In both the control and Alzheimer’s groups, significant inhibitions of adenylyl cyclase activity were produced by somatostatin (2P = 0.012; Wilcoxon’s matched-pairs signed ranks test and NPY (2P = 0.012). In the Alzheimer’s group, however, the degree of somatostatin enzyme inhibition was significantly lower than that for the control group. This difference was seen when both the absolute decreases in cAMP production and the percentage decreases in basal activity were compared (table). Furthermore, there was a larger spread in the observed somatostatin inhibitions for the Alzheimer’s group (compare the SEM values to the mean values in the table). In three of the Alzheimer’s cases, essentially no somatostatin inhibition of adenylyl cyclase activity was found, whereas the lowest percentage inhibition found in the control cases was 12%. For the control group, there were found to be no correlations (Spearman’s rank) between either basal activity, somatostatin or NPY inhibitions of basal activity and age or post mortem age.

The levels of 125I-1-Tyr-somatostatin-14 binding in the control and Alzheimer’s disease groups were not significantly different (table), a finding in accordance with some 6 but not with other reports. These data suggest that the lower degree of somatostatin inhibition of adenylyl cyclase activity in the Alzheimer’s group was not due simply to a lower receptor density. Important to note, was that the degree of NPY enzyme inhibition was similar in both groups, indicating that the observed deficit was specific to the somatostatin system and was unlikely to be a result of such factors as agonal status or drug treatment of the disease cases.

This study showing a reduced somatostatin modulation of adenylyl cyclase activity in Alzheimer’s disease is the first to our knowledge demonstrating a functional deficit of somatostatin receptor integrity in this disorder. Further experiments will be necessary to determine the mechanism underlying this dysfunction, such as for example studying the integrity of somatostatin receptor—“G”-protein—adenylyl cyclase interactions.

It will also be interesting to determine whether this dysfunction is found in other brain regions regulating dysfunctions in Alzheimer’s disease pathology and whether it is important for the cognitive decline seen in the disorder.

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Plasma dopamine-beta-hydroxylase activity in depressed patients: role of treatment

Dopamine-beta-hydroxylase (DBH) catalyses the hydroxylation of dopamine to noradrenaline and is known to be released with the neurotransmitter from the sympathetic nervous system. 6 It has been suggested that serum DBH could be an index of the activity of the sympathetic nervous system. 3 Moreover, several authors have established a relationship between central noradrenergic deficiency and the occurrence of depressive disorders. Plasma DBH measurements in depressive disorders has led to conflicting results although most authors found decreased DBH activity. 4,3 Large individual variations in plasma DBH activity can explain these discrepancies. Thus the aim of this study was to compare plasma DBH activity in the same depressed inpatients before and after antidepressant treatment.

Seventeen patients [two men and 15 women, mean (SEM) age: 40.5, (15.2) years] were included in this study. They all suffered from major depressive disorders according to DSM III criteria and were treated with tricyclic antidepressants. Patients treated with ECT or drugs acting on the autonomic nervous system (especially cardiovascular drugs or neuroleptics) were excluded. Plasma DBH was measured at rest after an overnight fast and five weeks after antidepressant treatment using the spectrophotometric method of Nagatsu and Udenfriend 6 with tyramine as substrate. The assays were performed blind to diagnosis. The changes were evaluated before and after treatment using a Wilcoxon test. The comparisons with a control group of 15 normal healthy volunteers [six men and nine women, mean (SEM) age: 34.8 (8) years] were performed using a Mann–Whitney test. The level of significance was p < 0.05.

All the patients were clinically euthyemic at the second DBH measurement (that is, five weeks after the beginning of the treatment). Mean plasma DBH activity (SEM) was 18.39, (2.02) µmol/min/l in controls; 6.43, (1.08) µmol/min/l in depressed patients before treatment (p < 0.01 when compared with controls) and 10.82, (2.56) µmol/min/l in euthyemic patients (that is, depressed patients treated by antidepressants) (p < 0.01 when compared with values obtained in these patients before treatment).

Although plasma DBH activity is a peripheral blood index, it more directly reflects the metabolism of catecholamines than other indices such as the metabolite MHPG or yield. It is needed to evaluate the role and indirect approaches of central noradrenergic activity. Plasma DBH activity may reflect the state of releasable stores of the enzyme in sympathetic nerve endings.

It may be concluded that plasma DBH activity is decreased in depressed patients when compared with age-matched controls. Whether this decrease is observed in every patient or in a subgroup remains a prospective for future studies.

The most interesting and original result is the increase in plasma DBH activity in euthyemic patients, that is, after five weeks of treatment with tricyclic antidepressants. The respective role of antidepressant drugs and thymic improvement remains unclear. However, the level of plasma DBH activity remains significantly (p < 0.05) lower in euthyemic patients than in control patients.

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