## Regional cerebral glucose metabolism in akinetic catatonia and after remission

K L Kahlbaum published in 1874 the first recorded description of catatonia. Akinetic catatonia is now defined as a neuropsychiatric syndrome principally characterised by akinesia, mutism, stupor, and catalepsy.[1] Even if some advances have been made in the recognition of catatonia, in particular by the development of different rating scales,[1] the pathophysiology of this syndrome is not clearly established.

A right handed 14 year old girl presented with akinetic catatonia during an episode of depression in the context of a bipolar type I disorder. Her catatonic status was characterised by akinesia with brief episodic spontaneous stereotyped movements, mutism, no spontaneous oral intake, catalepsy, waxy flexibility, and stupor with brief occasional eye contacts. This corresponded to a total score of 19 on the Northoff Catatonia Scale.[1] Electroencephalogram performed one day after onset of symptoms showed diffuse theta activity with sporadic diffuse delta activity. Cerebral magnetic resonance imaging was normal. Brain positron emission tomographies (PET) were obtained on a CTI-Siemens HR+ tomograph. A first PET (PET1) using (18F(-fluorodeoxyglucose (FDG) was performed on day 2 in a drug free state. Thereafter, intramuscular injection of 2 mg of lorazepam induced rapid clinical remission of the akinetic phase. Oral lorazepam was then given (3.75 mg/day) during five days. On day 8, a second PET with FDG was performed while the patient was treated by olanzapine (15 mg/day) and presented hyperactivity, logorrhoea, and disinhibition characterised by uncontrolled social interactions and physical contacts. Neuropsychological testing performed some days after remission revealed no apraxia or language disturbances but dysfunction of executive tasks manifested in the revised Wisconsin card sorting, the Tower of London, Stroop, and Trailmaking tests.

Voxel based analyses comparing patient's cerebral glucose metabolism with that of 29 right handed healthy controls (16 women and 13 men, mean age 32) were performed using Statistical Parametric Mapping (SPM99) (Wellcome Department of Cognitive Neurology, London, UK). Data from each subject were normalised to a standard stereotactic space and then smoothed with a 12 mm full width half maximum isotropic kernel. The analysis identified brain regions where glucose metabolism was significantly changed in each patient scan compared with the control group. All results presented are significant at $p<0.05$ corrected for multiple comparisons over the entire brain volume. In regions where we had a priori hypothesis—that is, regions implicated in awareness and motor control—we also considered results significant at $p<0.05$ after small spherical volume correction (radius 20 mm). PET2 analysis showed a relative decrease of metabolism in the precuneus, lateral parietal cortices (Brodmann area 40) and in the right superior frontal circumvolution (Brodmann area 6), see table 1. As PET2 was conducted after akinetic catatonia remission, it was used for an exclusive masking analysis of PET1 in order to search for metabolic changes characteristic of the akinetic catatonic state. This showed that a large area of the prefrontal cortex (mostly on the left side) including anterior cingulate, medial prefrontal, and dorsolateral cortices presented a relative decrease of metabolism in comparison with the control group (fig 1). This analysis also revealed relative hypermetabolism of the primary motor cortex, the rostral part of the striatum, and the vermis (fig 1). PET1 analysis also revealed that the precuneus and the left lateral parietal cortex (Brodmann area 40) presented a relative decrease of metabolism (table 1).

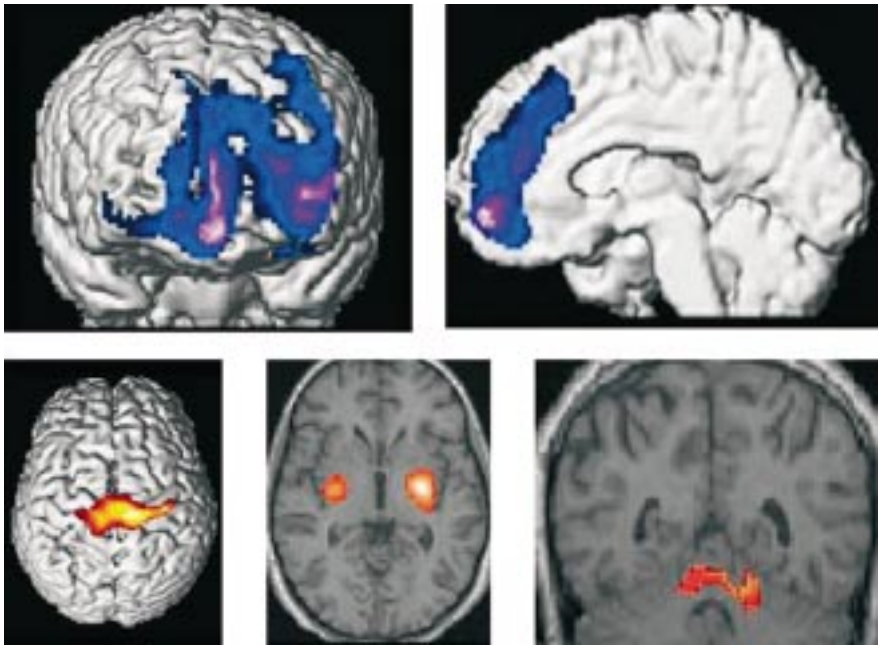

**Figure 1** Results of the exclusive masking analysis showing a decrease of metabolism in a large prefrontal area (upper row, on the right), the right anterior cingulate and the right medial frontal cortices (upper row, on the left). This analysis also showed a relative increase of metabolism in primary motor cortices (lower row, on the left), in the rostral part of the striatum (lower row, on the middle), and in the vermis (lower row, on the right). Dysfunctional brain areas have been coregistrated to the patient's magnetic resonance imaging.

In our opinion, these results might shed some light on the pathogenesis of akinetic catatonia. Indeed, exclusive masking analysis allowed us to determine in this case the metabolic changes characteristic of akinetic catatonia. Prefrontal cortical areas like anterior cingulate, dorsolateral, and medial prefrontal cortices are implicated in the planning, initiation, generation of voluntary movements and executive functions in general. Hypofunction of these brain areas, as demonstrated in our patient, could therefore explain symptoms such as akinesia, mutism, and absence of spontaneous oral intake, which are usual features of akinetic catatonia.[1] Moreover, the increased activity in primary motor cortices, the rostral part of the striatum and the vermis, associated with the deficit of internal initiation and generation of voluntary movements, might account for some particular motor features of catatonic states. These are

**Table 1** Results of SPM analysis of PET1 and 2

| | Hypermetabolism | | | | | Hypometabolism | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Cluster level | | Voxel level | | | Cluster level | | Voxel level | | |
| PET | p | Cluster size | p | Z | Coordinates x,y,z (mm) | p | Cluster size | p | Z | Coordinates x,y,z (mm) |
| 1 | 0.001 | 885 | 0.008 | 4.97 | 30, –8, –2 | 0.039 | 354 | 0.015 | 4.83 | 46, 18, 0 |
| | <0.001 | 2485 | 0.024 | 4.71 | 10, –24, 72 | <0.001 | 1752 | 0.001* | 4.49 | –4, –54, 30 |
| | <0.001 | 977 | 0.003* | 4.27 | 12, –52, –1 | <0.001 | 8720 | 0.002* | 4.40 | –24, 56, 18 |
| | 0.008 | 549 | 0.004* | 4.24 | –30, –12, –2 | 0.002 | 733 | 0.004* | 4.21 | –50, –60, 18 |
| 2 | | | | | | 0.005 | 628 | 0.016 | 4.81 | 40, –60, 44 |
| | | | | | | <0.001 | 1589 | 0.002* | 4.43 | –4, –54, 30 |
| | | | | | | <0.001 | 1057 | 0.005* | 4.16 | –48, –64, 32 |

*After small spherical volume correction (radius 20 mm).

the occurrence of episodic spontaneous stereotyped movements and the prolonged maintenance of posture (catalepsy). Previous functional cerebral imaging studies have reported the implication of the vermis in the maintenance of standing postures.[2] The high metabolic activity observed in the motor cortex could be related to reduced neuronal inhibition. Indeed, reduced density of inhibitory GABA receptors in this area has been reported in catatonia.[3] Previous imaging studies found dysfunctional posterior lateral parietal cortex in the catatonic state.[4] PET1 analysis showed hypofunction of this left region which persisted after clinical remission. So, this regional dysfunction is not sufficient to lead to akinetic catatonia but it might have participated in the disturbance of executive tasks planning.

Patients with akinetic catatonia are classically unresponsive to their environment.[1] This symptom characterises the stuporous state encountered in this syndrome. The exclusive masking analysis demonstrated reduced activity in the medial prefrontal cortex during akinetic catatonia. Previous functional imaging studies showed that the ventral medial prefrontal cortex is implicated in the integration of the visceromotor aspects of emotional processing with information gathered from the internal and external environments.[5] The dorsal medial prefrontal cortex has been involved in explicit representations of states of the "self".[5] Dysfunction of these brain areas might therefore explain the stuporous state observed in akinetic catatonia. Activity within the precuneus has been implicated in the representation of the world around us and the lateral parietal cortex is known to participate in conscious awareness.[5] PET1 analysis showed that these two regions presented a decrease of metabolism that persisted on PET2. This persistence could be related to the hypomaniac state presented at the time of PET2, a state, which differs from the resting state of the control subjects. Indeed, high level of glucose metabolism in the precuneus and lateral parietal cortex is the metabolic hallmark of the normal resting state.[5] Despite its persistence after catatonia remission, dysfunction of these regions during the akinetic catatonic state may be a prerequisite for the establishment of its stuporous aspect, as supported by studies on patients with reduced level of consciousness.[5]

In conclusion, some motor symptoms usually encountered in akinetic catatonia may be related to dysfunction of prefrontal cortical areas but also primary motor cortex, striatum, and vermis. This case of akinetic catatonia also brings new clues for the involvement of the medial prefrontal cortex in conscious awareness.

**X De Tiège, S Laureys, S Goldman**
PET/Biomedical Cyclotron Unit, Erasme Hospital, Free University of Brussels, Brussels, Belgium

**X De Tiège, I Massat, F Lotstra, J Mendlewicz**
Department of Psychiatry, Erasme Hospital, Free University of Brussels

**J-C Bier**
Deapartment of Neurology, Erasme Hospital, Free University of Brussels

**J Berré**
Intensive Care Unit, Erasme Hospital, Free University of Brussels

Correspondence to: Dr X De Tiège, PET/Biomedical Cyclotron Unit and Department of Psychiatry, Erasme Hospital, Free University of Brussels, Brussels, Belgium; xdetiege@hotmail.com

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