associated predominantly with hemangioblastomas of the central nervous system (HbI), angiomatosis retinae (AR), renal cysts, renal cancer, pancreatic cysts, pheochromocytoma and epididymal cystadenoma. Since paraneoplastic production of erythropoietin (EPO) or of erythropoiesis stimulating factors has been described in cerebellar HbI, renal cancer, renal cysts, and pheochromocytoma, we investigated whether the serum EPO concentration is an indicator of HLS, which might facilitate an early diagnosis of affected individuals.

Our study included 44 patients (23 females, 21 males) with positive gene carrier status of HLS. Their mean age was 38.7 (16-79) years. Five of the patients had HbI, 25 had AR, two had renal cancer, three had renal cysts, seven had pheochromocytomas; four had a history of surgical treatment for HbI, and 11 for pheochromocytoma. Fifteen subjects presented with multiple lesions. Three asymptomatic individuals were identified as gene carriers by pedigree analysis.

Serum for EPO radioimmunoassay was prepared from venous blood sampled without anticoagulant. The assay was carried out in duplicate using human urinary EPO standard, 125I-labelled recombinant human EPO (specific activity 11-33 TBq/mmol; Amer sham Buchler, Braunschweig, Germany) and antisera (1:5000) from a rabbit immunised with human urinary EPO. The antibody-bound 125I-EPO was precipitated with polyethylene glycol 6000 (160 g/l). The mean within and between assays coefficients of variation were 7% and 19% in the EPO range 40-50 mU/ml. The detection limit was 5 mU/ml.

Comparative measurements of immuno-reactive EPO were performed on serum samples from 14 normal subjects (five females, nine males; age 20-38 years). Their EPO values were essentially normally distributed with a mean (1 SD) of 18.1 (7.5) mU/ml. Thus, with the assay described, 95.5% of all normal values are in the range 31-33 mU/ml (mean ± 2 SD).

Serum EPO was elevated (> 33.1 mU/ml) in two of five (40%) patients with HbI, in two of 25 (8%) with AR, in one of seven (14%) with pheochromocytoma, but in none of the patients with renal and pancreatic lesions. No significant correlation was found between elevated EPO values and serum haemoglobin concentrations. One patient with AR and one patient with a history of pheochromocytoma surgery presented with erythrocytosis (haemoglobin > 180 g/l), but serum EPO was normal in both cases.

We conclude that EPO is not a suitable marker for identifying patients affected with HLS, either in asymptomatic or in symptomatic individuals, and subsequently does not support our recently published clinical screening programme.

Correspondence to: Dr Neu mann.


Application of gadolinium-DTPA magnetic resonance imaging for detection of a filum terminale myxopapillary ependymoma allowing successful surgical resection

Myxopapillary ependymomas of the spinal cord are histologically distinct low-grade gliomas which arise almost exclusively in the regions of the conus medullaris and filum terminale.¹²³ Radio graphic confirmation of these tumours has traditionally relied upon myelography and, more recently MRI.¹⁴¹ We report a further case that demonstrates the diagnostic value of Gadolinium-DTPA enhanced MRI.

A 41-year-old male teacher of gymnastics presented with a one and a half year history of low back pain which radiated intermittently and alternatingly to the right and left buttocks and thighs, and was exacerbated by valsalva manoeuvres. He did not complain of focal motor weakness, sensory or spasticinal disturbances.

Physical examination of the patient’s lumbar sacral region as well as his neurological examination were unremarkable. He had normal strength, sensation and rectal tone, as well as active and equal deep tendon reflexes throughout, with downgoing plantar reflexes and a normal gait. Leseuge’s test was negative bilaterally.

Plain radiographs and unenhanced CT scans of the entire lumbar sacral spine were repeated at our institution and were unremarkable. Intravenous enhanced lumbar sacral (L1-S1) CT also failed to show any intraspinal enhancing mass. Spin-echo

Figure (a) Spin echo pulse sequence, T1 (TR/TE = 600/20) and (b) T2 (TR/TE = 2500/80) weighted sagittal MRIs of the lumbar spine: the tumour was not apparent on T1, however, on T2 weighted image an intradural tumour extending from approximately mid L2 to the superior border of L3 could be seen. Note the signal intensity of the CSF below the mass which was brighter than the CSF above the tumour. (c) Post Gd-DTPA injection T1-weighted sagittal MRI of the lumbar spine: the location, margin and extent of the intradural tumour was readily identifiable due to the striking enhancement of the tumour. (d) Light microscopy of the tumour revealing papillary low columnar cells surrounding a central core of hyaline containing small vessels (Haematoxylin and Eosin × 40).
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 radiologically elusive spinal cord lesions.  

N MOSKOWITZ  
S UEMATSU  
Department of Neurosurgery  
AJ KUMAR  
H WANG  
Department of Radiology  
L HEDRICK  
Department of Pathology  
Johns Hopkins Hospital and  
Johns Hopkins University School of Medicine,  
Baltimore, Maryland, USA  

Correspondence: Dr Moskowitz, Johns Hopkins Hospital, Department of Neurosurgery, Baltimore, MD 21205, USA


Somatostatin receptors and the modulation of adrenylyl 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.  

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.  

A recent study on rat brain established that somatostatin modulation of neural function involves the inhibition of adrenylyl cyclase activity by the occupation of receptor sites negatively coupled, via GTP-binding ("G") proteins, to this enzyme.  

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 modulate adrenylyl 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 necropy. Tissue from the superior temporal cortex (Brodman area 22) was inspected, slowly frozen and stored at -70°C until used for the preparation of synapenic membranes. Adrenylyl cyclase assays were performed on washed synapenic membrane fractions (10-15 µg protein). Assays were terminated at 30°C in assay buffer consisting of 80 mM Tris acetate (pH 7.4), 0.5 mM ATP, 10 µM GTP 1 mM theophylline, 0.3% BSA, 0.5 mM EGTA, 5 mM phosphate, 30 units cyclic AMP phosphodiesterase, 2 mM MgSO4, with and without 100 µM somatostatin-14. Assays were terminated by boiling for 3 minutes and the cyclic AMP produced assayed using a commercial kit (TRK 432, Amersham). The concentration of somatostatin-14 used (100 µM) was the same as that reported necessary to achieve inhibition of rat cortical membrane adrenylyl cyclase.

Somatostatin receptor binding sites were determined using extensively washed and lysed membrane preparations (ca. 70 µg protein/assay) which were incubated for 60 minutes at 37°C in 50 mM Tris HCl (pH 7.4 buffer containing 10 mM MnCl2, 1 mg/ml BSA and 60 µg/ml bacitracin, with two different concentrations of [3H]-Tyr"-somatostatin-14 (30 and 110 pM). Non-specific binding was defined using 1 µM unlabelled somatostatin-14. Incubations were terminated after 10 minutes trituration and tissue bound radioactivity determined following washing of the pellet.

In addition to these experiments, the effects of 10 µM neuropeptide Y-36 (NPY) on adrenylyl cyclase activity were assessed, since this neuropeptide has also been shown to mediate inhibition of the enzyme.  

Such experiments were also considered important in view of the known co-localisation of somatostatin and NPY in some cortical neuronal sub-populations and the reported loss of NPY immunoreactive neurons in Alzheimer's disease temporal cortex.

Baseline adrenylyl cyclase enzyme activities in the control and Alzheimer's disease groups were not significantly different from each other (table). The large apparent difference (20%) between the control and Alzheimer's disease group basal activities was due to a single control case showing high activity (138±2 pmol cAMP/min/mg protein).

Table Somatostatin receptor function in Alzheimer's disease

<table>
<thead>
<tr>
<th>Somatostatin receptor</th>
<th>Control</th>
<th>Alzheimer's disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basal activity</td>
<td>48±6</td>
<td>43±7</td>
</tr>
<tr>
<td>% Somatostatin inhibition of basal activity</td>
<td>3.1</td>
<td>8.3</td>
</tr>
<tr>
<td>% NPY inhibition of basal activity</td>
<td>37.2</td>
<td>53.5</td>
</tr>
<tr>
<td>[3H]-Tyr Somatostatin binding</td>
<td>110</td>
<td>110</td>
</tr>
<tr>
<td>Somatostatin</td>
<td>30 µM [3H]-Somatostatin</td>
<td>30 µM [3H]-Somatostatin</td>
</tr>
<tr>
<td>Basal activity</td>
<td>19±4</td>
<td>14±7</td>
</tr>
<tr>
<td>% Somatostatin inhibition of basal activity</td>
<td>30</td>
<td>30</td>
</tr>
<tr>
<td>% NPY inhibition of basal activity</td>
<td>53±9</td>
<td></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 pmol cAMP/min/mg protein, mean (SEM).  
2 nmol/mg protein, mean (SEM).