

# This Week's Citation Classic®

Lader M H & Wing L. *Physiological measures, sedative drugs, and morbid anxiety*.  
London: Oxford University Press, 1966. 179 p.  
[Maudsley Hospital and Medical Research Council, London, England]

Studies in normal subjects and anxious patients related psychological state to physiological, mainly autonomic, measures. Sweat-gland activity measured electrically both spontaneous and in response to repeated auditory stimuli was abnormally active in the patients. Fairly precise estimates of the sedative effects of drugs proved feasible. [The *SCI*® and the *SSCI*® indicate that this book has been cited in over 350 publications.]

## Physiological Measurement of Psychopathology

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In 1960 a three-year research post funded by the US National Institute of Mental Health Extramural Program was offered to me, tenable at the Department of Pharmacology, University College London, and at the Institute of Psychiatry at the Maudsley Hospital. The main grant-holder was Professor Heinz Schild, a distinguished quantitative pharmacologist. He told me I was to develop ways of measuring psychotropic drug effects in man with a view to comparing new drugs with older ones, using classical bioassay techniques like those he used with bits of guinea-pig ileum. He also thought that Pavlovian conditioning might provide a useful stimulation paradigm. With the neophyte's enthusiasm, I started this task to find that no one had ever attempted anything quite so ambitious in psychopharmacology.

First, precise measures of drug response were not available. I was fortunate to be working with a technical wizard, J.D. Montagu, who taught me how to develop electrophysio-

logical techniques. Soon we had quite an array at our disposal, including skin conductance, which, using pharmacological dissection, we had shown was a measure of sweating. My reading of the literature soon convinced me that Pavlovian conditioning was a complex phenomenon, and I decided to investigate first what happened when simple unconditioned stimuli were repeated. Thirty years on, I have still not exhausted this topic!

With the stimulation procedure and the range of physiological and subjective measures, I established simple dose-effect curves for a barbiturate and in turn calibrated my measures. I was then ready to study anxious patients at the Maudsley Hospital. A small laboratory was set up in a basement with a Grass polygraph (pensioned off in 1988). My collaborator was Lorna Wing, a trained psychiatrist with an inexhaustible store of common sense, who found the patients, did the clinical ratings, and brought them down to my subterranean lair. We established differences between anxious patients and matched controls, showed that a barbiturate used in therapy lessened those differences, and then compared a new drug, chlordiazepoxide (Librium), with the barbiturate using classical staircase and two-plus-two-plus-one bioassays. Finally, in a twin study, we established a genetic component to some of the measures.

The studies were published as one of the prestigious Maudsley monographs. It was influential because it showed that psychiatric abnormalities such as anxiety could be quantified and contributed to the burgeoning of a whole new subject, clinical psychophysiology.<sup>1</sup> It established correlations between clinical and biological measures and gave psychiatry a new technology to exploit.<sup>2,3</sup>

I completed a formal training in psychiatry, went back full-time in research in 1966, and have pottered about happily ever since. The monograph, I believe, was instrumental in my being encouraged to continue with a research career. The irony is that my more recent work on benzodiazepine dependence has heavily criticized the drugs which first helped establish my career. The main vehicle for that criticism was also a Maudsley monograph,<sup>4</sup> and similar but more advanced techniques were used as those developed 30 years ago.

1. Cotes M G R, Donchin E & Porges S W, eds. *Psychophysiology. Systems, processes and applications*. Amsterdam, The Netherlands: Elsevier, 1986. 761 p.
2. Kelly D. *Anxiety and emotions: physiological basis and treatment*. Springfield, IL: Thomas, 1980. 424 p. (Cited 30 times.)
3. Raskin M. Decreased skin conductance response habituation in chronically anxious patients. *Biol. Psychol.* 2:309-19, 1975. (Cited 25 times.)
4. Petursson H & Lader M. *Dependence on tranquillizers*. Oxford, England: Oxford University Press, 1984. 130 p. (Cited 30 times.)