On the mechanism of action of electro-convulsive therapy: some behavioural and biochemical consequences of repeated electrically induced seizures in rats

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It is established that electro-convulsive therapy is an effective treatment for depression (M.R.C. 1965) although the role of the convulsion in the therapeutic effect is less clear and the mechanism of action remains obscure. However, recent studies have shown that repeated electrically induced convulsions in rats and mice potentiate behavioural responses mediated by brain monoaminergic systems (reviewed by Grahame-Smith, Green & Costain, 1978).

In the present experiments groups of rats were given 10 daily electroconvulsive shocks (150V; 50^c/s; 3 s) through crocodile clips applied to the ears and under halothane anaesthesia (ECS group). Control rats received anaesthetic only (Sham ECS group). Behavioural and biochemical measurements were carried out 24 h after the last shock. We confirmed the report of Evans, Grahame-Smith, Green & Tordoff (1976) that ECS rats ($n = 11$) show a slight but significant enhancement of the behavioural response (assessed by ratings of components of the behaviour) to increased dopamine synthesis following treatment with a monoamine oxidase inhibitor (tranylcypromine 10 mg/kg) and L-DOPA (50 mg/kg) compared to sham ECS rats ($n = 10$). In addition ECS rats ($n = 8$) were hyperactive in an open-field test compared to controls ($n = 8$).

Since repeated ECS has been reported to enhance behavioural responses to directly acting 5-HT and dopamine receptor agonists and does not affect 5-HT or dopamine synthesis, it has been suggested that the treatments either increase monoamine receptor sensitivity or change activity in a system modulating monoaminergic neurotransmission. The former possibility was evaluated by measuring [^{3}H]-LSD binding in membrane preparations of cortex and [^{3}H]-spiperone binding in striatum in ECS ($n = 11$) and Sham ECS ($n = 10$) treated rats. No differences emerged on these measures of 5-HT and dopamine receptor sensitivity. In addition possible ECS effects on monoamine modulating acetyl choline GABA and benzodiazepine receptor systems were investigated. However, no differences between groups were found in [^{3}H]-QNB, [^{3}H]-GABA or [^{3}H]-diazepam binding in the cerebral cortex. GABA concentrations in cerebral cortex were also unaffected by the ECS treatments.

The results confirm that repeated convulsions in rats increase functional dopaminergic neurotransmission. However, the results also rule out the possibility that ECS potentiated behavioural responses to monoamine agonists are due to generalized ECS effects on dopamine or 5-HT receptor sensitivity. Furthermore, acetyl choline, GABA or benzodiazepine receptors which may interact with monoaminergic neurotransmission are unaffected by repeated ECS.

References

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An iontophoretic study of the cholinoceptive properties of respiratory neurones in the rat medulla

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Units whose discharge pattern can be related to some phase of the respiratory cycle have been located in the cat medulla (Cohen & Wang, 1959, Merrill, 1970). Investigations of the pharmacological properties of these neurones by microiontophoresis include the effects of acetylcholine GABA and glutamate (Denavit-Saubie and Champagnat, 1978 and Kirsten, Satayavivad, St. John & Wang, 1978). The present study was undertaken to investigate the cholinergic properties of medullary respiratory units in the rat.

Experiments were performed on urethane anaesthetized male Wistar rats (200–400 grams). A diaphragm electromyogram was used as a record of central respiratory rhythm and was displayed on one channel of a dual beam oscilloscope. In this way the neuronal pattern of discharge could be linked to some phase of the respiratory cycle and be recorded on film.

Single units were recorded in the medullary reticular formation using conventional microiontophoretic techniques (Bradley & Dray, 1974). Drugs were applied from five-barrel micropipettes. The recording barrel contained 4M NaCl while the other barrels contained a selection of the following: acetylcholine