sequence T1-weighted sagittal and axial MRIs (TR = 600 ms; TE = 20 ms, matrix size 256 × 256, scan thickness 5 mm) obtained from a GE 1.5 Tesla super-conductive magnet (Signa) were non-specific and the tumour was not visualised, as the signal intensity of the mass was nearly isointense with the surrounding CSF (fig a).

The T2s (TR = 2500 ms; TE = 80 ms), however, revealed an intraspinall lesion which was outlined by the different signal intensities of the CSF above and below the tumour (fig b). The CSF signal to the tumour appeared brighter than the CSF superior to the tumour. There were no discernible signal differences between tumour and CSF, cephalad to the tumour. Thus the entire margin of the tumour was not well delineated (fig b). Following the injection of IV Gd-DTPA, at the dose of 0.2 ml/kg (0-1 mmol/kg) the T1-weighted MRI showed marked enhancement of the tumour with its margins well delineated from the surrounding CSF (fig c). The tumour extended from the middle of L2 caudal to the upper border of L3 and measured 14 mm in the AP dimension and 32 mm in the height. It was an intradural extramedullary lesion. Ependymoma and neurofibroma were the major differential diagnoses.

An L1 through L4 lumbar laminectomy was performed, exposing the dark-bluish dural. The dura was opened and the encapsulated 5 × 1.5 cm bluish-brown tumour was easily identified. The CSF caudal to the tumour was xanthochromic and proteinaceous, and clear cephalad to the tumour. It arose from the filum terminale and invaded the conus medullaris. Sharp microscopic techniques were employed to resect the tumour completely. The filum terminale was amputated and a 1 mm ventrally located tumour feeding the artery was divided. The dura was closed in a watertight fashion. The patient made an uneventful recovery. His neurological examination remained intact.

Light microscopic examination of the tumour using hematoxylin and eosin revealed papillary areas consisting of low columnar cells surrounding a central core of hyaline and connective tissue containing small blood vessels (fig d). The architecture of the cells was orderly without mitoses and was consistent with the previously pathological diagnosis of myxopapillary ependymoma.

Gadolinium DTPA is a paramagnetic contrast medium that decreases the relaxation time of T1 and T2 nuclei in tissues where it accumulates. T1 shortening increases the signal intensity of tissues, whereas T2 shortening decreases the signal. Fortunately, at lower concentrations, the T1 effect predominates. Like iodinated agents used for CT, Gd-DTPA serves as an indicator of blood-CSF barrier disruption for MRI. If this barrier is disrupted, the contrast molecules diffuse into the interstitial compartment, producing T1 shortening and enhancement of T1-weighted images. Spinecho pulse sequence T1-weighted images were not helpful in this case as the tumour and contrast material was seen evenly in the water and fat signal intensities. Differences of signal intensity between the tumour and CSF on T2-weighted images allowed the visualisation of the tumour lesion. Brighter signals were observed from the CSF below the tumour secondarily to its decreased flow, and increased protein content. Following Gd-DTPA injection, pronounced and its margins were well delineated from the surrounding CSF and from the conus medullaris. Although its enhancing characteristic was not specific for either a neurofibroma or ependymoma, the true extent and location of the lesion was readily identifiable.

This case confirms a previous study documenting the superior imaging capacity of Gd-DTPA MRI compared with unenhanced T1 and T2 MRI in diagnosing spinal cord ependymomas and other hitherto radiographically elusive spinal cord lesions.

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Somatostatin receptors and the modulation of adenylyl cyclase activity in Alzheimer's disease

The most consistently reported neuropeptide dysfunction in Alzheimer's disease is that affecting somatostatin neurotransmission, as characterised by a loss of somatostatin-like immunoreactivity and decreased numbers of somatostatin receptor recognition sites.1 Such changes in the number of receptor recognition sites, however, give no information as to the functional integrity of the receptor in the disease state.2 A recent study on rat brain established that somatostatin modulation of neural function involves the inhibition of adenylyl cyclase activity by the occupation of receptor sites negatively coupled, via GTP-binding ("G")-proteins, to this enzyme.3 As a result, in our study, we have assessed the integrity of somatostatin receptor function in Alzheimer's disease by assaying both the levels of receptor recognition sites and the ability of somatostatin to inhibit adenylyl cyclase activity.

Brains from a series of eight clinically diagnosed and histopathologically confirmed Alzheimer's disease cases (mean [SEM] age 81 [2] years, mean [SEM] post mortem delay 21 [4] hours) and eight control subjects (mean age 75 [2] years, mean post mortem delay 23 [3] hours) were collected at necropsy. Tissue from the superior temporal cortex (Brodman area 22) was dissected, slowly frozen and stored at -70°C for 1 year for the preparation of synaptic membranes. Adenylyl cyclase assays were performed on washed synaptic membrane fractions (10-15 µg protein) from each of the above groups over a concentration range of 10-80 µM inosine triphosphate (IPTP). The specific activity of cyclic AMP production was determined for each experiment as an average of two separate determinations and was calculated as the difference between the cyclic AMP produced from basal levels (specific activity of 0-5 µM IPTP) and the maximum amount of cyclic AMP produced at 100 µM IPTP. Control and Alzheimer's disease groups were each divided into two subgroups; one was used for the determination of cyclic AMP production while the other was used for the determination of cyclic AMP production in the presence of somatostatin.

Table Somatostatin receptor function in Alzheimer's disease

<table>
<thead>
<tr>
<th>Somatostatin receptor activity in Alzheimer's disease</th>
<th>Control</th>
<th>Alzheimer's disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basal activity</td>
<td>100 µM somatostatin</td>
<td>48.6 ± 8.8</td>
</tr>
<tr>
<td>% somatostatin inhibition of basal activity</td>
<td>11.7 ± 3.2</td>
<td>11.3 ± 2.1</td>
</tr>
<tr>
<td>Somatostatin activity</td>
<td>100 µM NPY</td>
<td>39.5 ± 2.6</td>
</tr>
<tr>
<td>% NPY inhibition of basal activity</td>
<td>20.8 ± 3.0</td>
<td>36.2 ± 2.5</td>
</tr>
<tr>
<td>Somatostatin binding</td>
<td>110 pM [3H]somatostatin</td>
<td>19.4 (9-4)</td>
</tr>
<tr>
<td>% Somatostatin binding</td>
<td>30 µM [3H]somatostatin</td>
<td>6.2 (1.3)</td>
</tr>
</tbody>
</table>

**p < 0.02 two-tailed Mann-Whitney U-test, with respect to corresponding control values.
*p < 0.05 two-tailed Mann-Whitney U-test, with respect to corresponding control values.

1 µmol CAMP/min/mg protein, mean (SEM).
1.0 mol/mg protein, mean (SEM).
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 NPV (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 even 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 highest percentage inhibition (59%) was seen in the control cases was 12%. For the control group, there were no to be no correlations (Spearman's rank) between either basal activity, somatostatin or NPY inhibitions of basal activity and age or post 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 study ing 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 showing distinct degenerative features in Alzheimer's disease pathology and whether it is important for the cognitive decline seen in the disorder.

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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 NE levels. The study is needed to evaluate this 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 euthy mic 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 euthy mic patients than that in depressed patients. This suggests that DBH activity may be an index of the sympathetic nervous system. Furthermore, the 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.3 Large interindividual 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 patients 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 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 15 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 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 euthymic patients (that is, depressed patients treated by antidepressants) (p < 0.01 when compared with values obtained in these patients before treatment).

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

Dopamine-beta-hydroxylase (DBH) catalyses the hydroxylation of dopamine to noradrena line and is known to be released with the neurotransmitter from the sympathetic nerve endings. It has been suggested that serum DBH could be an index of the activity of the sympathetic nervous system. Moreover, several authors have noted an increased DBH activity or significant DBH activity after treatment with antidepressants. In these patients, the DBH activity was significantly higher than in depressed patients and normal controls. The degree of depression was evaluated by the Hamilton Depression Rating Scale. DBH activity was measured from plasma by a sensitive assay using a competitive protein binding technique. DBH activity was significantly lower in depressed patients than in healthy controls and normal subjects. This suggests that DBH activity may be a marker of depressive states or at least clinical subtypes of depression.