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High Incidence of Initial Loss of Consciousness with Abnormal F-18 FDG and O-15 Water Brain PET in Patients with Chronic Closed Head Injury

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Background: The purpose of this study is to evaluate the incidence of loss of consciousness (LOC) with functional abnormalities by brain positron emission tomography (PET) in patients with closed head injury using fluorine-18 labeled fluorodeoxyglucose (F-18 FDG) and O-15 water PET imaging. **Methods:** 36 sequential patients referred from rehabilitation service without known brain disease who had cognitive complaints months after head injury and had F-18 FDG and O-15 water PET, CT and/or MRI imaging were included. The image findings were compared and correlated with the incidence of initial LOC. **Results:** Significant difference was found in the association of abnormal imaging findings with LOC between functional (PET) and anatomical (CT or MRI) modalities. There was also significant discrepancy between PET and CT/MRI findings. Of the 28 patients with normal CT or MRI, 10 patients or 36% had abnormal PET findings (p=0.007). However, there was, however, high concordance (92%) between perfusion and metabolic PET images. **Conclusion:** There are significantly more functional than anatomic abnormalities in chronic closed head injury. PET may help in confirming the diagnosis and subsequent management when CT/MRI is normal. Those with normal PET are less likely to have LOC at the time of initial injury.

Keywords: Perfusion; metabolism; PET; chronic head injury; loss of consciousness.

INTRODUCTION

Cerebral perfusion single photon emission tomography (SPECT) and metabolic brain positron emission tomography (PET) have been widely used for evaluation of functional abnormalities in patients with dementia and epilepsy[1] but less so for close head injury[2]. Computerized tomography (CT) or magnetic resonance image (MRI) is usually employed in the acute evaluation of brain injury and may clearly delineate the anatomic extent of brain injury.

Both F-18 FDG and O-15 water are clinically most relevant radiopharmaceuticals in PET brain imaging that reflect cerebral glucose metabolism and perfusion respectively. Because glucose is the brain's sole energy source, the cerebral uptake of F-18 FDG uptake is high and fairly constant among alive, conscious individuals. O-15 water is a diffusible perfusion tracer that only reflects changed blood flow without requiring an intact cellular metabolism and yet yielding a high extraction fraction[3]. PET scans with F-18 FDG and O-15 water provide the in vivo, noninvasive observation of local cerebral metabolic and perfusion status that may reveal pathologic conditions prior to traditional morphological manifestations seen on CT or MRI.

Traditional factors associated with outcome after closed head injury are only clues accounting for part of the total outcome variance observed[4]. While in assessing the initial brain injury severity, the presence and duration of loss of consciousness (LOC) and Glasgow Coma Scale scores at worst after resuscitation have been applied as major determinants and important "predictors" of morbidity and mortality[4], it is still not easy to recognize the occurence of LOC, especially in short of duration in the scene of accident. On the other hand, it is also reported that even in a mild traumatic brain injury, 15% to 29% of patients still can be experienced various degrees of complaints[5]. Although

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Table 1 The high incidence of loss of consciousness (LOC) with abnormal PET.

N=36 p=0.039	Normal PET	Abnormal PET
LOC	2	11
No LOC	12	11

earlier data indicate that functional SPECT is more sensitive than structural CT or MRI in detecting brain disorders during the chronic phase[6,7], new MR techniques such as magnetization transfer imaging, diffusion-weighted imaging and MR spectroscopy have made a remarkable progress in this aspect[10].

Even with all the progress, neurologists and rehabilitation physicians are still often confronted with diagnostic difficulties in the status of chronic closed head injury when CT or MRI is normal. Previous quantitative studies have demonstrated the abnormalities of perfusion[8] and metabolism[9] in traumatic brain injury. The definite time course of metabolic recovery has also been addressed in details[2]. While there is dissociation of the LOC and the metabolic reduction in the brain[2], to the best of our knowledge, the discrepancy in the incidence of LOC between functional and anatomical brain imaging especially using PET perfusion and metabolic means has not been investigated. The purpose of this study is thus to evaluate the incidence of LOC with functional abnormalities in patients with closed head injury by using both F-18 FDG and O-15 water brain PET imaging. ¡@¡@¡@

MATERIAL AND METHODS

Thirty-six sequential patients (40¡ 14 years) with cognitive complaint 9 months after head injury referred from rehabilitation service, who had F-18 FDG and O-15 water PET were included. Loss of consciousness for more than 3 minutes is defined as the initial loss of consciousness of the head trauma. All patients had CT and/or MRI. The injections of tracers and acquisition of PET images were performed with the eyes and ears open. The head was secured in standard position by a holder and a facemask. Cerebral perfusion PET images were first acquired by Siemens 951 PET camera thirty-five seconds after injection of an average of 3170¡ 195 MBq O-15 water in a 256 by 256 matrix with a pixel size of 0.117 cm. After the perfusion PET scan, cerebral metabolic PET scan was acquired by using the same camera in the same matrix on the same day one hour after injection an average of 369¡ 27 MBq F-18 FDG. After acquisition, the images were processed by linear back projection with a Hanning filter at cut-off frequencies of 0.4 and 0.5 cycles per pixel for O-15 water and F-18 FDG respectively and a uniform attenuation coefficient 0.095 cm^{-1}. The PET images of the patients with closed head injury were finally evaluated visually by displaying at a computer console by consensus approach, blind to CT or MRI. One color interval on PET images represent one standard deviation with mean in the center of the scale. Areas of decreased tracer uptake equal or more than two color interval on PET image are recognized as abnormal PET findings. The results were finally compared with anatomical imaging (CT and/or MRI) and correlated initial LOC. Fisher exact tests were used with a p-value < 0.05 being significant.

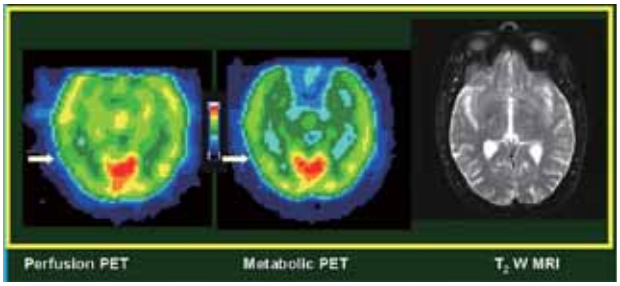

Fig. 1 A patient with closed head injury but without loss of consciousness has normal MRI and perfusion and metabolic PET (one color interval = one standard deviation with mean in the center of the scale).

RESULTS

There was significant difference in the association of abnormal imaging findings with LOC between functional (PET) and anatomical (CT or MRI) modalities (Table 1, Figure 1). For the 13 patients with documented initial LOC, eleven of them or 85% had abnormal PET findings while there was no such trend in with CT/MRI (p=0.039). There was also significant discrepancy between PET and CT/MRI findings (Table 2, Figure 2). Of the 28 patients with normal CT or MRI, 10 patients or 36% had abnormal PET findings (p=0.007). There was, however, high concordance (92%) between perfusion and metabolic brain PET images using O-15 water and F-18 FDG respectively. Only one out of a total of 36 patients had normal metabolic PET and abnormal perfusion PET. Conversely only two out of 36 patients had abnormal metabolic PET and normal perfusion PET. Among this rare functional imaging discrepancy, an interesting patient with luxury perfusion was found (Figure 3).

Table 2 The discrepancy between CT/MRI and PET in the incidences of loss of consciousness (LOC).

N=36 p=0.007	Normal PET	Abnormal PET
Normal CT/MRI	14	10
Abnormal CT/MRI	0	12

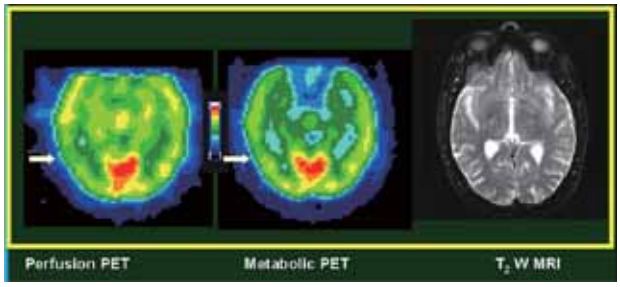

Fig. 2 A patient with close head injury and loss of consciousness and with normal MRI had however abnormalities (arrow) in both perfusion and metabolic PET (one color interval = one standard deviation with mean in the center of the scale).

DISCUSSION

In order to evaluate fully the functional abnormalities in traumatic brain injury, the current study employed both perfusion and metabolic PET imaging, instead of SPECT imaging. There may be some labile coupling between flow and metabolism. For instance, temporal lobe abnormalities in epilepsy patients have been noted to be less dramatic on perfusion PET scans than on glucose metabolic PET scans [10,11]. Takeda et al.[12] noted a lower level of hippocampal oxygen metabolism versus perfusion to the same region relative to the frontal cortex. Oku et al.[13] noted significantly lower uptake of the SPECT tracer using Tc99m-ethylcysteinate dimer (Tc99m-ECD) as compared to Tc99m-hexamethyipropyleneamine oxime (Tc99m-HMPAO) in the mesial temporal cortex. They postulated that Tc99m-ECD might be more sensitive to metabolic rate than Tc99m-HMPAO and that the differential uptake might reflect a difference in relative temporal perfusion and metabolism. Thus both metabolic and perfusion agents were employed for PET brain imaging in the current investigation.

In a recent study, Lewine et al. observed usefulness of MRI, SPECT and magnetoencephalography (MEG) in providing objective evidence of brain injury in adult patients with persistent post-concussive symptoms following blunt head trauma[9]. It revealed that perfusion SPECT, although less informative in cognitive symptoms than MEG, could provide objective evidence of brain injury in patient with post-concussive somatic and or cognitive symptoms.

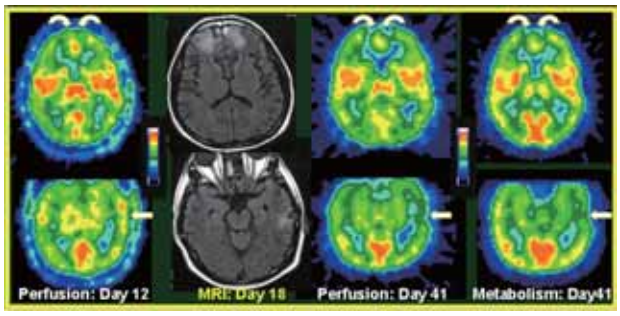

Fig. 3 A 37 year-old male with close head injury and loss of consciousness showed the rare discrepancy between perfusion and metabolic PET (luxury perfusion at day 12).

Notably, cerebral uptake of both SPECT perfusion tracers (Tc-99m ECD and Tc-99m HMPAO) depends on the efficiency of brain extraction and intracellular trapping; the latter requires an intact enzymatic metabolism so that altered uptake may not only reflect a changed blood flow[3]. Accordingly, PET scans using pure perfusion and metabolic tracers were necessary in the current study design. The use of both perfusion and metabolic PET images provides a more comprehensive tool for clinical diagnosis on traumatic brain injury patients than perfusion brain SPECT alone.

While lesion-based anatomic imaging modalities such as CT or MRI have made a great progression in diagnosis and management of patients with neurological disorders, brain lesions may only be present functionally rather than structurally. Clinical PET has served as an imaging tool that focuses more on molecular interactions of biologic and metabolic processes. Neurological applications using F-18 FDG and O-18 water PET thus enable us to perform neurochemical and metabolic studies of cerebral blood perfusion and glucose metabolism[3] that may not be seen on CT or MRI images[9]. The different imaging characteristics between PET and CT/MRI may explain at least in part the significant discrepancy between PET and CT or MRI findings in our current and the other studies[10]. Nevertheless, both modalities are complimentary in providing insight into structural and functional effects of closed brain injury and thus better define the disease.

In the present study, patients have chronic complaints regarding cognitive problems indicating some functional derangement that may not be necessarily displayed by

anatomic imaging modalities due to subtle or functional insults. A Previous PET investigation using ^{18}F FDG demonstrated a significant difference in glucose metabolism in the thalamus, brain stem, and cerebellum between comatose and noncomatose patients acutely after traumatic brain injury[14]. The metabolic rate of glucose in these regions significantly correlated with the level of consciousness using Glasgow Coma Scale scores at the time of PET[14]. Functional imaging such as F-18 FDG and O-18 water PET may be helpful to clarify the mechanism(s) in such cases although the relationship between clinical manifestations and imaging findings requires further exploration[9,10].

It appears less likely to detect patients at risk of developing posttraumatic problems based on clinical manifestations[10]. As significantly more functional than anatomic abnormalities were found in chronic closed head injury, PET might help in confirming the diagnosis and subsequent management in these group of patients, especially when CT/MRI was normal. Loss of consciousness at the time of initial injury is important in documenting the impact on brain injury. A normal pattern will make it less likely to happen during or after injury, which may have profound implications in the neuro-psychological or medico-legal evaluation.

CONCLUSION

There are significantly more functional than anatomic abnormalities in chronic closed head injury. Those with normal brain PET findings are less likely to have loss of consciousness at the time of initial injury.

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