Brain glucose utilisation in a patient with parkinsonism: a postmortem study with PET and SPECT.

Wechsler memory testing (limited by weight loss) showed lesions of the subthalamic nucleus. Science was shown to rest at with eyes closed, by means of 18-fluorodeoxyglucose, with a seven slice PET device of high resolution (5:5 × 5 × 5 × 9 mm, x, y, z, model TTV 03, LETI, Grenoble, France) in stereotactic positioning conditions relative to the Glabellas-Infion line. Attenuation correction was carried out by means of a transmission scan. The regions of interest were positioned directly over the MRI cross sections corresponding to the PET planes, by means of a software enabling MRI data acquired in 3D (FLASH procedure) to be resliced to the PET coordinates with respect to the patient's personal anatomical structures. The structures were identified on the MRI relative to the bicomissural line, and with Talairach's stereotaxic atlas of the human brain. The circular (14 mm diameter) regions of interest, 116 in number, aimed at analysing the main functional neocortical and subcortical structures, with averaging over both sides.

The absolute CMRglc values and the relative metabolic indices (region/neocortex) were compared with confidence intervals calculated in a sample of 10 healthy volunteers of mean age 51 (SD 9) years. The confidence intervals for single subject predictions were calculated as mean (SD), adjusting t to the sample size and the two tailed probability value chosen (t = 2.626 for 9 df, and p < 0.05 here).

Analysis of the absolute CMRglc values showed no significant abnormality, although the values for all the structures were close to the lower 95% confidence limit as calculated in our control group. Analysis of the “Region/Neocortex” indices (table) showed diminished values for the lateral prefrontal cortex, which just reached the p < 0.05 level. The temporal/neocortex index was significantly reduced (p < 0.05), and the occipital/neocortex index was significantly raised (p < 0.01); other regional metabolic indices showed no significant change. A lateral-prefrontal/neocortex ratio, calculated as the anteroposterior metabolic gradient, was significantly (p < 0.05) reduced (0.78% for a 95% lower confidence limit of 0.80).

Our patient's abnormal behaviour comes nearest to what has been described since the 1920s in the French literature as “athythormia” (in Greek, lack of thyroid, affect and lept, drive), initially in psychotic patients, subsequently in patients with bilateral lesions of the striatum. Laplante et al. described a similar presentation in patients with bilateral lesions of the pallidum or caudate, lose the ability to do what they called “loss of psychic self-activation” or “psychic akinesia”, also described recently after paramedian bilateral thalamic infarct. Both “athythormia” and “loss of psychic self-activation” share certain features that suggest frontal lobe dysfunction (for example, mental retardation, reduced initiative), but their hallmark is loss of drive (lack of interest in things of life) and a flat affect (lack of emotional response) and global mental deterioration. Reversal of this behaviour by external stimulation, however, seems less efficient in “athythormia”, which was rare in our patient.

The cerebral metabolic values in our patient showed minor changes, with a marginally significant relative lateral-prefrontal, and significant lateral-temporal hypometabolism, as well as a significant increase in relative metabolism of the occipital cortex, but without metabolic alterations of the precentral cortex or parietal lobe. This pattern suggests an abnormal anteroposterior metabolic gradient, also shown by a significantly reduced lateral-prefrontal/occipital ratio. Because this is the first report of metabolic changes in the brain in ADPPD, our findings can only be compared with previous literature in other related diseases.

Previous studies in patients with psychotic akinesia from mainly bipallidal or bithalamic lesions have also reported mild lateral prefrontal hypometabolism, suggesting disruption in the prefronto-striato- pallido-thalamo-prefrontal circuit at different levels results in a similar clinico metabolic picture. Neuropathological data in our patient’s two brothers (obtained at an advanced stage) indicate the presence of lesions at several locations in this circuit, with a possible cumulative effect on cortical function; moreover, this loop was presumably deprived of its modulating dopaminergic afferents, as is also the case in progressive

<table>
<thead>
<tr>
<th>Regional metabolic ratios (region/neocortex)</th>
<th>Patient</th>
<th>Controls (mean 95% confidence intervals)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frontobasal cortex</td>
<td>0.91</td>
<td>0.94 (0.73-1.15)</td>
</tr>
<tr>
<td>Prefrontal cortex</td>
<td>0.92</td>
<td>1.03 (0.86-1.15)</td>
</tr>
<tr>
<td>Whole prefrontal cortex†</td>
<td>0.92</td>
<td>1.01 (0.86-1.15)</td>
</tr>
<tr>
<td>Parietal cortex</td>
<td>1.03</td>
<td>1.00 (0.87-1.12)</td>
</tr>
<tr>
<td>Whole frontal cortex</td>
<td>0.94</td>
<td>1.02 (0.88-1.14)</td>
</tr>
<tr>
<td>Whole temporal cortex</td>
<td>0.88**</td>
<td>0.96 (0.89-1.01)</td>
</tr>
<tr>
<td>Whole parietal cortex</td>
<td>1.01</td>
<td>1.04 (0.97-1.11)</td>
</tr>
<tr>
<td>Whole occipital cortex</td>
<td>1.18***</td>
<td>1.00 (0.87-1.12)</td>
</tr>
<tr>
<td>Limbic cortex</td>
<td>0.95</td>
<td>0.87 (0.74-1.00)</td>
</tr>
<tr>
<td>Caudate nucleus</td>
<td>1.08</td>
<td>1.06 (0.83-1.34)</td>
</tr>
<tr>
<td>Lentiform nucleus</td>
<td>1.05</td>
<td>1.08 (0.83-1.34)</td>
</tr>
<tr>
<td>Basal ganglia</td>
<td>1.07</td>
<td>1.09 (0.86-1.31)</td>
</tr>
<tr>
<td>Thalamus</td>
<td>1.17</td>
<td>0.94 (0.70-1.16)</td>
</tr>
</tbody>
</table>

*p = 0.05; **p < 0.05; ***p < 0.01 vs normal controls.
†Includes the lateral prefrontal and frontal cortices.
‡Includes the prefrontal and the precentral cortices.
§Includes the caudate and lentiform nuclei.
supranuclear palsy, which also affects this loop and in which an abnormal anteroposterior metabolic gradient has also been documented. On the other hand, lesions essentially confined to the substantia nigra, as in Parkinson's disease, do not consistently alter cortical metabolism. It is tempting to envisage dysfunction in the prefronto-striato-pallido-thalamo-prefrontal loop as one possible mechanism underlying both "athymormia" and the abnormal anteroposterior metabolic gradient.

Mechanisms to account for the altered anteroposterior metabolic pattern in our case, other than disruption of this loop, include neuronal damage at the level of the frontal cortex. Thus although frontal atrophy was only questionable at MRI performed at the time of PET in our case, it was undoubtedly present in her two brothers at postmortem (at a much later stage of the disease), indicating frontal lobe degeneration is part of the entity. Also, the metabolic changes could reflect (and not cause) her abnormal behavior. Thus a similar metabolic profile has been reported in patients affected by schizophrenic or obsessive-compulsive disorders, where a flat affect and loss of drive are common features.

In conclusion, however disabling this abnormal behavior may be, it seems to be expressed as only mild anteroposterior metabolic imbalance.

Addendum
Since acceptance of this paper, the patient developed, and died from, central hypoventilation.

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Visual rating of hippocampal atrophy: correlation with volumetry

In a previous paper we described the use of visual rating of medial temporal and hippocampal atrophy as an early diagnostic marker for Alzheimer's disease. Other studies on this subject have used volumetric estimations of the hippocampal complex or temporal lobe. These techniques are refined but time consuming. To investigate the correlation between visual rating and volumetric estimation of the hippocampus, we assessed the volume of the hippocampus in 41 subjects (20 patients with Alzheimer's disease and 21 age-matched controls) of whom demographic data and MRI had been described elsewhere. The volumetric assessments were carried out by one author, who had been involved in the clinical part of the previous study but had not seen the images before. He performed the analysis blinded to the diagnosis and ages of the subjects.

After magnification of the hard copies of the MRIs by projecting them on a screen with an overhead projector, the outlines of the brain and hippocampus were drawn on transparencies. Only the second to the fifth slices of each MRI were used. These transparencies were then digitized on a Macintosh IIx with a ScanJet IIc flatbed scanner (Hewlett Packard) with a resolution of 72 dots per inch and were saved on an eight bit grey scale TIFF file (256 shades of grey). Postprocessing of the images was carried out with the public domain program IMAGE 1.35 (from W Rasband, NIH research services, Bethesda, Maryland, United States). The area of the hippocampus on each slice was measured and magnified by the slice thickness, thus producing an estimation of the volume. For analysis the eight volumes (four on each side) were added together and divided by four to produce a "mean total hippocampal volume".

The correlation between visual and volumetric assessment of hippocampal atrophy was excellent (figure; r = 0.83 p < 0.001, one-tailed).

From the figure it may be inferred that overlap occurs between some of the scores, especially between 2 and 3. Based on the volumetric assessments in 21 subjects, we had to modify to a 0-2 or 0-3 scale, which would simplify the rating, but could lead to loss of discriminative power. Although drawing from magnified hard copies may introduce several measurement errors, the correlation is surprisingly high. In future research, postprocessing will be carried out on images taken directly from the scanning console, bypassing the use of magnified copies.

In general, the main disadvantage of visual ratings in research settings has always been the low interobserver and intraobserver reliability. For clinical practice, however, visual ratings provide a useful and rapid assessment of hippocampal atrophy that correlates well with linear and volumetric measurements and may be used to aid the clinician in diagnosing or ruling out Alzheimer's disease.

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5 SERNUM concentrations of 2',5'-oligoadenylate synthetase, neopterin, and β-glucan in patients with chronic fatigue syndrome and in patients with major depression

Chronic fatigue syndrome is characterised by debilitating severe fatigue persisting for more than six months. Furthermore, it is associated with physical symptoms, such as muscle weakness, sore throat, arthralgia, and myalgia, as well as psychological symptoms such as headache, insomnia, depressive state, and neuropsychiatric symptoms. It has often been claimed that the onset of chronic fatigue syndrome follows an infection or for infection-like illness; hence a certain microorganism(s) or virus may cause it. Another possible candidate for inducing chronic fatigue syndrome is the cellular and humoral immune dysfunction, which has