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Correspondence

LITHIUM AND SEROTONIN UPTAKE BY PLATELETS

DEAR SIR,

Coppen *et al* (*Journal*, March 1980, **136**, 235-238) reported that the maximum velocity (Vmax) of serotonin (5-HT) uptake in blood platelet of depressed patients is significantly lower than normals, and that 6 weeks or one year of lithium treatment normalized this abnormality. They also reported that addition of lithium *in vitro* decreased 5-HT transport of normal human blood platelets. However, the following problems with the method used to study 5-HT uptake may invalidate their findings.

(1) EDTA was used as the anticoagulant. It has been previously reported that EDTA inhibits 5-HT uptake by platelets or produces a substantially lower rate of uptake of 5-HT than occurs, when acid citrate or citrate is used as the anticoagulant (Born and Gillson, 1959; Hardeman and Heynens, 1974).

(2) The rate of uptake was studied with 5-HT concentration in the range of 0.25 μM to 4.0 μM. Tuomisto and Tukiainen (1976), Tuomisto *et al* (1979) and Stahl and Meltzer Meltzer (1978) have reported that when 5-HT uptake is determined at concentrations greater than 1 μM of 5-HT the effects of passive diffusion cannot be entirely corrected. Thus, the data obtained at the higher concentrations of 5-HT cannot be used to determine active 5-HT uptake.

(3) Passive diffusion is temperature-sensitive (Pletscher, 1968; Sneddon, 1973; Gordon and Olverman, 1978); and is also dependent on the concentrations of 5-HT and of platelets. In the present study, 5-HT uptake was determined at 37°C whereas passive diffusion was determined at 0°C. This is a second reason why an appropriate correction for passive diffusion cannot be applied.

(4) No mention was made of the platelet concentration studied nor did the authors demonstrate linearity of 5-HT uptake with respect to incubation time at the platelet concentration studied, whatever it was.

We have also found decreased Vmax for 5-HT uptake in the platelets of 11 bipolar depressed patients compared to normal controls (Table I) as reported by Coppen *et al*. We have also studied the effect of treatment with lithium carbonate for 19.5 ± 8.5 days, on 5-HT uptake in these patients, using low concentrations of 5-HT (0.1 μM to 1 μM) and remaining within the linear range with regard to both platelet concentration and incubation time. The Vmax for 5-HT uptake was further decreased by lithium treatment, the opposite of the results of Coppen *et al* (Table I). No significant change was found in K_m, although a tendency towards a decrease was observed. We also did not observe any effects of the addition of lithium up to 1 μM *in vitro* on the 5-HT uptake of normal human blood platelets. Born *et al* (1980) also found no effect of lithium *in vitro* on uptake of 5-HT by human blood platelets.

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TABLE I

Platelet 5-HT uptake kinetics in normals and patients before and after lithium treatment

Group	Km* (μM)		Vmax* (pmoles/10^8 platelets/min)	
Normals	0.50 ± 0.12		116 ± 14.2	
Bipolar depressed				
Placebo	0.53 ± 0.16	P = ns	88.9 ± 26.2[1]	P < 0.05[2]
Lithium treatment	0.44 ± 0.19		65.7 ± 18.2	

* Mean ± SD.
[1] Lower than normals (student t-test) P < 0.005.
[2] Paired t-test.

MOURNERS WITHOUT A DEATH

DEAR SIR,

May I express my appreciation of the paper on Anticipatory Grief by Fulton and Gottesman (*Journal*, July 1980, **137**, 45-54) and my hope that it will be added speedily to the College's recommended-reading list. It is a very welcome change to come across a paper that (a) is couched in readable English, and (b) points out the futility of the currently-prevalent blinding by statistics, and does so in two important respects:

(i) the uselessness of trying to compare surveys which have not only taken widely differing groups but have studied those groups in non-comparable ways; and

(ii) even more important, in which the authors point out that it is the covert quality of a relationship which really counts in bereavement and *not* the overt formal ties. A pet may be a much more significant figure—and its loss far more traumatic—than a parent (or any other human being) with whom relationships are, almost by definition, ambivalent.

One very important area that has not, to my knowledge, been dealt with by any medical group is the effect on survivors, whom for the purpose of my theme I would like to term the NOBs (not-officially-bereaved), of blocked anticipatory grief. This must be an increasingly common phenomenon nowadays in view of the progress in resuscitatory techniques and of, often heroic, treatments of conditions which could reasonably be expected to prove fatal. Leaving aside the fact that these treatments often leave the patient a mutilated caricature of their previous whole person, with the adjustments in life-style and attitudes which this demands from the NOBs, I feel that there is a need for study of the effects on the NOB of having—sometimes repeatedly—to go through the processes of anticipatory grief, practical and legal as well as emotional, only to have to pick up again the cast-off threads and with the knowledge that the whole grisly process will have to be gone through again x times. The medical profession carries, but as a whole does not recognize, the greatest responsibility for inflicting this burden. It seems an egregious lacuna in medical education at both post- and under-graduate level that the issue is not a subject for continuous discussion and re-assessment. Instead we are actually taught to put prolongation of existence above quality of life and particularly the quality of life of the group of which the patient is a part, under the pseudo-scientific cloak of eschewing value-judgements—a term which now seems to be applied almost exclusively in a pejorative sense. In reality this is a totally unscientific nonsense involving the wilful refusal to take into account all known facts. A very large part of the life of higher mammals, human beings in particular, consists of making value-judgements (is it more pleasurable to curl up by the fire with a bowl of milk or to go out hunting?; is my over-riding loyalty to my country or my friend?). Surely an essential part of training should be to help people to make the most valid value-judgements possible in each circumstance rather than to encourage them to take the primrose-path of abrogating a common moral duty, cloaked in a blanket code of practice.

We are each entitled to take decisions that entail suffering for ourselves. What worries me is that