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5-HT AND 5-HYDROXYINDOLEACETIC ACID LEVELS IN SUCCESSIVE SAMPLES OF CISTERNAL CSF OF RHESUS MONKEYS*

M. S. KRISHNAMOORTHY** AND T. C. ANANDKUMAR‡

Neuroendocrinology Laboratory, W.H.O. Reproduction and Training Centre, All India Institute of Medical Sciences, New Delhi 110 016

ABSTRACT

The 5–HT and 5–hydroxyindoleacetic acid levels were assayed fluorometrically in successive samples—with no time interval between sampling—of cisternal CSF of anaesthetised rhesus monkeys. The basal levels were 39·78 ± 4·66 ng/ml and 68·29 ± 15·16 ng/ml respectively. The significance of the occurrence of 5–HT in CSF with regard to its possible role in regulating pituitary gonadotropin secretion is mentioned. The first 3 ml of CSF is found to be homogeneous with regard to 5–HT and 5–Hydroxyindoleacetic acid; successive samples collected subsequently contained higher levels of 5–HT and 5–hydroxyindoleacetic acid. Hence, a standardised sampling procedure is advocated to have comparable data.

INTRODUCTION

A CONSIDERABLE volume of evidence has accumulated to suggest that CSF may constitute a humoral link between different areas of the brain by transporting neural products affecting cellular function. Administered intraventricularly, 5–HT has been shown to inhibit pituitary leutinizing hormone secretion[1]. On the basis of this and other similar findings, it has been postulated that 5–HT of extrahypothalamic origin may reach the neural mechanism regulating pituitary gonadotropin secretion *via* CSF. However, on scanning the literature, very few references are found reporting the occurrence of 5–HT in CSF[2]; 5–HT as such has never been convincingly demonstrated in the CSF of rhesus monkeys. On the other hand, 5-Hydroxyindoleacetic acid (5–HIAA) has been repeatedly investigated in various psychopathological and neurological conditions[3–5].

Hence, in this work, we have assayed both 5–HT and 5–HIAA in successive samples collected on a single cisternal tap—without allowing any interval between successive sampling—mainly to look for the occurrence of 5–HT in CSF and also to look for any differences in 5–HT and 5–HIAA concentrations between successive samples.

MATERIALS AND METHODS

In this study, rhesus monkeys of both sexes were anaesthetised with 30 mg/kg *i.v.* nembutal sodium. Throughout the study, cisternal taps were done between 11 A.M. and 12 NOON to rule out diurnal variations. Successive 3 ml and 1·5 ml CSF samples were collected for 5–HT and 5–HIAA assay in the first and the second group of experiments respectively. Blood stained samples were discarded. Moreover, the samples were centrifuged in order to detect the presence of red blood cells; because it was difficult to see a coloration when a small amount of blood was present. The CSF samples were deproteinised and the solution was made 0·1 N with respect to hydrochloric acid[4]

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**Present Address : Department of Pharmacology, P.G. Inst. of Basic Medical Sciences, Taramani, Madras –42.

‡ Present Address : Department of Experimental Biology, W.H.O. Reproduction and Training Centre, All India Institute of Medical Sciences, New Delhi–16.

with concentrated perchloric acid; then 5-HT and 5-HIAA were assayed fluorometrically (excitation and emission wavelengths were 365,470 nm for both) according to Curzon and Green[7]. The activation and fluorescence spectra were compared and found to agree with that of authentic 5-HT and 5-HIAA. Since the assay method was not sensitive enough to estimate 5-HT in 1·5 ml CSF samples, only 5-HIAA was estimated in this group. All data were subjected to recovery corrections.

Results and Discussion

The mean 5-HT and 5-HIAA concentrations in the first of the two 3 ml successive samples, 39·78 ± 4·66 ng ml and 68·29 ± 15·16 ng ml respectively (Table I), could be taken as the basal CSF levels in anaesthetised rhesus monkeys. The significantly higher 5-HT and 5-HIAA levels in the second 3 ml sample compared to the first (Table I) may be attributed to the second sample consisting mostly CSF arising from levels rostral to the cisternal site which may have higher concentrations of 5-HT and 5-HIAA.

TABLE I

5-HT and 5-HIAA Levels in successive 3 ml cisternal CSF samples from Rhesus Monkeys

Sample	5-HT (ng/ml)	5-HIAA (ng/ml)
First	39·78 ± 4·66 (5)	68·29 ± 15·16 (6)
Second	51·24 ± 4·73* (5)	130·69 ± 32·67** (6)

The number of determinations is indicated between brackets. Each value is the mean ± S.E. of the specified number of determinations. Significance of differences between the first and the second samples, by paired-sample *t*-test. In view of the changes occurring being proportional, 5-HIAA values were log transformed prior to *t*-test.

* $p < 0·01$.
** $p < 0·001$.

In the majority of the previous studies, one of the reasons for the inconsistency of data concerning the presence of 5-HT in CSF might be the restriction of the estimations to lumbar CSF only. Indeed, Schain[8] advocated that cisternal CSF should be assayed more often since it might yield positive data while lumbar CSF was negative. He also stated that since 5-HT in blood is almost entirely bound to platelets, it is not likely that it reflects the plasma level. If 5-HT in CSF is shown to be of neural origin as is shown for acetylcholine[8], this would be an evidence for the role of CSF as a possible transport medium for biologically active substances in CNS.

In the second group (Table II), there was no signn ficant difference in 5-HIAA concentrations betweei the first and the second 1·5 ml successive samples. These two values (72·06 ± 18·80 ng/ml and 80·42 ± 14·80 ng/ml) were not significantly different from that of the first 3 ml sample reported in the first group (68·29 ± 15·16 ng/ml), suggesting that the initial 3 ml of CSF—collected either as a single or as two successive samples on a single cisternal tap—is homogeneous with regard to 5-HIAA concentration. While 5-HIAA level in the third sample was significantly higher than that of the second sample, the level in the third sample was not significantly different from that of the fourth sample.

TABLE II

5-HIAA Levels in successive 1·5 ml cisternal CSF samples from Rhesus monkeys

Sample	5-HIAA (ng/ml)
First	72·06 ± 18·80
Second	80·42 ± 14·80
Third	104·02 ± 24·86*
Fourth	88·35 ± 4·06

Each value is the mean ± S.E. of five determinations. Significance of differences between the first and the second, the second and the third and the third and the fourth successive samples, by paired sample *t*-test.

* $p < 0·05$.

The existence of a gradient in amine metabolite concentrations from a high level in the ventricular fluid to a low level in the lumbar fluid has been alluded to in earlier studies[5, 9–11]. Recently, Siever *et al.*[12] stated that the presence of a gradient has relatively been neglected so far as a topic for clear examination. The present findings indicate that the cisternal CSF does not represent a homogeneous system with reference to 5-HT and 5-HIAA levels. The concentration differences were suggested to reflect differences in amine metabolite transport phenomena or in brain amine activity in terms of release, turnover or metabolic route, resulting in different diffusion rates down the brain CNS axis[12]. Since the concentration differences between successive samples were significant with reference to 5-HT and 5-HIAA levels, even small variations in volume of cisternal CSF sample might lead to variable results. Eventually, this phenomenon will probably explain the differences between the basic values of amine metabolites in CSF reported by different authors. In view of this finding a standardised sampling procedure regariding the cisternal CSF sample volume is advocated to have comparable data and to avoid misinterpretation it is absolutely essential that the amount of CSF withdrawn should be mentioned in reports about amine metabolites in CSF.

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SYMPOSIUM ON 'EINSTEIN—A HUNDRED YEARS'

To mark the birth centenary of Albert Einstein, the greatest scientist-philosopher of this century, an informal group of faculty members of Loyola College, styled as Forum for Academic Growth organised a one-day Symposium on 24th March 1979, where eminent physicists of India participated and brought out the life and achievements of Einstein, in popular language to a 300-strong audience of nonphysicists and physicists.

Professor Alladi Ramakrishnan (Director, Matscience Madras) in his presidential address explained how Einstein successfully gave shape to Newtonian principles. He called for a spirit of boldness, sincerity and investigation among the Indian students of science; the quality, he attributed, as a strong reason for the tremendous success of not only Einstein, but also of Raman and Bhabha.

Professor S. Ramaseshan (Jawaharlal Nehru Fellow, Raman Research Institute, Bangalore), in his keynot eaddress 'Einstein the man' elaborated on the biography of Einstein, and touched upon his qualities as a 'man'. He gave a critical account of the famous letter Einstein wrote to President Roosevelt which made the latter decide in favour of the atom bomb. The speaker also drew an illuminating comparison between the two titans in the evolution of physics as a science, namely, Newton and Einstein. The talk was interspersed with many interesting anecdotes from Einstein's life and his idiosyncracies.

Professor P. M. Mathews, (Senior Professor of Theoretical Physics, University of Madras, Madras) while speaking on 'Einstein, relativity and space-time' expounded the concepts of special and general theories of relativity which involve (*i*) light and the equality of inertial and gravitational masses and (*ii*) gravitational effects as the manifestation of the curvature of space-time. Establishing an interesting continuum to Professor Mathews's talk, Professor R. Srinivasan, (Head of the Department of Physics, Indian Institute of Technology, Madras) spoke on 'Einstein's Theories and Cosmology'. He said that the basic ideas behind the interpretation of gravitation as a distortion of the geometry of space-time are developed leading to Einstein's Gravitational Field Equations in empty space and the modification of these equations in the presence of matter and variation leads to the corresponding equations for the nonempty space. He analysed the relevance of these equations to cosmology and the various static and nonstatic models of the universe deduced therefrom. He also compared the models with the observational data available. Giving the concluding lecture, 'Post Einsteinian World—An Assessment', Dr. G. Venkatraman (Principal Physicist, Reactor Research Centre, Kalpakkam) dwelt at length on the sociological problems in relation to the impact of science and technology on modern society. He reinforced that the most important of these is the threat of a nuclear holocaust. He concluded with a brief reference to the type of education needed for the present society as also proposed by Einstein.

An exhibition displaying a few photographs and articles relating to Einstein was arranged by American Center, Madras and Albert R. Mann Library, New York.

By organising this programme, the Forum for Academic Growth celebrated the birth centenary of a great scientist who belonged to the whole world, in a unique way and it provided an opportunity to a number of young students to meet some of the leading scientists of India. Attempts are being made to bring out the proceedings of the Symposium.

The Forum thanks Rev. Fr. L. Correya, S.J., (Rector) and Rev. Fr. J. Kuriakose, S.J., (Principal) Loyola College, Madras, for their encouragement and the donors for their financial support.

Loyola College, A. RAMAN.
Madras 600 034.