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 degree decreased 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 in the lowest percentage inhibition found in the control cases was 12%. For the control group, there were no to be found (Spearman's rank) between either basal activity, somatostatin or NPY inhibitions of basal activity and age or postmortem interval.

The levels of 251-Tyr-somatostatin-14 binding in the control and Alzheimer's disease groups were not significantly different (table), a finding in accordance with some but not all other studies. 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 population. Importantly, of 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 important to determine whether this dysfunction is found in other brain regions involved in different degenerative processes. 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. Whether serum DBH activity is increased in patients with melancholic or atypical depression, and whether DBH activity is increased or decreased in other depression subtypes, has been discussed extensively in the literature, as has been the role of DBH in the pathophysiology of depression.

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 (2) years] were included in this study. They all suffered from major depressive disorders according to DSM 3 R 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 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 five normal healthy volunteers [six men and nine women, mean (SEM) age: 34, (8) years] were performed using a Mann Whitney test. The level of significance was p < 0.05.

All the patients were clinically euthymic at the second DBH measurement (that is, five weeks after the beginning of the treatment). Mean plasma DBH activity (SEM) was 6.39, (2.02) pmol/min/l in controls; 6.43, (1.08) pmol/min/l in depressed patients before treatment (p < 0.01 when compared with controls) and 10.82, (2.56) pmol/min/l in euthymic 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 urinary levels. Studies are needed to elucidate the role of DBH and other 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 euthymic 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 euthymic patients than in depressed patients. Whether these findings will lead to a genetic component in the pathophysiology of depressive states could be suggested since altered plasma levels of DBH may reflect a genetic susceptibility. Further, further studies will be necessary to determine whether this is the case.

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