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SINGLE ELECTROCONVULSIVE SHOCK AND DOPAMINE AUTORECEPTORS

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SUMMARY

Dopamine (DA) autoreceptor downregulation has been suggested to mediate the therapeutic effect of antidepressant treatments including electroconvulsive therapy (ECT). Suggestion has also been made that a single ECT may have antidepressant potential via such a mechanism. The present study was therefore conducted to assess the effects of a single electroconvulsive shock (ECS) on dopamine autoreceptors in the rat brain. Using the low dose, apomorphine-induced hypomotility behavioural paradigm, DA autoreceptor function was studied one and eight days after a single true ECS, and 8 days after a single sham ECS. No significant difference was observed between the groups. The results suggest that single ECS exerts neither acute nor time-dependant DA autoreceptor effects; however, the issue in certain aspects remains open for further study.

The cognitive adverse effects of electroconvulsive therapy (ECT) are a source of concern to clinicians, and have necessitated the search for techniques of ECT administration which, while maintaining optimal efficacy, are associated with reduced cognitive morbidity. Towards this end, modification of stimulus parameters and electrode placement have been recommended, but a newer approach has been to deliver fewer treatments, spaced at wider intervals, with the expectation that the beneficial effect of ECT is time dependant. As an extension of this concept, the administration of a single ECT has been mooted for the management of endogenous depression (Andrade, 1990).

Depression, the most important indication for ECT today, has been characterized as a hypodopaminergic state, and amelioration of depression by antidepressant drugs or ECT has been suggested to result from enhanced dopaminergic neurotransmission (Willner, 1983; Swerdlow and Koob, 1987).

The present study therefore sought to assess the acute and time-dependant effects of a single ECS on dopamine (DA) autoreceptors in the rat brain.

Material and Methods

The methodolgy adopted in the present study was the same as that in an earlier study (Andrade et al., 1990), except for the following: (1) low-dose apomorphine (100 g/kg) was used as a specific DA autoreceptor challenge (Srinivasan et al., 1989), (2) saline or apomorphine-injected animals were monitored 1 and 8 days after a single true ECS, and 8 days after a single sham ECS, in a factorially designed experiment. (3) Two computer-assisted parameters of motility were scrutinized: distance travelled, and time spent resting, by the animals during the period of monitoring.

Results

The intensity of the delivered current ranged from 20 to 50 mA depending on the interelectrode impedances, and the duration of the motor seizure ranged from 15 to

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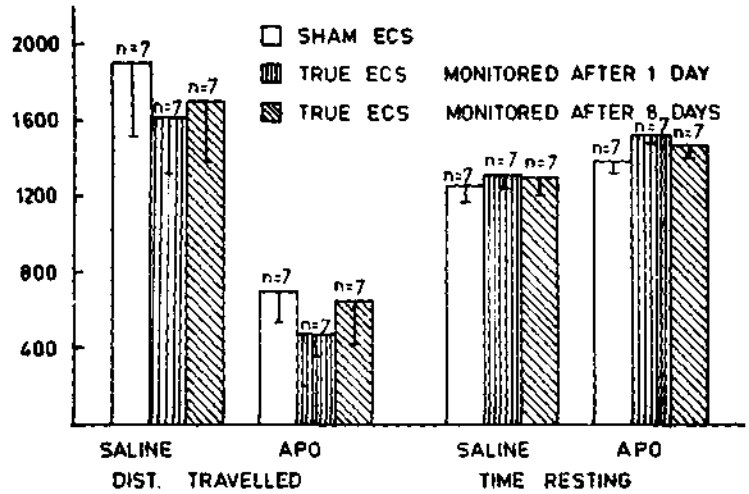

Mean-SEM distance travelled (cms)/time spent resting (secs) by saline and apomorphine-injected rats in true (monitored 1 and 8 days after ECS) and sham (monitored 8 days after ECS) single ECS-treated groups.

25 secs. By conventional standards, therefore, all animals received adequate stimuli and experienced adequate convulsions.

The 'distance travelled' and 'time resting' data in each of the 2 true and 1 sham ECS-treated categories are presented in the figure. A two way ANOVA revealed, expectedly as low dose apomorphine is known to sedate via DA autoreceptor mechanisms), a significant drug effect ($p < 0.001$), but neither a significant main effect for ECS nor a significant ECS × drug interaction in either, 'distance travelled' or 'time resting' paradigms. In other words, while the expected apomorphine effect was obtained, there was neither acute nor time-dependant ECS effect observed.

Discussion

The absence of consensus in the field stimulated these attempts to study the effects of a single ECS on DA autoreceptors. Chiodo and Antelman (1980), using an electrophysiological approach, found that a single ECS produced no discernable change one hour after its administration, while significant DA autoreceptor downregulation resulted 8 days later. In a comparable study, Tepper et al. (1982) reported that a single ECS downregulated DA autoreceptors 1 day later, which effect was also observable 8 days later.

Behavioural approaches have however failed to confirm these findings. Serra et al. (1981) demonstrated that a single ECS did not alter DA autoreceptor functions 1 apd 2 days later, while Creese et al. (1982) reported that a single ECS produced no delayed effect on these receptors.

The present study, also a behavioural approach although differing in methodology, confirmed that a single ECS produces neither acute nor time-dependant change in DA autoreceptor functioning. It would therefore seem that single ECS-induced time-dependant dopaminergic effects are confined to DA postsynaptic receptors (Andrade et al., 1990). It would further seem that the DA autoreceptor hypothesis for mechanism of action of ECT (Chiodo and Antelman, 1980; Wilbur, 1983) is less robust than believed, as earlier suggested (Gangadhar et al., 1989).

While these findings are important for the understanding of the mechanism of action of ECT, other neurotransmitter systems also need to be investigated for time-dependant effects of a single ECS, as such may have an important bearing on the optimal reduction in the number of ECTs required to produce a given clinical response.

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