Effect of Choline on Central Dopaminergic Function in Normal Subjects

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With 1 Figure

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Summary

Oral administration of choline (10 g) had no effect on basal serum growth hormone or prolactin concentrations in normal subjects (N = 5). Choline significantly enhanced the increase in growth hormone secretion induced by apomorphine HCl (0.5 mg s.c.). These data suggest that cholinergic mechanisms may enhance hypothalamic-pituitary dopaminergic function in man in contrast to their inhibitory effect on dopaminergic function in the basal ganglia.

Introduction

There is some evidence suggesting that the acetylcholine precursor, choline, enhances central cholinergic function and modifies striatal dopaminergic function (Haubrich et al., 1979; Davis et al., 1978) in the rat although it is not yet clear that such changes relate to increased brain acetylcholine concentrations. In man, oral administration of choline increases cerebrospinal fluid choline concentrations (Growdon et al., 1977 a) and, at least in some patients, improves tardive dyskinesia, Huntington’s chorea (Davis et al., 1976; Growdon et al., 1977 b) and memory impairment in Alzheimer’s disease (Signoret et al., 1978; Etienne et al., 1978). These clinical conditions are associated with hypocholinergic function and, in the case of the involuntary movement disorders, striatal dopaminergic hyperactivity.
These observations suggest that choline may also modify central dopaminergic function in man by increasing cholinergic activity.

Apomorphine, a dopamine receptor agonist in animals (Sourkes and Lal, 1975) and man (Tsang and Lal, 1977), stimulates growth hormone (GH) secretion (Lal et al., 1972, 1973, 1977) and this response has been used as a clinical index of central dopaminergic function (Lal and Nair, 1979). In the present study we have investigated the effect of choline on basal and apomorphine-induced GH secretion in normal subjects. In addition, because prolactin secretion is modulated by an inhibitory dopaminergic mechanism (Martin et al., 1974), we have also looked at the effect of choline on prolactin (PRL) secretion.

Subjects and Methods

Five physically healthy non-obese male volunteers, aged 30 to 45 years and on no medication served as subjects. In initial studies the effect of oral administration of choline on plasma choline concentrations and on basal GH and PRL secretion was investigated. Following an overnight fast, at 8 a.m. a 19-gauge scalp vein needle was inserted into an arm vein and kept open with heparin-saline. At 9 a.m. and 9.15 a.m. (i.e. −15 and 0 min), samples of blood were drawn for measurement of baseline control parameters. Immediately after the 9.15 a.m. sample choline (10 g of the base), given as the bitartrate in 200 ml water, or an equal volume of water alone, was ingested. Further samples of blood were drawn at 15, 30, 45, 60, 75, 105 and 135 min. Following these preliminary studies, the effect of choline on apomorphine-induced GH secretion was investigated in five subjects, four of whom were volunteers for the initial experiments. Choline (or water alone) was ingested 60 min before apomorphine HCl (0.5 mg s.c. at time 0 min). Samples of blood were drawn at −60, −45, −30, −15, 0, 15, 30, 45, 60, 90 and 120 min.

Serum GH and PRL were measured by radioimmunoassay (Friesen et al., 1970; Hwang et al., 1971). Plasma choline was determined by a radioenzymatic assay method adapted from procedures described before (Kato et al., 1975). Hormonal samples from the same subject under the different experimental conditions were measured in the same assay and without knowledge of the treatment code. Data were analyzed by the paired t-test. Results are presented as the mean ± S.E.M.

Results

Following administration of choline there was a rapid increase in plasma choline levels (Table 1). At 15 min the values were already significantly elevated compared with baseline values. From 45 min