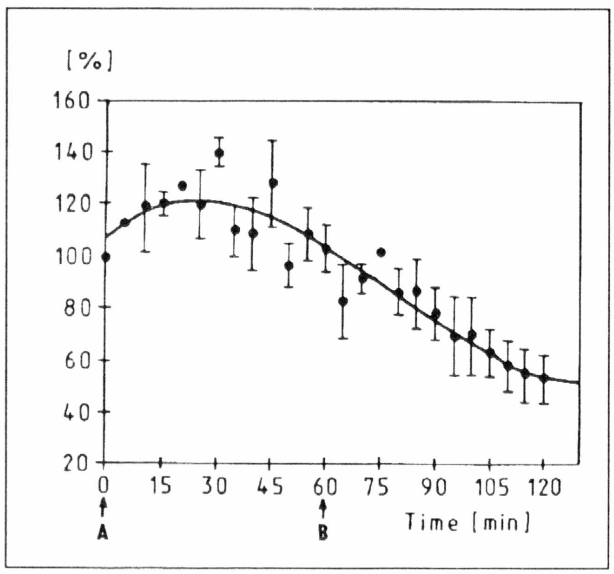

Fig. 1
Third order regression line of dopamine oxidation current (S.E.M.) after first (A) and second (B) dose of alcohol administration (n=8). Statistical significance calculated against initial value (0 min), at 30 min ($p < 0.01$) and 120 min ($p < 0.01$).

A parallel group of rats was cannulated (into the tail artery) and received the same alcohol dose as did the experimental group. Blood was taken at 60 and 120 min of ethanol administration and sent for chromatographic determination of blood ethanol concentration (Institute of Forensic Medicine, Comenius University Medical School, Bratislava).

Changes in dopamine oxidation potential were expressed as percentages of the control value. Third-order regression line was constructed (Sigmaplot V.10 Jandel) and Student's t-test was used to evaluate the results. Mean values and standard errors are shown).

Results

The analysis of blood alcohol levels showed an increase from zero levels (control samples) to 0.20 % and 0.35 % at 60 and 120 min respectively.

The centre of the ascorbic acid oxidation potential peak was detected at +120 mV, and that of dopamine at +380 mV polarizing voltage. At preliminary calibration, the +380 mV peak increased upon microinjection of 2 nm solution of dopamine standard into the vicinity of the working microelectrode impaled into the striatum.

The dopamine oxidation current reached a maximal value at 30 min after the first alcohol dose (140 % as compared to the control value, $p<0.01$, see Fig. 1), with a subsequent decrease of dopamine oxidation current amplitude towards the initial levels at 60 min following the first alcohol administration. In our previous experiments we found, that after a single alcohol dose the increased dopamine oxidation current values – after decreasing back to initial levels – keep oscillating from 3 to 5 % around the initial levels for the next 1-2 hours (Murgaš and Diaz 1991).The second alcohol administration was followed by a decrease of the dopamine oxidation current peak amplitude, reaching 50 % of the initial value at 120 min.

Discussion

None of the techniques used previously to monitor the dynamics of neurotransmitter concentration in neuronal tissue structures could fully reflect these processes. For example, the widely used punch technique (Palkovits 1973) allows postmortem biochemical analysis of neurotransmitter concentration in defined nuclei or substructures of cerebral nuclei; however, the data thus obtained refer to total contents of the respective structure supplying only an indirect picture of the dynamic pattern (Murgaš at al. 1989). The push-pull cannulation technique or intracranial microdialysis(Goddum 1961), while offering the possibility of abandoning postmortem analysis of neurotransmitter turnover, presents a number of problems, mainly concerning the establishment of balanced inflow/outflow of the perfusion liquid and washout of neurotransmission products (Redgrave 1977).

The voltammetric technique is only moderately invasive as far as mechanical damage to the structure is concerned and from 15 to 20 minutes after implantation of the electrodes the oxidation current becomes stabilized for many hours provided no external stimulation occurs (Murgaš *et al.* 1989); on the other hand, acute experiments require anaesthesia the effect of which is but incompletely defined. In chronic experiments, restraint is unavoidable to prevent the animals damaging the leads connecting them to the analyzer.

The choice of routes of alcohol administration (peritoneal or intragastric administration) presents no problems in our experimental layout: the previous experiments showed that oxidation current amplitudes in anaesthetized animals are not affected by either of the two routes of administration. The intragastric administration emulates, to a certain degree at least,

the most common route of alcohol ingestion and the absorption rates (Wise 1977).

Alcohol administration has a significant effect on the turnover of biogenic amines both in the periphery and in the central nervous system. Vogel and Mokhtari (1983) observed decreases of plasma noradrenaline and adrenaline levels following peritoneal administration of low alcohol doses (0.5 g/kg), whereas the levels of the two transmitters were reported to increase following larger doses. Alcohol administration is also followed by changes in biogenic amine concentration also in the nervous system; changes in the hypothalamus subsequently affect secretion of the pituitary tropic hormones (De Turck and Vogel 1982).

The increased amplitudes of dopamine oxidation currents observed during the first 60 min after alcohol administration, with a maximum at 30 min, and the gradual decrease, especially after the repeated dose, resemble the known effect of alcohol on human behaviour. During the first postalcohol consumption stage excitation appears (due to reduced tension as claimed by several investigators, e.g. Cappel and Herman 1972), followed by a general depression during the later stages although a direct correlation between dopamine oxidation current peaks and locomotor activity is not necessarily causal. Indirect correlation concerns the decreased noradrenaline and adrenaline levels in the hypothalamus at 5 and 10 min after alcohol administration to rats as reported by Vogel and Mokthari (1983), and the raised dopamine release from the striatum during the early stages after alcohol administration observed in our experiments. Even if the structures are not identical, it is probable that the toxic effects of alcohol on neural tissues are universal, very likely due to changes in the level of nerve cell membrane polarization (Murgaš and Pavlásek 1989).

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