Diurnal variations of whole blood serotonin content in patients with depression and neurosis

Clinical studies have provided evidence that serotonin (5-hydroxytryptamine, 5HT) is implicated in the state of depression, as its precursors, selective inhibitors of uptake and $5HT_2$ receptor blockers are very effective in its treatment.[1,2] There is some evidence that disturbances in the regulation of circadian rhythms may be of prime importance in the pathophysiology of affective disorders.[3] Furthermore, depression is believed to be linked with brain serotonin metabolism.[4,5]

As human blood platelets may be regarded as a reliable model for serotonergic synaptosome because of their specific biochemical mechanisms for uptake, storage, metabolism and release of amine, the whole blood measurement of serotonin (that is, mainly platelet serotonin, since very little is detectable outside the platelets) provides a peripheral model for the study of processes in the brain.[6,7] However, it is still an open question as to whether blood platelet parameters reflect those in the brain. The daily fluctuations of behaviour in affective disorders have stimulated us to search for circadianism of serotonin.

We examined at five time points whole blood 5HT levels in psychiatric patients in hospital and control volunteers. The group of patients consisted of 18 subjects (12 with depression and six with neurosis). They were diagnosed and treated in the Department of Psychiatry, Hamamatsu University School of Medicine. At the time the blood samples were taken, patients were in a depressive state, confirmed by a mean score of 18·7 (range 12–24) on the 24-item scale of Hamilton Depression Rating Scale.[8] None of them were receiving any drug, except for small does of bezodiazepines, for at least 10 days before blood was taken. Before entering the trial, the patients were in good physical health and gave voluntary consent to participate. Ethical committee approval for this study was obtained from the Hamamatsu University School of Medicine. The control group matched for age and sex with the patients was made up of 30 volunteers, who showed no clinical signs of depression or organic disease, and were drug-free.

Quantitative analysis of 5HT in the blood was performed by HPLC as described by Anderson *et al.*[9] Analytical recoveries were 85% (SD 4·5%, CV 5·6%). Amount and response for standards were linearly related.

As shown in the figure, whole blood serotonin level was significantly reduced in depressed patients at 8:30, 10:30, 12:30, and 14:30 ($p < 0·01$), as well as in patients with neurosis at 8:30, 10:30, and 12:30. The values at 16:30 were similar in all groups. The blood concentration of 5HT showed a circadian change. In the depressed patients group the lowest value was obtained at 8:30 and the level progressively increased to 16:30. The values at 10:30, 12:30, 14:30 and 16:30 were significantly higher than that at 8:30 ($p < 0·05$). Fluctuation in whole blood serotonin level was observed in a group of patients with neurosis. The highest values were obtained at 8:30 and14:30. From 8:30 it decreased gradually to 12:30 and showed a significantly lower value at 10:30 and 12:30 ($p < 0·05$). From 12:30 serotonin level in neurotic patients increased to 14:30 and remained at almost the same level at 16:30. The different pattern was shown in the control group. The highest value was obtained at 8:30 and it decreased gradually and showed a significantly lower value at 12:30, 14:30, and 16:30 ($p < 0·01$).

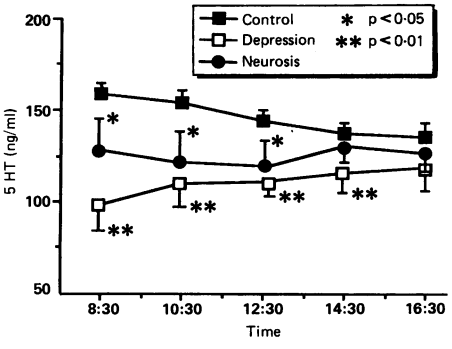

Figure Diurnal variations in whole blood serotonin concentrations. Each point represents the mean ± SE value (Duncan's muliple range test).

Since the characteristics of MAO activity, 5HT uptake, imipramine and alpha 2-adrenergic receptor binding are similar in platelet and brain, the platelet is one of the most researched biological markers in psychiatry. Platelet serotonin content is most likely regulated by the 5HT transport activity. Daily variations in serotonin uptake in depressed patients have been reported by several groups.[10–12] A diurnal variation in the transport capacity is suggested by data reported by Modai *et al.*[12] The findings in our study support these observations. The second diagnostic feature of blood platelet is imipramine binding. Recent findings of reduced ^{3}H-imipramine binding in platelet of depressed patients compared with healthy controls have been proposed as a biological marker of depression. However, there was no evidence for significant diurnal of circannual variation in the binding parameters in any of the diagnostic category.[13]

In conclusion, our data indicate that the clear distinct pattern of diurnal rhythm could be established in a group of patients with depression, neurosis as well as in a control group. Moreover, we found general differences in the circadianism of 5HT between depressed and neurotic patients, which may have practical implication in the differential diagnosis.

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BOOK REVIEWS

All titles reviewed here are available from the BMJ Bookshop, PO Box 295, London WC1H 9TE. Prices include postage in the United Kingdom and for members of the British Forces Overseas, but overseas customers should add £2 per item for postage and packing. Payment can be made by cheque in sterling drawn on a United Kingdom bank, or by credit card (Mastercard, Visa or American Express) stating card number, expiratory date, and your full name.

Benjamin's Son: Benjamin Archer Kent MD. (1808–1864). By PETER H SCHURR. (Pp 193; £12.95 H/Back; £7.95 S/Back.) 1991. London, Royal Society of Medicine Services Ltd. ISBN 1-85315-146-7/1-85315-145-9.

This is a painstaking and devoted account of the life of an unusual physician of the 19th Century and his family connections. It is a fascinating document of social and medical history, and will therefore have specific appeal to those who have aptitude and inclination in this field. This book may not be read widely, which is a pity and I commend it to a wider public despite a certain ponderous idealism which clings to the early 19th Century and knowing of the general lack of sympathy for simple scientific methodology that prevails in our enlightened age.

The MD Thesis contained in translation in the Appendix with associated reviews of contemporary knowledge of the sympathetic ganglia by Peter Schurr, and the historical review of nervous disorders by Edward Hare, have the sympathetic ganglia as their

Groove Meningiomas are dealt with in two brief paragraphs while Tuberculum Sellae Meningiomas occupy a page and Petroclival Meningiomas likewise a page. In a book claiming to address the principles of neurosurgery, descriptions which fall between excessive brevity and over-detailed attempts lead inevitably to the feeling that one is driven to the usually quite extensive reference lists for further information. The chapter on Trigeminal and Glossopharyngeal neuralgias and Hemifacial Spasm on the other hand addresses the subject briskly and yet comprehensively.

Some of the recommendations in the chapter on Management of Head Injury would, I think, raise eyebrows even in the most dedicated neurosurgical units in the United Kingdom but it is clear that the Monitoring of Intracranial Pressure is retained more in fashion across the Atlantic than here. By the same token, the detailed description of Ventriculography, a procedure which is hardly ever performed now, particularly in the context of head injuries, is quite surprising. Other chapters address Spinal Cord Tumours, Vascular Malformations, Syringomyelia and Neural Tube Defects and while brief are reasonably comprehensive and pleasant to read. The book finishes with brief chapters on Traumatic Lesions of the Spine and Spinal Cord and on Peripheral Nerve Disorders and, again reflecting its American origin, two of the best chapters are by Watts and his associates on Disc Disease and Spinal Canal Stenosis.

The reviewer found it difficult to know quite what to make of this book. It does not set out to be a compendious review of neurosurgery and yet the chapter on CNS Infection, includes 431 references. It might profitably form bedside reading for a junior neurosurgical resident but it is likely that its main interest would be the remarkable series of references appended to most of the chapters. In the presence of so many more clearly focussed texts I wonder whether it will be bought by more than a handful of fairly rich trainees.

LINDSAY SYMON

Advances in Neurosurgery Vol 19. Edited by W J BOCK, Ch LUMENTA, M BROCK AND M KLINGER. (Pp 283; Price: DM88.00.) 1991. Heidelberg, Springer-Verlag. ISBN 3 540 53311 7.

This issue of advances in Neurosurgery is described as dealing with three major topics. The first is concerned with vascular malformations of the brain where Neuroradiological interventions and microneurosurgical treatment present major advances. The second covers treatment patterns for various supratentorial tumours in childhood. The interdisciplinary aspects of neurosurgical intensive care, particularly electrophysiology and anaesthesia, are treated extensively as the third topic. The book is made up of papers from the Proceedings of the 41st Annual Meeting of the Deutsche Gesellschaft für Neurochirurgie, Dusseldorf, May 27–30, 1990.

Unfortunately two other sections have been added. The first deals with the co-ordination of Neurosurgical training in Europe of the 1990's and the second consists of the winning poster presentations at the proceedings. Neither of these two added sections fit into the described format of the book and the section on training has no place in this type of presentation.

The remaining sections I found to be disappointing. Each section consists of a disparate collection of papers varying in quality, originality and scientific context. The sections on vascular malformations of the brain and supratentorial tumours in children will provide a discerning reader with some information of modern approaches and treatments for a variety of pathological entities. The section on Neurosurgical Intensive Care I found to be unclear and it failed to convey the importance of an interdisciplinary approach in this area. I would not recommend this volume to young Neurosurgeons in training, though some of the papers may be of interest to Researchers.

NEIL DWYER

Information in the Brain: A Molecular Perspective. By IRA B BLACK. (Pp 225; Price: £26.95.) 1991. London, The MIT Press. ISBN 0 262 02321 0.

Ira Black is a major contributor to modern neurobiology. His book contains a very intelligent and readable core which summarises a 1990 view of the chemistry of neural function. He moves from the signalling of rapid events by way of evanescent transmitters to the intracellular consequences which have longer and longer time epochs. He describes with great clarity the interaction of these imposed changes with the inherent genetic make up of the cells. He shows precisely how these transient changes may produce longer and longer term events within single cells and outside them. The roles of transmitters, intracellular messengers, enzymes, nuclear potentialities, peptides and growth factors are displayed with admirable clarity.

This core is submerged in a more speculative surround in which it is proposed that the properties of the molecules determine the potentiality of the organism and that the behavioural repertoire of the organism depends on its possession of specific molecules. This provocative suggestion leads to much more specific hypotheses such as the proposal that Alzheimer's disease is basically an error in the handling of nerve growth factor which prevents the proper function of cholinergic basal neurons. I hope he is right in his guess. Even beyond this surround, the book contains an attack on "Functionalist Fallacy and Muddled Metaphor". I find his solution as unsatisfactory as the target of his attack but that does not detract from the value of his core summary.

PATRICK D WALL

Nerve Endings and Mitochondria Missing Links. By DAVID HOPKINS. (Pp 182; Price £12.00.) 1991. London, Neuropress. ISBN 0 9515290 0 5.

The title of this book is an unusual juxtaposition of words and intriguing which is why I agreed to review it. It is presented, I hesitate to say written, in a curiously disjointed style of numerous short paragraphs with a note-like use of words. It is easy to read with limited and highly selected references to the literature.

The underlying hypothesis is presented in chapter 4 and is essentially that vesicles containing neurotransmitters localised in the nerve ending originate on the nerve ending mitochondria by a process which is not clear. The evidence put forward for this suggestion is largely morphological and of a very speculative kind. Molecular mechanisms as to the manner by which phospholipids and cholesterol are incorporated into the vesicle membranes from the mitochondria are conspicuous by their simplicity and vagueness. Indeed in chapter 15 one of the proposals may be interpreted as meaning that the coupling of mitochondrial oxidative phosphorylation changes on nerve stimulation. Furthermore in chapter 16 (sec.16.1.2) the Fo fraction of the mitochondrial ATP synthase is described as *mostly* of intramembrane subunits of mitochondrial genetic origin. In fact only two of the seven known components are coded for by the mitochondrial genome.

It is these types of suggestion and inaccuracies, together with the highly selected references quoted which lead one to view the speculative hypothesis propounded in this book with some sceptism if not incredulity. Whilst I found the book interesting to read, I could not on balance recommend any serious reader to purchase a copy, despite its relatively low price (£12.00).

J B CLARK

SHORT NOTICES

Revue Neurologique
Published by Masson, Paris. Abstracts of Articles for 1990 and 1991 available in English as a supplement.

Basic Histopathology: A Colour Atlas & Text. 2nd Edition. By PR WHEATER, HG BURKITT, A STEVENS, JS LOWE. (Pp 252 Illustrated; Price Not Indicated) 1991. Edinburgh, Churchill Livingstone. ISBN 0 443 04237 3.

World Health Forum: An International Journal of Health Development Vol. 12, No.3. (Pp 374; Annual subscription Sw.fr 68.–/US$54.–) 1991. Geneva, World Health Organisation. IX ISSN 0251 2432.