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 sign rank 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 seen 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 postmortem delay.

The levels of 125I-Tyr1-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 reports.2 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 in this group. 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 glial 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 to establish 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—adenyl cyclase interactions. It will also be interesting to determine whether this dysfunction is found in other brain regions showing different degrees of Alzheimer’s disease pathology and whether it is important for the cognitive decline seen in the disorder.

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Letters to the Editor

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 peripheral sympathetic nerves.2,3 It has been suggested that serum DBH could be an index of the activity of the sympathetic nervous system. 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 Large inter-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 [ten men and 15 women, mean (SEM): age 45.5 (15.2) 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 Udenfriend5 with tyramine as substrate. The assays were performed blind to diagnosis. The changes were evaluated before and after treatment using a Wilcoxon test. The comparison with a control group of 15 normal healthy men (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 euthymic 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; 4.33 (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 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. Studies are needed to evaluate the relationship between these indices and the clinical state or response to treatment. Thus, the DBH activity could be a marker of depressive states or at least clinical subtypes of depression.

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