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 ($p < 0·01$).

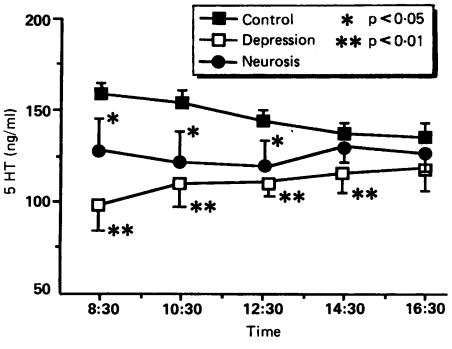

Figure Diurnal variations in whole blood serotonin concentrations. Each point represents the mean ± SE value (Duncan's muliple range test).

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

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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