Diurnal Changes in Dopamine-β-Hydroxylase, Homovanillic Acid and 3-Methoxy-4-Hydroxyphenylglycol in Serum of Man

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Summary

Dopamine-β-hydroxylase activity (DBH) and concentrations of homovanillic acid (HVA) and 3-methoxy-4-hydroxyphenylglycol (MHPG) were measured in serum of 11 normal volunteers at 8 a.m., 2 p.m., 8 p.m. and 2 a.m. DBH was higher at 8 a.m. (p < 0.05) and lower at 2 a.m. (p < 0.0025). MHPG followed the same course, while HVA was higher at 8 p.m. (p < 0.05). The mean values for the eleven volunteers were: DBH 65.8 ± 25.8 nanomoles hydroxylated tyramine per ml serum and hour (at substrate concentration 0.05 mM), HVA 89.9 ± 57.3 ng/ml serum and MHPG 10.9 ± 3.4 ng/ml, with variation coefficients of 38.6, 63.8 and 30.1 respectively. The circadian variations found in serum parallel the data from estimations of MHPG and HVA in urine by other investigators. It is suggested that the diurnal variations of DBH, MHPG and HVA reflect the alternating activity of the catecholaminergic neurons in the peripheral as well as the central nervous system.

Introduction

A large body of evidence indicates that the catecholamines noradrenaline (NA) and dopamine (DA) play a crucial role in mediating certain types of mood and behavior. Approaches to obtain adequate information on their metabolism within the central nervous system of man can be made by measuring their metabolites in the body fluids.
Dopamine-β-hydroxylase (DBH), is the enzyme which catalyzes the hydroxylation of dopamine to noradrenaline. It is released from the sympathetic nerve terminals together with NA by the process of exocytosis (for review see Geffen and Livett, 1971, and Axelrod, 1972). DBH is found in various tissues of the sympathetic system and in the serum of humans and animals (Weinshilboum and Axelrod, 1971), and it has been suggested that serum levels of the enzyme may reflect peripheral sympathetic activity in man.

Methods have been developed to measure DBH activity in serum (Molinoff, Weinshilboum and Axelrod, 1971; Nagatsu and Udenfriend, 1972); however, various limitations and drawbacks in DBH measurement have been described by another investigator (Laduron, 1975).

Homovanillic acid (HVA) is the main metabolite of DA in brain (Carlsson, 1959) and it has been demonstrated that there exists an active transport system from brain to blood in dog (Ashcroft et al., 1968). However, no conclusive information is available as to what extent HVA in blood derives from brain.

3-methoxy-4-hydroxyphenylglycol (MHPG) has been shown to be the major metabolite of NA in brain of various species (Mannarino et al., 1963; Rutledge and Jonason, 1967; Schanberg et al., 1968; Schanberg et al., 1968 a). In man, MHPG has been measured in cerebrospinal fluid (Gordon and Oliver, 1971), urine (Wilke et al., 1967) and plasma (Dekirmenjian and Maas, 1974). Using different strategies in man and animals, it has been estimated that 30 to 50 percent of the urinary MHPG may originate from the metabolism of NA in brain pools (Gitlow et al., 1971; Maas et al., 1973), however not all reports do support this conclusion (Breese et al., 1972; Bareggi et al., 1974). No information is available to what extend MHPG in plasma may represent the metabolism of NA in brain.

The purpose of this study was to estimate the diurnal variations of DBH, HVA and MHPG in the serum of healthy volunteers under controlled conditions. The variations and correlations of those three parameters may yield some basic information necessary for further studies on catecholaminergic functions in physiological and pathological states.

**Materials and Methods**

Eleven male volunteers, aged 19 to 22 years, were housed under identical conditions on a ward of our hospital. Medical examination prior to the study did not reveal any substantial psychiatric or somatic diseases. All participants had normal blood pressures between 115 and 130 mm Hg.