between the antidepressive efficacy and seizure duration without confounding seizure duration with the actual number of ECT treatments administered. However, because existing studies comparing methohexitone (Malsch *et al*, 1992; Fear *et al*) or thiopentone (Mitchell *et al*, 1991) to propofol anaesthesia have found no seizure duration effect with the same number of treatments, one must conclude that seizure duration is irrelevant to the antidepressive efficacy. Furthermore, no other well-controlled ECT study to date has demonstrated a relation between seizure duration and antidepressive efficacy.

What appears to be important with respect to therapeutic efficacy, as discussed elsewhere (*BJP*, May 1983, **142,** 536–537), is not the precise duration of seizure activity, but rather the administration of 5–12 adequately generalised tonic–clonic seizures of at least 20 seconds duration (American Psychiatric Association, 1990). In this regard, two points should be made. Firstly, in the two studies comparing propofol with methohexitone anaesthesia (Malsch *et al*, 1992; Fear *et al*), adequate numbers of seizures were administered (approximate mean number of treatments across studies: 7.7 (methohexitone) and 7.3 (propofol)) which were of adequate duration (mean seconds of seizure activity: 46.9 (methohexitone) and 37.1 (propofol)).

Secondly, electrically induced seizures may vary in degree of generalisation (*BJP*, May 1983, **142,** 536–537). More precisely, seizure generalisation may increase in a curvilinear fashion (i.e. quadratic curve) until an asymptote ("ceiling effect") is reached with respect to the amount of electrical energy delivered (Sackheim *et al*, 1993). When this asymptote is reached, the antidepressive efficacy of ECT has probably reached its maximum; seizure duration at this point is probably just a correlate of the causal relationship between seizure generalisation and electrical energy, the latter of which alleviates depression.

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W. F. DANIEL

Department of Psychology
University of New Mexico
Logan Hall
Albuquerque, New Mexico
USA

AUTHORS REPLY: We thank Dr Daniel for his correspondence, which is broadly supportive of the points made in our paper. It is encouraging to see that the evidence concerning seizure duration and the efficacy of ECT continues to be critically appraised, since it is only through this that an understanding of the mechanisms underlying effective ECT will be ascertained. There are some points raised in the letter which merit further consideration.

There are significant problems in interpreting the literature with respect to the relationship between antidepressive efficacy and seizure duration. In addition to the error of combining the effects of seizure duration with those of treatment numbers so as to obscure the true effect of each, it is difficult to know how it would be possible to show, simply, a positive correlation between antidepressive efficacy and seizure duration. Clearly it is far easier to show statistically that two samples differ rather than to prove that they do not. There is, however, increasing evidence that seizure duration in current ECT practice is not clinically relevant so long as a seizure occurs. Perhaps useful progress could be made in attempting to define what constitutes a seizure, since existing literature is conflicting, and this would represent an important step in the standardisation of ECT research.

Daniel inadvertently illustrates this point in calculating mean seizure durations across two recent studies (Malsch *et al*, 1992; Fear *et al*). These figures are not directly comparable since they invoke different methods of measuring seizure duration. The first study used the purely motor manifestations of a seizure to measure its duration, using the "cuff technique", whereas in the second, both physical (unspecified method) and EEG durations were measured. In a third paper (Mitchell *et al*, 1991), physical measurement was performed "by an experienced psychiatric nurse without use of the 'cuff' (isolated arm) method". Under these circumstances, it is not valid to say that the seizures were of adequate duration since the comparability of their durations is uncertain.

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While evaluative studies and clinical experience both support a course of 5–12 treatments where generalised tonic–clonic seizures occur, the often-quoted 20–25 second minimum seizure duration is based only upon presumptive evidence (Swartz, 1992) and has not been supported by clinical outcome studies. Furthermore, we contend that this 'guesstimate" is without meaning and largely untestable unless and until a standardised mode of measurement is agreed and added. Motor timings are known to be shorter than EEG timings but, since many studies looking at EEG seizure durations use only a single lead EEG of the frontal/anterior temporal field, there is little information concerning the effects of left–right distribution of seizure activity (Fink & Johnson, 1982).

Clearly there is considerable scope for further work in this area with immediate consideration needed of the standardisation of seizure measurement, and larger, well-controlled studies to test the effect of seizure duration on antidepressive efficacy. Following this, EEG studies of seizure generalisation may prove more illuminating still.

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C. F. FEAR

Queen Elizabeth Psychiatric Hospital
Mindelson Way
Birmingham B15 2QZ

C. S. LITTLEJOHNS

Deeside Community Mental Health Team
North Wales Hospital
Denbigh, Clwyd LL16 5SS

Toxic serotonin syndrome or extrapyramidal side-effects?

SIR: In the review article by Arya (*BJP*, December 1994, **165**, 728–733), a significant omission is the failure to take account of the toxic serotonin syndrome (TSS). There is now a growing literature concerning the extrapyramidal-like side-effects of selective serotonin reuptake inhibitors (SSRIs). However, it has previously been suggested that some of the cases in which extrapyramidal side-effects have been described following SSRI administration may be part of (or a mild form of) TSS (Dursun *et al*, 1993).

It is likely that TSS remains underreported and rather misdiagnosed because the full behavioural profile and clinical features have not been studied and reported widely. In clinical practice most patients receive multiple medication, thereby rendering the identification of the causative drug more difficult. We would like to draw attention to this intriguing syndrome, and suggest that TSS should be kept in mind during SSRI treatment when adverse effects occur. Its early recognition leads to the possibility of correction of the biochemical/receptor dysfunction by discontinuing the SSRI medication and using a non-selective serotonin receptor(s) antagonist: methysergide, cyproheptadine or propranolol (Sternbach, 1991; Dursun *et al*, 1993).

Although at present there is no widely accepted diagnostic criteria for TSS, a set of criteria has been suggested for this purpose (see below). Prospective studies are required to establish a definitive scale for TSS, and the re-evaluation of cases which resemble this syndrome may contribute further to understanding TSS and its differentiation from extrapyramidal symptoms.

Suggested diagnostic criteria for TSS: by Sternbach (1991), with additional clinical features from Insel *et al* (1982) and Dursun *et al* (1993).

(a) Coincident with the addition of or increase in a known serotonergic agent to an established medication regimen, at least three of the following clinical features are present:

uncontrollable shivering
incoordination
restlessness in feet while sitting
initial involuntary contractions followed by myoclonic-like movements in legs
hyperreflexia
frightened, diaphoretic hyperarousal state
agitation
oculogyric crisis
diarrhoea
fever

(b) Other aetiologies (e.g. infectious, metabolic, substance abuse or withdrawal) have been ruled out.

(c) An antipsychotic drug had not been started or increased in dosage prior to the onset of the signs and symptoms listed above.

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