Cerletti carried out fundamental research into the effects of E.C.T. during the subsequent twelve years and described his findings at the International Congress of Psychiatry in Paris in 1950. His main conclusions were that the treatment was cheap and safe and that there were many indications for it, including not only depression but also mania and most forms of schizophrenia as well as confusional psychoses.

Cerletti subsequently claimed that certain substances were found in the brains of animals which had been subjected to numerous electroshocks; this was based on the ability of such brain extracts to diminish the virulence of rabies and also, he asserted, a temporary feeling of well-being when injected into melancholic patients. This work however was not generally accepted. On one occasion when asked whether these "acroagonines" might not be merely hormones found in the brain and resulting from the stimulation of the pituitary by E.C.T., Cerletti answered that this was quite possible and he hoped that further work would be carried out to test the validity of this hypothesis.

Although his account of "acroagonines" did not find general acceptance, it has been generally agreed that E.C.T. has been the most valuable of all the physical methods of treatment in psychiatry and that it has relieved an immense amount of suffering. In 1948, at a meeting at Warlingham Park Hospital convened by the late T. P. Rees to celebrate ten years of E.C.T., many psychiatrists testified how the whole aspect of a typical mental hospital had been transformed by these treatments, as L. C. Cook later described in his Presidental Address to the R.M.P.A. in 1958.

Cerletti received many honours in recognition of his achievements. As well as being President of the Italian Psychiatric Association, and Honorary President of the Neurological Society, he received a special award from the Academy of Italy for his psychiatric discoveries. He received many honorary degrees abroad. He visited the U.S.A. in 1959 and in 1961 and travelled widely in that country.

He visited England in 1960 and met many of the leading psychiatrists. He showed an interest in improved techniques developed in this country from his own discoveries. He paid a pious visit to the Nightingale Museum at St. Thomas's Hospital, for he had done much to reorganize and reform nursing in Italy. He was enchanted by this first (and as it turned out, his last) visit to England. He showed the greatest interest in social conditions under the Welfare State and he said that he was impressed by the friendliness and good sense of the average citizen, "such as he had never encountered elsewhere". A visit to an art gallery displayed Cerletti's knowledge of art. He recognized each painter by his works and he could give a thumbnail sketch of the life and characteristics of each artist.

In 1963 the West London Medico-Chirurgical Society decided to award him the Triennial Gold Medal for his distinguished services to medical science. Under the rules of the Award the medal could also be awarded for exceptional heroism in the discharge of medical duties. Cerletti qualified on both counts, for he had won the Italian Military Medal in the 1914 war. Other recipients had included Sir Ronald Ross who had discovered the life cycle of the plasmodium which causes malaria, Professor Neisser of Breslau, Sir Hugh Cairns and Sir E. C. Dodds. Cerletti wrote on 1 July, 1963 that he would arrive on 28 July. However within a few days he had become ill and he died on 25 July. He received the medal posthumously.

He leaves a widow and a daughter, and a son who is Professor Paolo Cerletti, a biochemist in Rome.

Yours faithfully,

A. SPENCER PATERSON.

2 Devonshire Place, W.1.

AMITRIPTYLINE AND IMIPRAMINE

DEAR SIR,

The findings of W. Browne, L. C. Kreeger and N. G. Kazamias (1963) in the September issue of the *Journal* under the title "A Clinical Trial of Amitriptyline in Depressive Patients" are very surprising, because they are not only contrary to the impressions and experience of most clinicians, but also quite out of keeping with results reported by almost all previous investigators. The literature up to the date of the appearance of the report by Browne *et al.* had been summarized by C. G. Burt *et al.* (1962) and by J. W. Garry *et al.* (1963). From these summaries it appears that amitriptyline, like imipramine, is quite effective in endogenous depressions (affective psychoses), but only marginally so in psychogenic reactions (which I presume is what Browne *et al.* mean by "reactive depression"). Their findings that endogenous depressions do not respond significantly better to amitriptyline than they do to a placebo is startling, so much so as to make one wonder whether a printing or other technical error had caused their two clinical groups of "endogenous" and "reactive" depressions to be switched round and so become linked to the wrong results. This would adequately explain not only their otherwise unexpected findings,

but also the fact that the opposite results previously reported have not been mentioned in their paper.

Is it possible for these authors to throw some light on the discrepancy between their findings and those of all other workers?

Yours faithfully,

J. HOENIG.

References

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Burt, C. G., Gordon, W. F., Holt, N. F., and Hordern, A. (1962). *J. Ment. Sci.*, **108**, 711–730.

Garry, J. W., and Leonard, T. J. (1963). *Brit. J. Psychiat.*, **109**, 54–55.

Dear Sir,

Dr. Hoenig asks us "to throw some light on the discrepancy between our findings (in a clinical trial of amitriptyline) and those of all other workers".

We have checked our results very carefully, and believe that we have excluded any technical or printing error.

The paper of Garry and Leonard described the use of amitriptyline in chronic depressive states, their patients having been ill for a mean period of 7·5 years. We feel that it would serve no purpose to compare their results with ours, as we were dealing with more acute cases.

With regard to the paper of Burt *et al.*, this was published after our paper had been accepted. We did at that time consider putting in an addendum to our paper, but finally decided to let it stand as it was. In comparing these two papers, it is clear that the results in cases of endogenous depression (affective psychosis) differ. Burt *et al.* found improvement in 18 out of 25 cases (72 per cent.) whilst in our series improvement resulted in only 9 out of 19 (45 per cent.). There are, no doubt, many possible causes for this discrepancy, for example, differences in diagnostic formulation or in assessing changes objectively. However, the most important, in our view, is that we compared amitriptyline with a placebo, whereas Burt *et al.* compared it with imipramine, on the basis that imipramine was well-tried and generally regarded as the most effective anti-depressant drug available at that time. We feel that there may well have been a considerable difference in the subjective attitudes of the workers in these two trials. Perhaps we experienced a greater anxiety for those patients with severe depression who were not showing a good response to treatment, because we knew that some of them might be having the placebo tablets. Burt *et al.* knew that every patient in their trial was receiving an anti-depressive drug, either amitriptyline or imipramine. It is possible that they felt more secure and could therefore allow a longer period of time to elapse before having to consider removing a patient from the trial.

Dr. Hoenig suggests that amitriptyline is of marginal value only in cases of reactive depression (psychogenic reaction), and because of the high rate of response in our cases, 13 improved out of 16 (81 per cent.), he questions whether we accidentally got our results switched around. We would point out, however, that Burt *et al.* found improvement in 11 out of 12 cases of reactive depression, that is 92 per cent. It is clear that their improvement rate in these cases was higher than ours. In our paper we mentioned that we gained the impression that amitriptyline had a tranquillizing effect in these patients, and suggested that a trial comparing it with chlorpromazine would appear worthwhile. Such a trial would indicate whether amitriptyline has a specific anti-depressant action or not in cases of reactive depression.

We wonder if Dr. Hoenig is correct when he states that the impressions and experience of *most* clinicians are contrary to our findings. In questioning our colleagues, we find that the majority consider amitriptyline to be one of the less useful drugs in the treatment of endogenous depressive states.

We do not believe that discrepancies in controlled trials are so uncommon. For example, compare the results of two trials on imipramine. Ball and Kiloh (1959) found it superior to a placebo, whilst Roulet *et al.* (1962) were unable to demonstrate any significant differences between the drug and placebo group. (We are aware that Roulet *et al.* were dealing mostly with depressive reactions, and had very few psychotic depressives in their trial.)

The whole subject of double-blind trials is complex, and requires a good deal of re-thinking. Cromie (1963) in his paper "The Feet of Clay of the Double-Blind Trial" considers some of the pitfalls that beset us.

Yours faithfully,

M. W. BROWNE.

Netherne and Fairdene Hospitals, Coulsdon, Surrey.

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