Journal of Neurology & Neurophysiology

Bund et al., J Neurol Neurophysiol 2016, 7:1
DOI: 10.4172/2155-9562.1000355

Case Report | Open Access

Additional Value of FDG PET and Resting State-functional MRI for the Assessment of Consciousness Disorders in Hypoglycemia-induced Coma

Bund C[1], **Roquet D**[2], **Noblet V**[2], **Schenck-Dhif M**[3], **Schneider F**[3], **Kremer S**[2,4,5] **and Namer IJ**[1,2,5*]

[1]*Department of Biophysics and Nuclear Medicine, University Hospital of Strasbourg, Strasbourg, France*

[2]*ICube, University of Strasbourg / CNRS (UMR 7357), Strasbourg, France*

[3]*Medical Intensive Care Unit, University Hospital of Strasbourg, Strasbourg, France*

[4]*Radiology and Hospital Hautepierre Service, University Hospital of Strasbourg, Strasbourg, France*

[5]*Translational Medicine Federation Strasbourg (WFSW), Faculty of Medicine, Strasbourg, France*

***Corresponding author:** Izzie-Jacques Namer, Biophysics Department and Nuclear Medicine, University Hospital of Strasbourg, Hospital de Hautepierre, 1, avenue Molière, 67098 Strasbourg Cedex 09, France, Tel: +33388127550; Fax: +33388128342; E-mail: Izzie.Jacques.NAMER@chru-strasbourg.fr

Received date: January 28, 2016; **Accepted date:** February 10, 2016; **Published date:** February 17, 2016

Abstract

Background: Consciousness disorders in brain-injured patients are sometimes complicated to understand. The accuracy of the distinction between coma, vegetative state, minimally conscious state and locked-in syndrome can be improved by using functional imaging modalities, which is important because of the therapeutic impact.

Case presentation: We report a case of a 34 years old diabetic Caucasian woman whose glycemia had been previously tightly controlled with an insulin pump and who developed a profound coma overnight (spontaneous ventilation and Glasgow score 6) with transient ocular revulsions and intermittent crawling movements triggered by noxious stimuli at admission. At the 3rd day, 18F-fluorodeoxyglucose (FDG) PET and resting-state functional MRI (rs-fMRI) were performed when the patient spontaneously opened her eyes, but no evidence of awareness of the environment could be obtained. Awareness recovered progressively and follow-up imaging was performed on the 7th day when the patient presented only certain cognitive disorders. We demonstrated that rs-fMRI and FDG PET are non-invasive imaging tools that are helpful in the assessment of consciousness levels and residual cognitive disorders in patients with metabolic severe coma.

Keywords: Coma; Hypoglycemia; Metabolic coma; PET; FDG; fMRI

Introduction

Consciousness disorders in brain-injured patients are sometimes complicated to understand. In fact, it could be a border zone between awareness and consciousness. The accuracy of the distinction between coma, vegetative state, minimally conscious state and locked-in syndrome can be improved by using functional imaging modalities, which is important because of the therapeutic impact. Many functional MRI and FDG PET data have been published over the last few years and have helped us in the understanding of consciousness disorders [1].

The case presented illustrates the additional value of rs-fMRI and FDG PET for the assessment of consciousness disorders in hypoglycemia-induced coma.

Case

Our patient was a 34 years old diabetic Caucasian woman whose glycemia had been previously tightly controlled with an insulin pump. She's diabetic since her 8th birthday and has a diabetic retinopathy. There were no other significant medical histories.

She developed a profound coma overnight (spontaneous ventilation and Glasgow score 6) with transient ocular revulsions and intermittent crawling movements triggered by noxious stimuli at admission (Table 1). She was transferred in a medical intensive care unit, where she was intubated. It's important to precise that she never required sedation or anesthesia. Cerebral CT at admission didn't show any remarkable signs. After treatment by glucose infusion and insulin (Table 2) she stayed in a prolonged coma, with a bilateral, symmetric and diffuse but slow activity on EEG, which is why she was included in an imaging protocol for patients presenting prolonged coma.

So, at the 3rd day, FDG PET and rs-fMRI were performed when the patient spontaneously opened her eyes, but no evidence of awareness of the environment could be obtained.

A morphological brain MRI (including sagittal T1, axial T2, axial and coronal FLAIR, axial gradient echo T2 and diffusion weighted MR images) with rs-fMRI (405 whole-brain T2*-weighted echo planar images) was first performed. The first five images of rs-fMRI were removed to account for T1 partial saturation and the 400 remaining images were then motion corrected using SPM8 (Welcome Department of Cognitive Neurology, London, UK). Functional connectivity was analyzed using independent component analysis (FMRLAB toolbox 2.3, Swartz Center for Computational Neuroscience, San Diego, CA, USA) after reduction of the dimensionality from 400 to 250 by principal component analysis. Functional connectivity networks maps were manually selected following validated criteria [2] and classified according to the atlas from Kalcher et al. [3].

	Initial management	Arrival in medical intensive care unit	Day 3: First FDG PET	Day 7: Second FDG PET
Glasgow score	6	3	no evidence of awareness of the environment	disorientation in time and space
Glycemia (mmol/L)	1.78a	6.39	5.56	4.44
Blood pressure (mmHg)	80/50	97/60	108/62	99/60
Cardiac frequency (beats per minute)	134	134	109	77
SpO2 (%)	-	97b	97b	100
T (°C)	-	37	37.3	37.1
Potassium (mmol/L)	-	3.74	4.41	3.87
CPK (UI/L)	-	719c	110	56
Creatinine (μmol/L)	-	68.8	76.2	68.9
Hemoglobin (g/dL)	-	11.7	10.3	8.7d
Blood platelets (G/L)	-	186	267	316
Leucocyte (G/L)	-	5.1	6.3	4.91

Table 1: Vitals and blood sampling results during hospitalization at key moments (**a.** Capillary blood glucose, **b.** Tracheal intubation + oxygen therapy, **c.** CPK (creatine phosphokinase) were elevated, up to 2718 UI/L in the first 24-hours, suggesting that coma was prolonged before the patient was found, **d.** During the hospitalization, an anemia was discovered on blood sample linked to an iron-deficiency anemia, which was then supplemented).

Initial management	Reanimation	Output medical treatment
Subcutaneous insulin pump: insulin glargine	Glucose infusion 30% then Perinutriflex 1250 mL/24 h	Intravenous rapid insulin infusion by an electric syringe pump in doses controlling glycemia at 4.4-8.3 mmol/l
Potassium chloride: 600 mg	Intravenous rapid insulin infusion by an electric syringe pump in doses controlling glycemia at 4.4-8.3 mmol/l	Potassium chloride: 1200 mg
Nicotine patch	Amoxicillin and clavulanic acid: 3 g	Amoxicillin and clavulanic acid: 3 g
	Low molecular weight heparin in thromboembolism prevention	Vitamins B1 and B6
	Esomeprazole: 40 mg	Ferrous sulphate

Table 2: Insulin dosing and medications prescribed to the patient.

While no abnormalities were seen on morphological MRI, four functional connectivity networks were observed on rs-fMRI: occipital, frontal and temporal networks, and left latero-fronto-parietal network (FPN). The internal awareness network, also called default mode network (DMN) was not identified (Figure 1A). Brain FDG PET showed hypometabolism of bilateral precuneus, left pre- and postcentral regions, left insula, left temporal regions and bilateral occipital regions (the patient's eyes were closed) (Figure 2B).

Awareness recovered progressively and follow-up imaging was performed on the 7th day when the patient presented only certain cognitive disorders, in particular disorientation in time and space (with a mini mental state examination at 15/30). The morphological MRI was normal. On rs-fMRI, five functional connectivity networks were observed including the DMN and the dorsal attentional system (C.04 and C.10 of the Kalcher's atlas, respectively), that were absent at the first MRI session (Figure 1B). FDG PET showed a marked improvement of previously observed metabolic abnormalities as only the left temporal pole remained hypometabolic (Figure 2C).

Restoration of spatial and temporal orientations, of normal cognition required an additional week of supportive care.

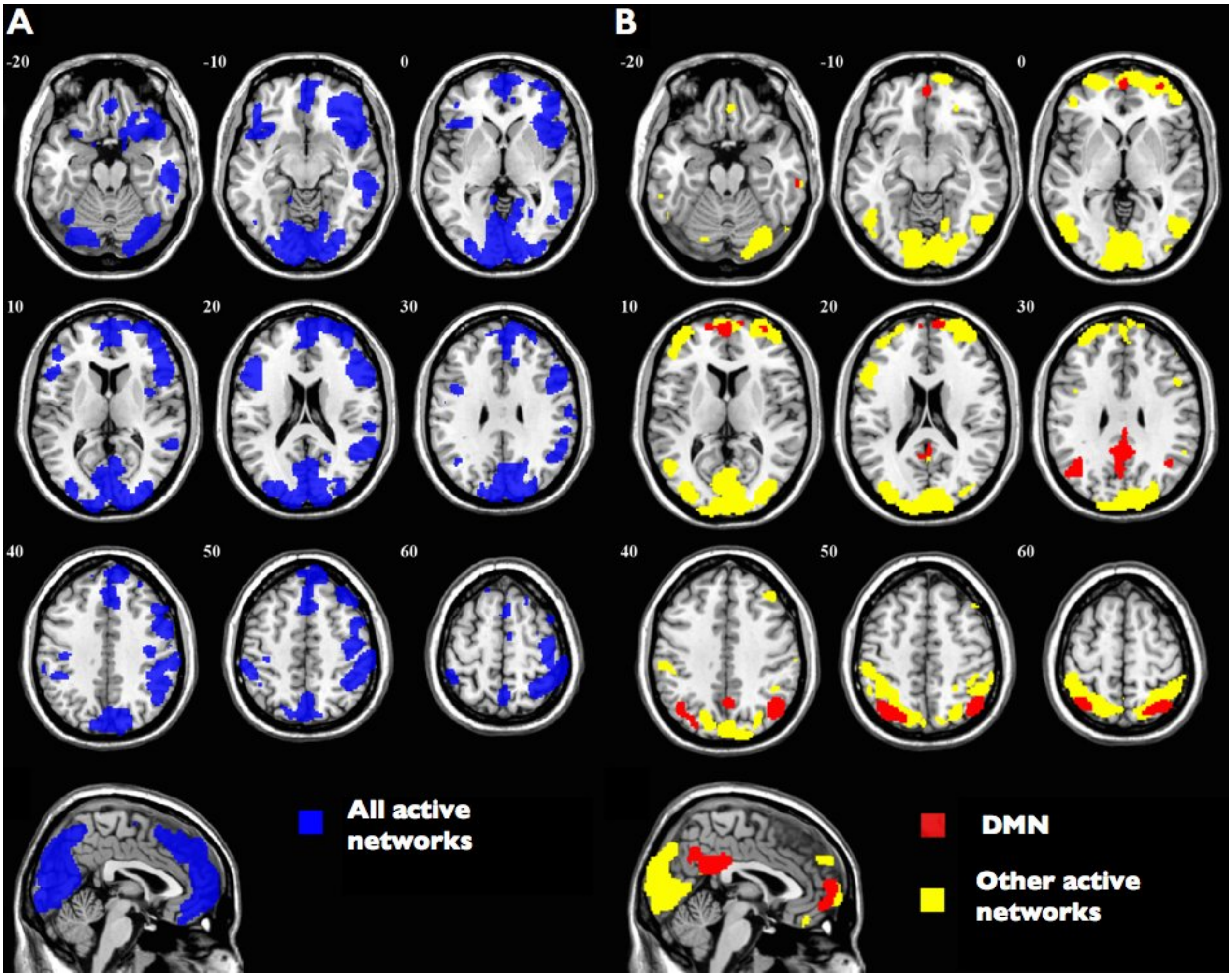

Figure 1: Networks from rs-fMRI acquisition during (A) and after (B) the hypoglycemic coma episode. During the coma episode (A) four functional connectivity networks (in blue) were observed on rs-fMRI (occipital, frontal, and temporal networks) including the left-FPN but not the DMN. After the coma episode (B), we observed four functional connectivity networks observed previously (in yellow) as well as the DMN and the dorsal attentional system (in red), which were absent at the first fMRI session.

Discussion

Detection of DMN was linked to better awareness. In fact, the last few years two main functional connectivity networks have been identified: the external awareness network (FPN) which subserves consciousness of the environment and the internal awareness network or default mode network (DMN) that appears to be related to self-related processes [4]. rs-fMRI studies have pointed out the importance of the DMN to distinguish coma, vegetative state, minimally conscious state and locked in syndrome as DMN connectivity correlates with the degree of consciousness [5].

FDG PET can demonstrate the relationship between functional activity and glucose energy metabolism in the central nervous system [6-9], as approximately 75% of brain's energy consumption goes into signal transmission, while the remaining 25% serves to maintain basic cellular activity [10]. FDG PET has proven able to distinguish the different levels of consciousness disorders by showing that glucose metabolism in the frontal and parietal cortex correlates with behavioral scores [11]. In our case, although rs-fMRI was considered as normal at the second session, FDG PET still showed left temporal hypometabolism that could explain the persistence of some cognitive disorders.

So, FDG PET could be used to see if patients would be emerging from minimally conscious state, which is not easy to do at bedside clinical examination. Recovery of the DMN metabolic activity was studied in severe brain damaged patients [12] and also in traumatic diffuse brain injuries [13]. Both studies showed that FDG PET was useful to distinguish between the different states of coma by studying hypometabolism. rs-fMRI showed similar results, although it seems to be less sensitive [12].

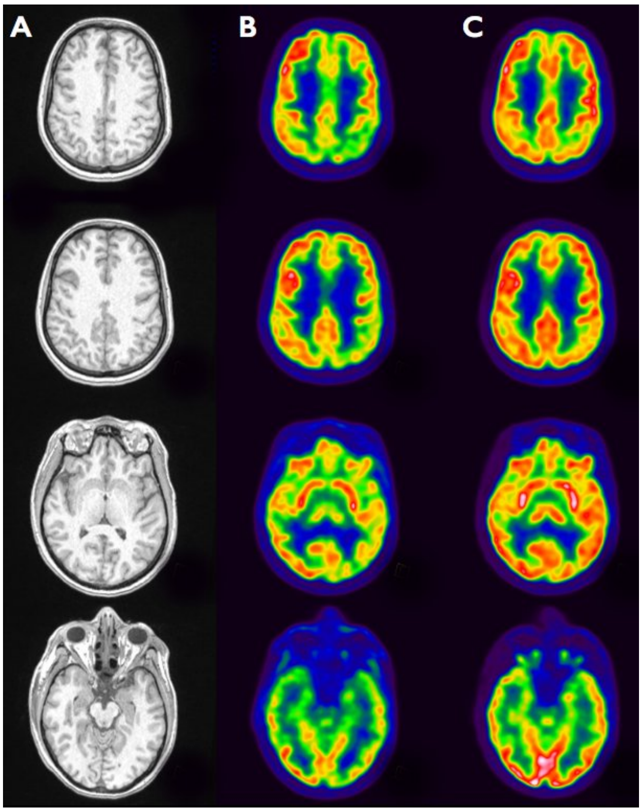

Figure 2: Matched transverse slices showing multimodal brain imaging: T1-weighted MRI (A), FDG PET during (B) and after (C) the hypoglycemic coma episode. During the coma episode (B) FDG PET showed hypometabolism of bilateral precuneus, left pre- and postcentral regions, left insula, left temporal regions and bilateral occipital regions (the patient's eyes were closed). After the coma episode (C), FDG PET showed a marked improvement of previously observed metabolic abnormalities as only the left temporal pole remained hypometabolic.

In conclusion, FDG PET and rs-fMRI are non-invasive imaging tools that are helpful in the assessment of consciousness levels and residual cognitive disorders in patients with metabolic severe coma. They both indirectly measure neuronal activity and have been recently used in a study to demonstrate differences in neuronal activity between commonly used mouse strains [14]. The detection of the DMN on rs-fMRI and levels of cortical metabolism in frontal and parietal regions on FDG PET seem to be the most accurate markers of consciousness disorders when compared to currently available markers. Combining both methods with the development of PET/MRI may be more accurate and combine advantages of the two methods [15].

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