

Relevance of the enhanced 5-hydroxytryptamine behavioural responses in rats to electroconvulsive therapy

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When rats are given a daily electroconvulsive shock (150 v sinusoidal for 1 s through ear clip electrodes) for 10 days they show enhanced behavioural responses to tranlycypromine and (–)-tryptophan or tranlycypromine and L-DOPA 24–72 h after the final shock (Evans, Grahame-Smith, Green & Tordoff, 1976; Green, Heal & Grahame-Smith, 1977). These drug schedules are considered to raise the functional activity of central 5-hydroxytryptamine (5-HT) and dopamine respectively (see Green & Grahame-Smith, 1976). Other evidence suggests that repeated electroconvulsive shock (ECS) increases post-synaptic 5-HT and catecholamine mediated behavioural responses, and it has been suggested that these changes may have relevance to the mechanism by which electroconvulsive therapy (ECT) produces its antidepressant effect (Evans *et al.* 1976; Green *et al.* 1977; Modigh, 1975, 1976).

We now report further results which are consistent with this hypothesis. In all experiments the hyperactivity response to tranlycypromine (10 mg kg⁻¹) followed 30 min later by (–)-tryptophan (50 mg kg⁻¹) was measured on LKB Animex activity meters (sensitivity and tuning 30 µA) as described by Green & Grahame-Smith (1976).

In agreement with the suggestion that a central nervous system induced convulsion (whether or not modified by neuro-muscular blockade) is an essential component for the therapeutic response (Fink, 1974) we find that 150 v sinusoidal for 1 s applied daily to the feet for 10 days fails to enhance the 5-HT induced hyper-activity response.

Enhancement is produced by both alternating sinusoidal current, and monophasic pulsatile current applied through the earclip electrodes.

Multiple ECS (8 shocks at hourly intervals) in a single day does not enhance the behavioural response

when the animals are tested either 24 h later or up to 10 days subsequently. This is in line with the clinical impression that multiple ECT is rarely therapeutically justified (Abrams, 1974).

A clinical response to ECT is normally elicited by between six and eight treatments given either two or three times per week. When rats were given a total of eight ECS over 17 days or five shocks over 10 days the same degree of enhanced hyperactivity was seen 24 h after the final shock, as when 10 daily shocks had been given. The rate of accumulation of 5-HT in the brains of the control and ECS treated rats was the same in both studies.

These data strengthen our view that enhanced monoamine responses following repeated ECS may have relevance to the anti-depressant action of ECT.

References

- ABRAMS, R. (1974). Multiple ECT: What have we learned? In *Psychobiology of Convulsive Therapy*, eds. Fink, M., Kety, S., McGaugh, J. & Williams, T.A. pp. 79–84. V.H. Winston & Sons, Washington DC.
- EVANS, J.P.M., GRAHAME-SMITH, D.G., GREEN, A.R. & TORDOFF, A.F.C. (1976). Electroconvulsive shock increases the behavioural responses of rats to brain 5-hydroxytryptamine accumulation and central nervous system stimulant drugs. *Br. J. Pharmac.*, **56**, 193–199.
- FINK, M. (1974). Induced seizures and human behaviour. In *Psychobiology of Convulsive Therapy*, eds. Fink, M., Kety, S., McGaugh, J. & Williams, T.A. pp. 1–17. V.H. Winston & Sons, Washington DC.
- GREEN, A.R. & GRAHAME-SMITH, D.G. (1976). Effects of drugs on the processes regulating the functional activity of brain 5-hydroxy-tryptamine. *Nature (Lond.)*, **260**, 487–491.
- GREEN, A.R., HEAL, D.J. & GRAHAME-SMITH, D.G. (1977). Further observations on the effect of repeated electroconvulsive shock on the behavioural responses of rats produced by increases in the functional activity of brain 5-hydroxytryptamine and dopamine. *Psychopharmacology*, **52**, 195–200.
- MODIGH, K. (1975). Electroconvulsive shock and post-synaptic catecholamine effects: increased psychomotor stimulant action of apomorphine and clonidine in reserpine pretreated mice by repeated ECS. *J. Neural Transm.*, **36**, 19–32.
- MODIGH, K. (1976). Long-term effects of electroconvulsive shock therapy on synthesis turnover and uptake of brain monoamines. *Psychopharmacology.*, **49**, 179–185.