CATECHOLAMINE METABOLITES IN CSF

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THE ONLY metabolites of monoamines in cerebrospinal fluid (CSF) known to be of practical value today are homovanillic acid (HVA), methoxyphenylethylglycol (MOPEG)-sulphate and 5-hydroxyindoleacetic acid (5-HIAA).

The efflux of these from CSF to blood has obviously three main components, which are due to diffusion, bulkflow of CSF and active transport. The third phenomenon is at least due to one, but possibly two or three, active transport mechanisms. How these functions act on the efflux of HVA and 5-HIAA is rather obscure, and very little is known about the outflow of MOPEG-sulphate.

In dogs has been shown that while the value of CSF-5-HIAA rises to the same level in the hydrocephalic dog, where the outflow of 5-HIAA is almost completely blocked, and in the normal dog pretreated with probenecid and examined when reaching a steady state level of this drug in blood, the HVA concentration in the normal dog under same conditions reaches only half of the hydrocephalic level (ANDERSSON, VON ESSEN and ROOS, 1973). This phenomenon could be due to the higher lipid solubility of HVA. A relatively larger part of HVA than of 5-HIAA might be eliminated from the CSF by diffusion which is suggested to take place mainly on the convexities of the brain. In experimentally induced hydrocephalus, where the normal flow from the ventricular system is blocked, the acids cannot reach the diffusion sites which has different consequences for the elimination of HVA than for 5-HIAA.

Recently VON ESSEN in our laboratory has shown a significant increase in cerebral blood flow after dopamine intravenously to dogs and, which is more important in the clinic, a decrease after haloperidol and pimozide. The increase and the decrease is about 25 per cent of the normal flow (VON ESSEN, 1972).

The bulk flow carrying both large and small molecules by the same route is, of course, of some importance also for 5-HIAA and HVA, but the difference in the type of efflux between the acids cannot be explained in this way. Drugs reducing the intracranial pressure might possibly change the rate of disappearance of the acids via the bulk flow.

Probenecid blocks the active outtransport of 5-HIAA and HVA from CSF to blood. This has been used in clinical studies both in Parkinsonism (OLSSON and ROOS, 1968; for rev. see KORF, 1971) and manic-depressive psychosis (ROOS and SJÖSTRÖM, 1969; SJÖSTRÖM and ROOS, 1972; for rev. see SJÖSTRÖM, 1973). Also the basic levels of both 5-HIAA and HVA have been studied in many different conditions and I would like to review some of our recent findings.

Results of screening of material from 154 neurological patients (JOHANSSON and ROOS, 1973, in preparation) show that low basic values of both HVA and 5-HIAA can be seen in parkinsonism, in multiple sclerosis and in amyotrophic laterial sclerosis. (ROOS and STÖRTEBECKER, 1973, in preparation) low values for HVA were also seen in two cases with spinal cord tumor.

In material of depressed and manic patients we matched 15 depressed and 17 manic pairs (one male and one female in every pair) and compared them to 11 pairs of control patients and 11 pairs of healthy volunteers (SJÖSTRÖM and ROOS, 1972). There was a significant difference in the levels of 5-HIAA between depressed and manic male and female patients. Females had higher level of 5-HIAA in CSF than males. In material of young schizophrenic patients SEDVALL (personal communications) and his coworkers have recently seen changes in CSF-HVA in the similar direction. Females had significantly higher levels of the acid metabolite in lumbar CSF (SEDVALL, 1973, in preparation). In a material of 63 Parkinsonian patients, however, no such sex differences could be seen (GRANERUS, MAGNUSSON, ROOS and SVANBORG, 1973). The same negative finding is seen in our control material, (GOTTFRIES, GOTTFRIES, JOHANSSON, OLSSON, PERSSON, ROOS and SJÖSTRÖM, 1971) in which 100 patients are investigated according to 5-HIAA and 84 according to HVA in lumbar CSF. The results are thus divergent, but a recent study with autopsy material (GOTTFRIES, ROOS and WINBLAD 1973, in preparation) might throw some light upon the problem and give new information. There seems to be a sex difference of distribution of 5-HIAA in some parts of the human brain but not in all. In cortex lobus occipitalis and in cortex lobus hippocampi as in hypothalamus there are significantly higher levels of 5-HIAA in female than in male. In all the other parts investigated we could not find any difference. Sharman (personal communication) has seen the same difference in 5-HIAA in mice during the oestrus cycle. In a small series, where we studied HVA in caudate nucleus and putamen, we could see a tendency towards higher levels of HVA in these two nuclei in females. Our material is now bigger and a new statistical evaluation seems to show that the difference might be even more significant than in the first preliminary study. Our finding will possibly give new data to the discussion about the biological background to the psychological differences between males and females. We could tentatively speculate about what we know about disturbances in the balance between catecholamines and serotonin-release as a possible cause of aggressive behaviour. Maybe we should, until we know more, say only 'vive la différence'.

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