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5-Hydroxyindole acetic excretion in newborns, infants and children

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The 5-hydroxyindole acetic acid excretion of healthy prematures, term newborns, infants, and children up to 15 years of age was investigated. Comparison of the results with healthy adult values suggests that more exact information can be obtained on excretion values of children if they are calculated for bodyweight. The results obtained in the different age groups point to an increased activity of serotonin metabolism in newborns, infants and children. During the important phases of somatic and psychomotor development an increased urinary output of 5-hydroxyindole acetic acid was found as compared with adult values.

In man, serotonin (5-hydroxytryptamine, 5-HT) is produced from tryptophane by several enzymic steps. 5-hydroxyindole acetic acid (5-HIAA) is a final product of the catabolism of this important biogenic amine. Serotonin is first transformed to 5-hydroxytryptophan acetaldehyde by monoaminooxidase, and this in turn to 5-HIAA by aldehyde dehydrogenase [11, 23, 29]. This product of catabolism is not stored by the cells, consequently it appears in the plasma and is excreted by the kidneys [4, 12, 13, 18, 28]. It is noteworthy that 5-HIAA was found in urine well before the discovery of serotonin [10]. The daily output of healthy adults is 2—8 mg 5-HIAA [11, 23]. The excretion rate is increased in pregnancy, an even more marked elevation can be observed in toxaemia, and extremely high excretion may be encountered in carcinoidosis [3, 11, 14, 16, 20, 21, 22, 24]. There is little information about its excretion in infants and children and data referring to 5-HIAA excretion of term and preterm newborns are even more scarce [1, 2, 19, 27]. As no normal values for infants and children are available, this has prompted us to perform the present study.

Patients and Methods

Healthy term babies, symptom-free prematures, infants and children treated in the corresponding departments of the Hospital of County Bács-Kiskun participated in the study. All patients below 4 years were boys, both sexes were represented in the age group 4—14 years. Urine was collected on the first five consecutive days from newborns, and from infants of 1, 2, 6 and 12 months of age. Beyond infancy the data were grouped for each completed year of age. Infants or children affected by malabsorption, metabolic disease, epilepsy,

mental or motor retardation of any origin or having been treated by any drug suspect of interfering with serotonin metabolism before admission, were excluded. The newborns and infants received a diet normal for their age. No cheese or tomatoes were given to older infants or children, these foods having a high serotonin content. Results obtained in 10 healthy adults served as control values. All age groups comprised 15 patients each.

The 5-HIAA content of the 24 h urine specimens was determined according to the method of Lynch et al [17]. For statistical analysis Student's *t*-test was used.

Results

5-HIAA excretion of preterm babies was significantly less on each day within the first five days than that of term infants (Fig 1). Newborns and infants had a significantly lower excretion than adults ($p < 0.01$). Healthy newborns had a higher excretion on the 4th day of life than ever during infancy. If the peak of the fourth day is disregarded, there was a gradual slow increase from the first day up to 12 months of age. At one year the mean value of 5-HIAA output was 1.3 mg $\pm$ 0.24 mg daily. During the four years following the first one, there was a marked increase, about 1 mg per year (Fig 2). The total increment from 5 to 9 years was as small as 1 mg. There was a sharp increase in daily output around the 14th year of age, more than 2 mg from the 13th to the 14th year. The mean excretion of children of 14 years was 7 $\pm$ 4.2 mg per 24 hours 5-HIAA. This was higher than in adults, but the difference was not significant statistically. In children one year of age, the daily 5-HIAA excretion was significantly lower than that of the healthy adult controls ($p < 0.01$).

If excretion is related to weight and expressed in mg/kg/24 h, the highest values for children were encountered

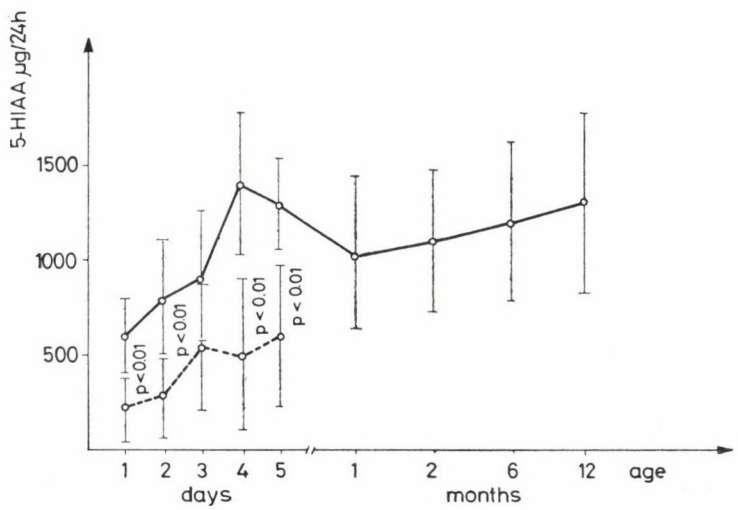

Fig. 1. Daily 5-HIAA output of newborns and infants: ○—○ of premature newborns: ○- - -○ on the first five days of life. Each group comprised 15 infants

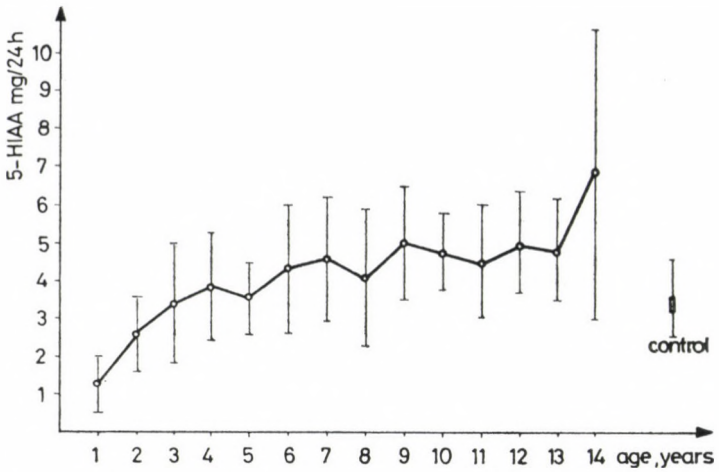

FIG. 2. Daily 5-HIAA outpout expressed in mg/24 h, of children compared with healthy adult control values. The number of adults was 10, each group of children comprised 15 individuals

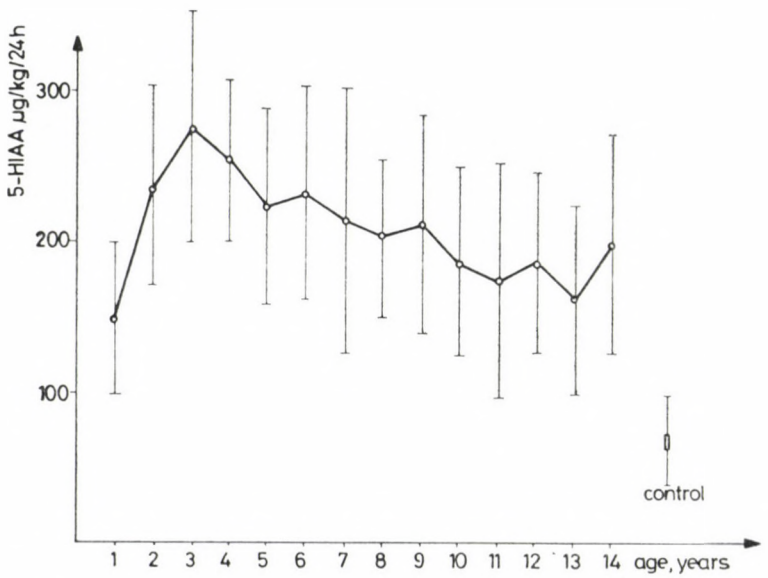

FIG. 3. Comparison of weight-related daily 5-HIAA excretion of children and adults, expressed in 5-HIAA µg/kg/24 h. The number of control individuals was 10, each age group comprised 15 children

in individuals of 2,3 and 4 years of age (Fig 3). Their mean values were significantly higher than the adult control values ($p < 0.01$). After 4 years, there was a gradual decrease in the weight-related 5-HIAA excretion. In general, children had higher values than adults, but by 13 years of age the difference disappeared. Children of 14 years of age showed a moderate increase again, but the difference was not significant statistically.

Discussion

Serotonin is an important biogenic amine and is one of the transmitter compounds playing an important role in the regulation of the central nervous system, especially in vertebrates [9]. 5-HIAA can be much easier measured than serotonin. Erspamer has shown that metabolism of 0.92 mg serotonin results in 1 mg 5-HIAA [5]. Therefore, excretion of 5-HIAA is a fairly good indicator of serotonin metabolism.

In a previous study [25] we showed that serotonin plays a great role in the adaptation of newborns to extrauterine conditions. Also, we compared the plasma serotonin level and 5-HIAA excretion of prematures affected by the idiopathic respiratory distress syndrome: there was a strong correlation between the two values and both changed with the severity of stress of adaptation [26].

The present results have confirmed our previous findings. Tu and Wong followed the 5-HIAA excretion of newborns up to the tenth days of life; they found a markedly increased excretion rate during the first 4 days, exceeding the mean values of healthy children of school-age [27]. Their results are only partly in agreement with our results. It is true that after the period of adaptation we found a gradual increase up to the end of the first year of life. The daily output of newborns calculated for 1 kg of bodyweight, however, did not exceed the corresponding mean values observed in school-children. The increased values of the first few days of life may be attributed to adaptation to extrauterine life. In our experience the daily output of 5-HIAA is parallel to the degree of adaptation stress and the increase is a good indicator of commensurate adaptation.

After completion of the first year, there is a considerable increase under normal conditions. In subsequent years the increase is less pronounced, only at about 14 years of age is there a rapid steep increase. The value of daily output of 5-HIAA is a crude indicator of serotonin metabolism, the weight-related value gives much more information. There is a strikingly high output between 2 and 4 years as compared to the adult values. In addition to somatic development, serotonin also plays an important part in learning and memory processes [9, 30]. It has been shown in many animal experiments that if serotonin metabolism is inhibited in the brain, the animal learns with difficulty and there will be a reduction in memory capacity [6, 7, 8, 15]. Our data showed

that in addition to adaptation to extrauterine conditions serotonin may also play an important part in the biological maturation process of the organism. Its presence may be determinant in somatic development, in learning the motion process, in learning and retaining data in the memory.

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