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 cataplexy. Even if some advances have been made in the recognition of catatonia, in particular by the development of different rating scales, 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, cataplexy, waxy flexibility, and stupor with brief occasional eye contacts. This corresponded to a total score of 19 on the Northoff Catatonia Scale. 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 $[^{18}F]$-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 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).

PET2 analysis also revealed a relative decrease of metabolism in the precuneus, lateral parietal cortices (Brodmann area 40) and in the right superior frontal circcumvolution (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 hypometabolism 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).

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. 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 |

<table>
<thead>
<tr>
<th>PET</th>
<th>Hypermetabolism</th>
<th>Hypometabolism</th>
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<tr>
<td></td>
<td>Clustering</td>
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<tr>
<td>1</td>
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<td>0.008 549</td>
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<tr>
<td>2</td>
<td>0.005 628</td>
<td>0.016 4.81</td>
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</table>

*After small spherical volume correction (radius 20 mm)
Lateral parietal cortex is known to participate in consciousness.

PET analysis showed hypoactivation 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. This symptom characterizes 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. The dorsal medial prefrontal cortex has been involved in explicit representations of states of the “self”. 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 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.

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.

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References


Mirth and laughter arising from human temporal cortex

Laughter and mirth are essential in our enjoyment of daily life and in facilitating communication. Various studies have been done relating to the emotional processing that takes place in the human cerebral cortex, but few have explored the cerebral origins of mirth. Some reports on pathological laughter have implicated the hypothalamus, brainstem, and temporal lobe.

As part of the presurgical evaluation of patients with epilepsy, electric cortical stimulation is used to delineate the functional cortical areas, and sometimes this elicits various emotional responses. However, only two stimulation studies have been conducted with a focus on mirth and laughter. Arroyo et al. suggested that the motor act of laughter and the processing of its emotional content were separately represented in, respectively, the anterior cingulate area and the basal temporal area (the fusiform gyrus or parahippocampal gyrus, or both). Fried et al. suggested not only that laughter and mirth were represented in the presupplementary motor area, but also that there was close linkage between the motor, affective, and cognitive components of laughter.

We report a patient in whom electric cortical stimulation applied to the inferior temporal gyrus produced mirth alone or laughter preceding by mirth, depending on the intensity of the stimulation.

Case report

A 24 year old right handed woman with medically intractable complex partial seizures underwent implantation of subdural grid electrodes on the cortical surface of the left temporal cortex and a depth electrode into the right mesial temporal lobe. Long term video/EEG monitoring with scalp electrodes done before this invasive monitoring showed late ictal lateralization at the left anterior temporal area, and thus a right temporal onset could not completely be excluded. Magnetic resonance imaging showed high intensity and atrophy in the left anterior and right posterior hippocampus. Interictal FDG-PET (fluorodeoxyglucose positron emission tomography) showed hypometabolism in the left temporal lobe. An intracarotid amobarbital test revealed the dominance of language and memory in the left hemisphere.

The seizures started with an epiclastic rising sensation, followed by loss of awareness combined with hand and oral automatisms. Laughter or the feeling of mirth was not seen during the patient’s habitual seizures. Video/EEG monitoring showed that the epileptogenic focus was in the left mesial temporal cortex (A1, 2, 9, and 10) (red electrodes in fig 1). Electrical cortical stimulation (50 Hz, alternate polarity of square pulses) was done to delineate the functional areas, with special emphasis on language function.

Stimulation of the basal aspect of the inferior temporal gyrus between A4 and A12 (yellow electrodes in fig 1) at low intensity and short duration (5 mA, 1 s) consistently produced mirth without laughter, and it was always accompanied by a melody that she had heard in a television programme in her childhood. The duration and intensity of the mirth increased in proportion to the duration and intensity of stimulation (15 mA, 3 s), and she eventually smiled during the latter part of a 5 second stimulation. The patient said that the tune appeared funny to her and made her feel amused, but only during the electrical stimulation, and we were able to confirm this. When maximum intensity at longer duration (15 mA, 5 s) was applied, it disrupted a variety of language tasks, but neither alternating hand and foot movements nor vocalisation was disturbed. During this maximum stimulation condition, the patient felt mirth, but the performance of various language tasks obscured apparent laughter. Stimulation of the adjacent pairs of electrodes (A3–A11, A6–A13, and B2–4) (blue electrodes in fig 1) affected only language tasks but was not consistently accompanied by a feeling of mirth.

Comment

Our observations suggest that mirth is represented in a relatively small distinct area in the temporal neocortex (the basal surface of the inferior temporal gyrus), which is in part consistent with the observations of Arroyo et al.1

Figure 1 Brain magnetic resonance imaging showing the arrangement of electrodes on the surface of the left basal temporal cortex. A11 and B1 are overlapping. The electrodes A4 and A12 (yellow) are located on the basal aspect of inferior temporal gyrus where the electric stimulation induced mirth with or without laughter. A1, A2, A9, and A10 (red) were epileptogenic foci and were ultimately resected. Electrical stimulation of blue electrodes disrupted or arrested speech and other language tasks.
Our study clearly showed that mirth was represented in the inferior temporal gyrus, and was closely linked with a particular context (a certain tune in this patient). This association with a specific event was not observed in the patients reported by Arroyo et al. Because the temporal lobe is involved in memory function in human, it is reasonable that both the context of the mirth and laughter and the induced mirth and laughter are represented. In the present case, we could not identify any site where the electric stimulation elicited laughter without mirth. Importantly, the fact that the stimulation with higher intensity and longer duration elicited mirth with laughter might suggest different thresholds for mirth and laughter, postulating a hierarchical organisation or serial processing of mirth and laughter in the human temporal cortex. Laughter might be situated at a higher order than mirth, at least in the temporal neocortex. It is possible that laughter might be caused by further activation of the frontal motor cortices, including the anterior cingulate gyrus, through corticocortical projections, such that electrical cortical stimulation could elicit laughter without mirth.

With regard to the characteristics of induced mirth in this patient, the melody which made her feel funny was not amusing by itself, although the mirth elicited in present case can be judged to reflect normal function of the epileptogenic foci. Thus this particular patient's symptoms are indeed caused by stimulation through an undetermined process.

Although it should be taken into account that the mirth elicited in the present case might not necessarily have reflected the representation of mirth and laughter in the normal brain, no mirth was seen during the patient's habitual seizures. While the electrical cortical stimulation could elicit laughter without mirth, the mirth elicited in the present case might have been caused by further activation of the frontal motor cortices, including the anterior cingulate gyrus, through corticocortical projections, such that electrical cortical stimulation could elicit laughter without mirth.

In the present case, the mirth represented in the temporal lobe and may be stored together with the context inducing mirth in the same area, suggesting a close relation between mirth and memory function. As far as the temporal neocortex in the present patient is concerned, laughter seems to be situated at a hierarchically higher order than mirth.

### References

### Table 1: Incidence of different types of Parkinsonism in necropsy series (percentages)

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<thead>
<tr>
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<tr>
<td>Lewy body dementia</td>
<td>20%</td>
<td>14%</td>
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<tr>
<td>Progressive supranuclear palsy</td>
<td>3%</td>
<td>2%</td>
<td>3%</td>
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<tr>
<td>Postencephalitic parkinsonism</td>
<td>2%</td>
<td>2%</td>
<td>2%</td>
</tr>
<tr>
<td>Posttraumatic Parkinson’s disease</td>
<td>2%</td>
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<td>2%</td>
</tr>
<tr>
<td>Unclassified/no lesion</td>
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<td>10%</td>
<td>10%</td>
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*With SN lesion 3.0.

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Table 2: Misdiagnosis in necropsy series of clinical Parkinson's disease (with or without dementia)

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<tr>
<th>Pathology</th>
<th>Hughes et al&lt;sup&gt;a&lt;/sup&gt; (n = 100)</th>
<th>Rajput et al&lt;sup&gt;a&lt;/sup&gt; (n = 41)</th>
<th>Jellinger (1971–88)&lt;sup&gt;b&lt;/sup&gt; (n = 380)</th>
<th>Jellinger (1989–2001)&lt;sup&gt;c&lt;/sup&gt; (n = 260)</th>
<th>Hughes et al&lt;sup&gt;d&lt;/sup&gt; (n = 143)</th>
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<td>6</td>
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<td>5</td>
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<td>MIX encephalopathy (AD+VaE)</td>
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<td>0</td>
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<td>0</td>
<td>1</td>
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<td>Normal (essential tremor)</td>
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<td>0</td>
<td>0.4</td>
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<td>Others (pallido-nigral degeneration, toxic, etc)</td>
<td>0</td>
<td>2</td>
<td>1</td>
<td>0.4</td>
<td>0.4</td>
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<tr>
<td>Postencephalic parkinsonism</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0.4</td>
<td>0.4</td>
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<tr>
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<td>24</td>
<td>22</td>
<td>15.3</td>
<td>11.5</td>
<td>15.2</td>
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</table>

Values are % unless stated.

AD, Alzheimer’s disease; VaE, vascular encephalopathy.

References


Smoking and cognitive change from age 11 to age 80

Age-related cognitive decline affects people’s quality of life and the ability to live independently. A recent review stated, “[w]e are aware of no studies on the relationship between smoking and cognitive decline associated with normal aging or studies of the effect of smoking on cognition in normally aging individuals.” Some previous studies examined smoking in relation to pathological cognitive aging, but lacked cognitive data before the initiation of smoking, and used crude clinical cognitive assessments. Among middle-aged subjects, current smoking was associated with poorer cognitive performance on tasks of psychomotor speed and cognitive flexibility. Smoking has been identified as a possible risk factor for accelerated cerebral degenerative changes, cognitive decline, and dementia. Here we show that smoking contributes to normal cognitive change from age 11 to age 80.

Participants, methods, and results

The Scottish Mental Survey of 1932 (SMS1932) tested mental ability in people born in 1921 (n = 87 498). The SMS1932’s Moray House test (MHT) was validated against the Scottish Binet test and includes verbal reasoning, numerical, spatial, and other items. From 1999 to 2001 we traced and rettested 530 people from Edinburgh who were born in 1921 (the Lothian birth cohort 1921). All lived independently. We excluded people with mini-mental state examination scores below 24 and those with known dementia. We traced their scores from SMS1932, readministered the MHT using the same instructions and time limit as the SMS1932, and collected information on smoking. In all, 470 people (194 men) provided full data.

We examined the effect of smoking on cognitive change from age 11 to age 80 using general linear modelling (analysis of covariance; SPSS version 11). Age corrected MHT score at age 80 was the dependent variable, smoking (never = 205; current = 34; ex-smoker = 231)) and sex were between subject variables, and age corrected MHT score at age 11 was a covariate. Among the current smokers the mean (SD) age at starting smoking was 18.9 (5.5) years (range 9 to 40). The ex-smokers’ mean age at starting smoking was 18.2 (5.2) years (range 7 to 60), and the mean age at stopping smoking was 49.6 (16.1) years (range 19 to 79 years). Only six of these ever-smokers (current and ex-) began smoking before the age of 11. The mean (SD) MHT scores for each smoking related subgroup at age 11 and age 80 are shown in table 1. MHT scores at age 11 had a large effect on scores at age 80 (F<sub>4,1006</sub> = 332.2, p < 0.001, η<sup>2</sup> = 0.418). There was a significant, independent effect of smoking (F<sub>3,997</sub> = 3.3, p = 0.039, η<sup>2</sup> = 0.014), but not of sex.

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The sex by smoking interaction was not significant ($F_{1,103} = 1.7$, $p = 0.17$, $\eta^2 = 0.007$). Current smokers had significantly lower MHT scores at age 80 than never smokers ($p = 0.013$; mean difference $= −5.2$, 95% confidence interval (CI) $−9.4$ to $−1.1$) and ex-smokers ($p = 0.016$; mean difference $= −5.0$, 95% CI $−9.0$ to $−0.9$). These group comparisons remained similar in effect size and significance after entering years of full time education to the model.

This finding adds to those of a previous study which found that, among middle aged participants, current smokers had reduced cognitive performance when compared with never smokers. It might be expected that smoking affects cognitive change detrimentally from age 11 to age 80, with an effect that is similar in size to other contributors, such as the $e_4$ allele of the APOE gene. An advantage of this study is that the initial cognitive assessments were made when only a tiny percentage of the subjects had begun smoking. This finding adds to those of a previous study which found that, among middle aged participants, current smokers had reduced cognitive performance when compared with never smokers. It might be expected that smoking affects cognitive change detrimentally from age 11 to age 80, with an effect that is similar in size to other contributors, such as the $e_4$ allele of the APOE gene.

A competitive interest: none declared.

Table 1 Moray House test scores at age 11 and age 80 by smoking status

<table>
<thead>
<tr>
<th>Smoking Status</th>
<th>n</th>
<th>IQ age 11 (SD)</th>
<th>IQ age 80 (SD)</th>
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<tr>
<td>Never smoked</td>
<td>205</td>
<td>101.6 (13.8)</td>
<td>100.8 (14.5)</td>
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<td>Ex-smoker</td>
<td>231</td>
<td>99.8 (15.2)</td>
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<tr>
<td>Current smoker</td>
<td>34</td>
<td>98.4 (15.5)</td>
<td>94.3 (17.5)</td>
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Scores were converted to IQ-type scores (mean = 100; SD = 15) at each age separately.

References