CASE REPORT

INCREASED CEREBELLAR PET GLUCOSE METABOLISM CORRESPONDS TO ATAXIA IN WERNICKE–KORSAKOFF SYNDROME

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Abstract — Aims: To investigate a possible relationship between cerebellar glucose metabolism and recovery from ataxia in the first months of acute Wernicke–Korsakoff syndrome. Methods: Two cases of alcoholic Wernicke–Korsakoff syndrome were followed up with the clinical status and cerebral glucose metabolism over a 4- and 9-month period. Results: Initially both patients showed severe ataxia and elevated cerebellar glucose metabolism that decreased corresponding to the restitution of stance and gait. Conclusion: Increased cerebellar glucose metabolism at the onset of the illness may reflect the reorganization process of disturbed motor skills and may indicate cerebellar plasticity.

METHODS

PET data acquisition and analysis

PET images were obtained under standard resting conditions (eyes closed in dimmed ambient light) using a Siemens ECAT EXACT scanner (CTI, Knoxville, TN, USA). Acquisitions were in 3D-mode with an axial field of view of 16.2 cm. To obtain transaxial images parallel to the intercommissural line, the patients were positioned with the cantomeatal line parallel to the detector rings. Thirty minutes after an injection of 180 MBq 18F-FDG, a sequence of three 5-min frames was started and later combined to a single frame. Thereafter the images were corrected for attenuation, scatter and dead time.

An automated analysis of the 18F-FDG-PET images was performed using a program that generates standardized three-dimensional stereotactic surface projections of the individual dataset followed by a pixelwise comparison with a normal database resulting in parametric z-score images. This routine has been described previously and evaluated with dementing disorders and epilepsy (Bartenstein et al., 1997).

To quantify changes in glucose metabolism in different brain regions during the course of the disease, an additional ROI based analysis was performed using standardized anatomical regions. The sensorimotor cortex was chosen as a reference region because this area is less likely to be affected by the disease than other brain areas (thalamus, cerebellum) that are frequently used as reference regions (Kril et al., 1997). The sensimotor cortex has been shown to yield stable results in this kind of analysis (Santens et al., 2001). In contrast to normalisation to global mean, the choice of a single stable reference region avoids the effect that severe reduction in supra-tentorial regions produces an artificial increase in the cerebellar glucose metabolism.

Case 1

The 40 year old male patient had a 20-year history of alcohol dependence according to DSM IV criteria. Based on the information provided by the father of the patient, the average amount of alcohol consumption was six pints of beer per day during the last months prior to hospitalization. When the patient was admitted to the emergency unit of our hospital, he was found to be unable to walk and to care for himself. This acute syndrome began about 3 days before admission. In the absence of an acute alcohol intoxication the patient showed ataxia of stance and gait, ocular muscle weakness (right external rectus muscle) with horizontal and vertical nystagmus, and a global apathetic-confusional state with fluctuating levels of consciousness. Cranial MRI showed general atrophy of the cerebrum and cerebellum including bilateral thalamic lesions. Over a 9-month period, the clinical status and cerebral glucose metabolism of the patient were followed up four times.
Case 2

The 58-year-old female patient was hospitalized after 4 days apathetic-confusional state with acute onset. On admission, she showed horizontal and vertical nystagmus and severe ataxia of stance and gait without alcohol intoxication. According to the information that was provided by her husband, she had a 10-year history of alcohol dependence (DSM IV criteria) and drank about two bottles of wine or champagne daily. Cranial MRT detected general atrophy of the cerebrum and cerebellum without other lesions of brain tissue. Clinical status and cerebral glucose metabolism were followed up over a 3-month period.

RESULTS

Clinical follow up

Under treatment with 100 mg/d.i.e. thiamine intravenously over 20 days, ocularmotor function normalized in both patients within the first 2 weeks. Orientation improved, but at the end of the observation period both patients were not clearly orientated to time.

FDG–PET (Figs 1, 2)

Both patients initially showed clearly reduced cortical glucose metabolism resembling an Alzheimer-typical finding whereas the cerebellar glucose metabolism was increased.

The first PET scan of patient 1 showed a substantial decrease of regional cerebral glucose metabolism bilaterally (an average decrease of more than two standard deviations compared to the normal database) in the parietal and temporal cortex extending into the occipital lobe (visual association areas) as well as in the frontal cortex, cingulate and the thalamus.

The first PET scan of patient 2 showed less severe disturbances of the cortical glucose metabolism but significant glucose hypometabolism in both parietal regions as well as...
mesial and frontal bilaterally. Cortical glucose hypometabolism tended to normalize in both patients over time. Cerebellar glucose hypermetabolism tended to normalize in the follow-up PET scans corresponding to the restitution of ataxia in both patients.

**DISCUSSION**

We present follow-up investigations of two patients with severe Wernicke–Korsakoff syndrome with acute onset, partial remission and a persisting memory deficit. Ocular symptoms and ataxia disappeared completely during the first 2 months under thiamine substitution in both patients. Thus, our findings reflect the typical clinical course of this syndrome.

Both patients initially showed widespread cortical (frontal, parietal, temporal) glucose hypometabolism that tended to normalize in parallel to the improvement of clinical functioning. This impairment of cerebral glucose metabolism was expected and it has been demonstrated in several animal studies showing decreased global cerebral glucose metabolism under thiamine deficiency and its (partial) restitution under thiamine substitution (Hakim et al., 1981). Additionally, neuroimaging studies assessing cerebral glucose metabolism in Wernicke–Korsakoff patients using FDG–PET have shown significant hypometabolism in regions belonging to the Papez/limbic circuits, in the bilateral thalamic nuclei, in the mesial prefrontal cortices and the temporo-parietal regions (Joyce et al., 1994; Paller et al., 1997; Aupée et al., 2001; Fellgiebel et al., 2003).

In contrast to these studies, we made an unexpected observation in both patients with regard to cerebellar glucose metabolism. At the time of admission, both patients showed cerebellar glucose hypermetabolism in the state of severe ataxia of stance and gait. Interestingly, we also observed a restitution of the increased cerebellar glucose metabolism in parallel to the improvement of ataxia in both patients.

Using functional MRI, Parks et al. (2003) found increased cortical and cerebellar activation associated with slower self-paced finger tapping in alcohol-dependent patients compared to normal controls. Parks speculated that the greater activation is compatible with compensatory alterations of cortical-cerebellar circuits. Elevated cerebellar activation measured by fMRI or PET was also found in motor sequence learning and motor adaption (Doyon et al., 2003). Moreover, better performance tasks have been shown to be associated with decreased cerebellar activation (Imamizu et al., 2000).

**CONCLUSION**

Our findings suggest that the increment of cerebellar glucose metabolism in the acute stage of Wernicke encephalopathy and it’s normalization parallel to the restitution of motor symptoms could reflect a functional reorganisation process of disturbed motor skills and may indicate cerebellar plasticity.

**REFERENCES**


