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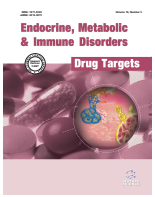
RESEARCH ARTICLE

18F-FDG-PET Correlates of Impulse Control Disorder in a Diabetic Patient



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Abstract: ***Background*:** Studies have already shown that hyperglycemia and insulin resistance are significantly associated with the impairment of cerebral glucose metabolism that may secondary lead to cognitive disturbances. In this study, we aimed to evaluate the neurometabolic correlates of diabetes in a patient with Intermittent explosive disorder (IED).

***Methods*:** We have investigated the cerebral glucose metabolism *via* 2-[18F]-fluoro-2- deoxy-D-glucose positron emission tomography (FDG-PET) in a diabetic patient with aggressive outbursts.

***Results*:** We have found significantly reduced glucose uptake in left temporoparietal region, pontin area, and left nucleus lentiformis.

***Discussion*:** Our present results indicate decreased cerebral glucose metabolism in specific cerebral cortical and subcortical areas. The main limitation of this report is that, this is a single case study and that these findings need to be replicated in well- conducted randomized controlled studies by using additional neuroquantitative methods.

Keywords: Diabetes mellitus, FDG-PET, impulse control disorder.

INTRODUCTION

Recent studies have already shown that hyperglycemia may result in the impairment of cerebral glucose metabolism [1-3] that may lead to cognitive dysfunction during diabetes. This is in line with the previous studies showing that impaired insulin resistance and increased fasting glucose levels are well-known risk factors for cognitive dysfunction [1-5]. This is suggested with a recent work indicating a strong link between intermittent explosive disorder and diabetes diagnosis while the underlying mechanism is still unclear [6]. Studies until now have already reported that dysregulation of glucose metabolism in cortico-subcortical networks is involved in intermittent explosive disorder and borderline personality [7] although the role of brain stem, a main subcortical region, in emotional processing remains still an enigma [8]. This may relate to difficulties to evaluate the association between brain stem lesions and human emotion partly because of the life-threatening conditions related even to small brainstem lesions [8]. In addition to their pacemaker function for motoric cortical centers, it has been already shown that pons and nucleus lentiformis play a major role in emotional processing (i.e., reflexive emotional reactions) through their functional interactions with amygdala and prefrontal cortex [9]. This is in accordance with the recent evidence showing that decrease in the neocortical gray matter volume may be associated with psychiatric disorders [10-15]. All the evidences suggest that a dysconnection between specific cerebral areas, rather than an impairment in the isolated areas, may lead to acting out attacks. This is in agreement with our previous study showing that an isolated pontin ischemic lesion lead to a poststroke depression which was correlated with impaired metabolism in frontal and temporoparietal cortical regions [16].

CASE

We reported a 36-year-old man who experienced acting out attacks one year after he was diagnosed with type 2 diabetes for 5 years. According to his clinical history (i.e severe physical and verbal violence precipitated by little provocation), he fulfilled the DSM-IV diagnostic criteria for the intermittent explosive disorder. His neurological and psychiatric examination revealed that he was fully cooperative and oriented while he displayed an appropriate emotional status. The patient scored eight points on Modified Overt Aggression Scale and Mini-Mental State Examination and the original Beck's Depression Inventory scores were found in normal limits. Detailed blood tests revealed significantly elevated HbA1c levels (13 %).

MATERIAL AND METHODS

Cranial MRI was taken using an 1.5 Tesla imager (Philips) with an eight-channel head coil. Spin-echo horizontal

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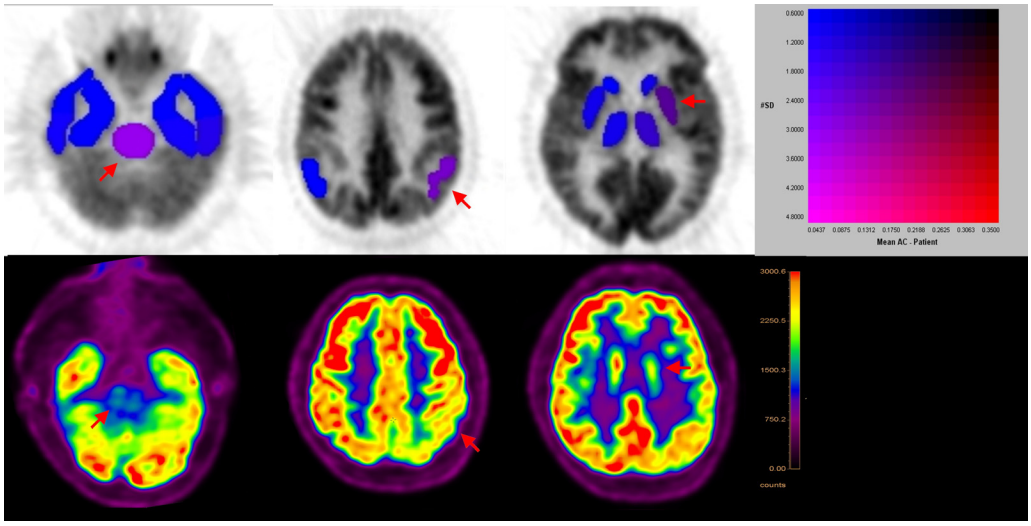

Fig. (1). The raw FDG-PET data (B) were processed using NeuroQ software (A) (Version 3,5. Syntermed, Inc Atlanta. USA) and the average pixel values in standardized regions of interest (ROI) were calculated automatically as mean counts. Focal/whole cerebral ratios were statistically compared to the normal values in the control database after spatial normalization of PET image that automatically defined significantly hypometabolic brain regions as a decrease of more than 1.65 SDs of regional brain metabolism. Please see coincident red arrowheads in raw FDG-PET data (B) and NeuroQ software (A) indicating to a hypometabolism on the pons, left temporoparietal cortex and left lentiform nucleus.

T1-weighted, horizontal, and coronal T2-weighted and sagittal FLAIR slices were obtained. Brain (F18) FDG PET-CT images were taken using PET/CT equipped with 16 slice CT (Philips Gemini).

Brain fludeoxyglucose positron emission tomography (F18) (FDG PET-CT) images were taken using Philips Gemini TF PET/CT equipped with 16 slice CT. The patient had a glucose level below 160 mg/dl, and ^{18}F FDG was administered intravenously at a dose of 0.1 mCi (3.7 MBq)/kg. After injection, the patient was allowed to rest quietly in a dimly lit room for at least 30 minutes during the uptake phase. At 60 min after the injection, data were acquired, and PET images were reconstructed with CT data for PET attenuation correction. We have not included an additional control group since the NeuroQ software includes a normal brain ^{18}F-FDG PET database consisting of 50 healthy adults which spans a wide age spectrum (20-89 years old without neuropsychiatric disorders).

Brain ^{18}F-FDG PET images in axial, coronal, and sagittal slices and the quantitative results of NeuroQ analysis were visually evaluated by 2 blinded nuclear medicine physicians. The NeuroQ program calculated the average pixel values in standardized regions of interest (ROI) as mean counts and statistically compared these counts with the control database following spatial normalization of PET images. As a result, significantly hypometabolic brain regions were automatically defined as a decrease of more than 1.65 SDs of regional brain metabolism [17]. It should also be noted that the major limitation of our analysis was we compared our patient to a database that was obtained with another PET-CT with different acquisition parameters.

RESULTS

A magnetic resonance imaging scan of the brain revealed no morphological abnormality while decreased glucose uptake in PET was prominent on the left temporoparietal cortex, pontin area and left nucleus lentiformis (NeuroQ software, Syntermed, standard deviation > two below the mean of the asymptomatic control group) (Fig. **1**).

DISCUSSION

In contrast to our previous work [18] showing lower cerebral glucose metabolism in cortical regions, we have also demonstrated reduced glucose metabolism in basal ganglia and brain stem which did not entirely parallel morphological changes. In contrast to previous studies suggesting that patients with DM may have tendency to decreased brain glucose metabolism in specific areas [3-5], our present findings show that reduced glucose metabolism in subcortical emotional circuits is associated with acting out attacks. Based on these findings it can be hypothesized that diminished glucose metabolism in the related cortical regions may indicate to secondary impairments due to decreased functions of emotional networks including also the brain stem and striatum [18-23]. This is also suggested by previous studies showing that central pontine myelinolysis associated emotional incontinence may involve the disruption of the corticopontine and related neurotransmitter pathways suggesting the functional role of brain stem not only in higher cognitive processes but also in emotional regulation and depression [8, 16, 23].

We also have demonstrated decreased glucose metabolism in the left temporo-parietal region. This finding is interesting in the light of recent data which indicated that intermittent explosive disorder and borderline personality are associated with an increase in glucose metabolism in the limbic system and a decrease in prefrontal regions [7]. These findings are in agreement with previous findings showing that decreased cortical glucose metabolism may be associated with diminished functions of the cortical part of emotional circuits which

have been already shown to play a major role in the pathogenesis of aggression [20, 22]. It has been already known that diabetes mellitus lead to significant microvasculature brain damage [24] that may result in disturbed cerebral metabolism including also the temporoparietal regions [1-5]. Additionally it has been already demonstrated that impaired insulin resistance and higher glucose levels are associated with the diminished glucose metabolism in specific brain regions which play a significant role in cognitive function [1-5]. These findings together may support the role of dynamically interacting central networks in the generation of psychiatric symptoms during various neurometabolic disorders suggesting that the decreased glucose metabolism in specific brain regions may indicate a conversion risk from predegenerative to degenerative disease (i.e., MCI and AD). This is in line with the previous studies showing that low cerebral glucose metabolism may predict the severity of vascular and degenerative Parkinson's Disease (PD) as well as the conversion risk from MCI to AD Alzheimer's Disease although the neuro-psychometric evaluation of our patient was in normal limits [25-27].

CONCLUSION

As a result, we present here the cerebral metabolic correlates of acting out attacks in a 36-year-old diabetic patient. In contrast to subjective radiological evaluation which is limited with conventional neuroimaging modalities (i.e., MRI and CT), this type of quantitative analysis can give us valuable neurometabolic information. Since this is only a single case report and it is difficult to say that diabetes and IED may secondary lead to cerebral hypometabolism, future well-conducted randomized controlled studies confirming our preliminary findings would be the exciting future steps to be taken in the field of psychoneuroendocrinology research. This type of early neurometabolic data might enlighten possible specific networks involved by diabetes and intermittent explosive disorder.

CONFLICT OF INTEREST

The authors confirm that this article content has no conflict of interest.

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