The Effect of Anaesthesia on ^{18}F-FDG Uptake in the Rat Brain: A Fully Conscious Dynamic Study using Motion Correction

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***Abstract*—Anaesthesia is used in preclinical positron emission tomography (PET) studies to ensure that no motion of the animal occurs during the scan. The effect of the anaesthesia in brain imaging on the tracer or drug under study is not always known, and this may confound the results of the study and how they are translated to the clinic. Using developed motion correction techniques, we present results from a study of the effect of isoflurane on FDG uptake in the rat brain using fully awake tube-bound, but unrestrained, rats. The study involved dynamic scans of both awake and asleep rats. We report here on 2 rat studies. A consistent increased uptake at steady-state of FDG in the awake rat brains was observed, when compared to the asleep scans.**

I. Introduction

In preclinical positron emission tomography (PET) studies an anaesthetic, such as isoflurane, ketamine, or chloral hydrate, etc., is usually used to ensure that the animal remains still for the duration of the scan. The effect of the anaesthesia on the tracer or drug under study is not always known, and this may confound the results of the study and how they are translated to the clinic, where anaesthesia is usually avoided. There have been reports on the effect of anaesthesia, summarised in [1], where the animals were infused with the tracer or drug while awake and then anaesthetised and scanned after some time, thus acquiring a static scan where the tracer or drug uptake was not affected by the anaesthesia [2]; or where the animal was physically restrained (particularly the head for brain imaging) such that motion was impossible [3]. To fully quantify the effect on the tracer or drug a dynamic scan is necessary from the time of infusion. While restraining the animal does allow for this, the effect of stress on the uptake is another confounding factor which is difficult to quantify. As stated in [1], a study involving fully awake, unrestrained animals would be ideal for quantifying the effect of the anaesthesia.

In this work we report on a proof of principle study of fully awake, tube-bound, but unrestrained, rats, undergoing dynamic scans to evaluate the effect of anaesthesia on the tracer uptake in the brain. An external stereo-optical camera is used to track the motion of the rat's head, and a list-mode based motion correction reconstruction is then performed to achieve a reconstruction free of motion artefacts [4]–[6]. The effect of the anaesthetic isoflurane on the uptake of the tracer ^{18}F-FDG in the rat brain was investigated.

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Fig. 1. The awake rat inside the tube while being scanned. The marker on the rat's forehead was tracked by the MicronTracker to derive the motion of the rat's brain. In the foreground the reference marker can be seen, which allows for the conversion from MicronTracker coordinates to PET coordinates.

II. Method

All animal experiments were approved by the ethical committee of the K.U. Leuven and performed in accordance with the European Communities Council Directive (86/609/EEC).

PET measurements were performed using the microPET Focus 220 small animal PET scanner (Preclinical Solutions, Siemens Healthcare Molecular Imaging, Knoxville, TN, USA). To track the motion of the rat's head the MicronTracker Sx60 (Claron Technology Inc., Toronto, Canada) camera was used. The MicronTracker (MT) is a stereo-optical camera which can track preregistered markers, deriving the 6 degrees-of-freedom from two slightly offset images. It was used to track a small marker (2.2×1.7 cm) attached to the rat's head, at a frequency of 25 - 30 Hz. Female Wistar rats were used (270 - 280 g). Seven to ten days before the scan a surgery was performed on each rat to insert a catheter into the jugular vein, with an access port protruding from between the shoulder blades. Following this the rats were put on a 3 day course of antibiotics and analgesics, and allowed to recover before continuing with the experiment.

Each rat was acclimatised to having the tracking marker attached to its head, as well as being inside a tube suspended

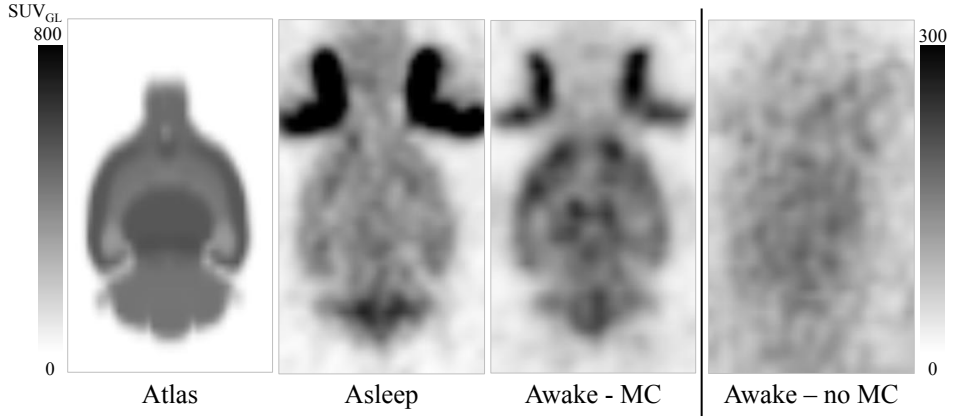
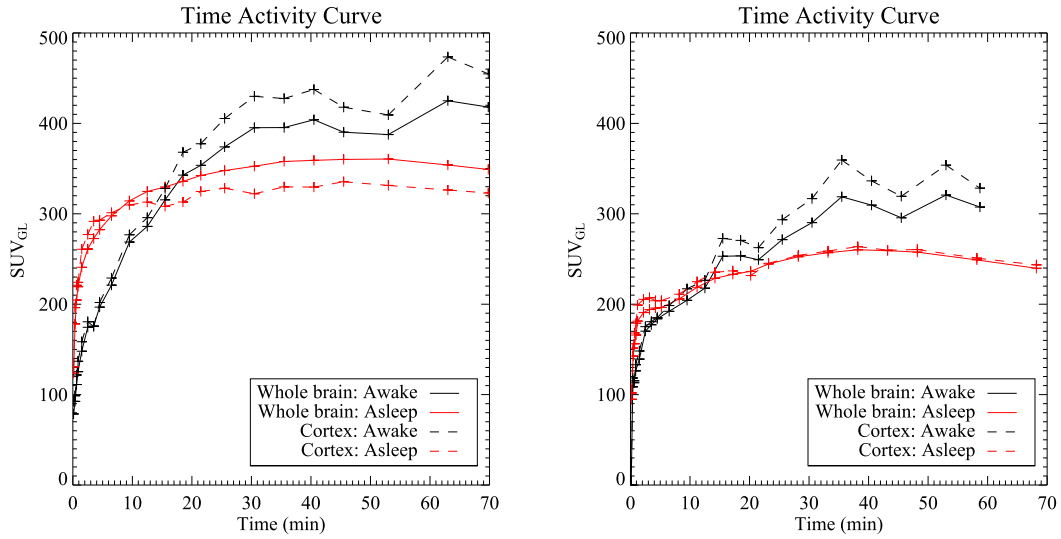


Fig. 2. Reconstructions of a single frame 60 minutes after tracer infusion for the asleep scan and the awake scan with and without motion correction (MC).



(a) Rat 1

(b) Rat 2

Fig. 3. Time activity curves for two rat studies. The time shown is from after the tracer infusion.

in the scanner (as can be seen in figure 1), over a period of 3 days leading up to the scan. The rats were not restrained inside the tube. The acclimatisation involved placing the rat into the tube and putting it back into the tube if it were to jump out. The rats were fasted for 12-15 hours prior to the scan. The whole blood glucose level was measured using a glucose counter (GlucoCard Memory 2, A. Menarini Diagnostics, Italy) with blood taken from the tail vein. The glucose measurements were done in duplicate when possible both immediately before and after the scan. The rats were infused with 0.6 - 0.8 mCi of FDG in a total injected volume of 0.8 ml (including saline for flushing) using an infusion pump over 24 seconds at a rate of 2 ml/minute, and were scanned for 60 - 75 minutes, starting from before the tracer infusion. Three to four days after the awake scan the rats were again scanned with the same procedure, but while under anaesthesia, namely isoflurane (2.5%, 2 L/min O_2). The anaesthetic was administered before the tracer infusion and constantly throughout the scan. The reconstructions were performed using OSEM, without attenuation and scatter correction. The Johnson rat brain atlas [7] was aligned to the asleep and awake scan reconstructions and used to delineate regions-of-interest (ROIs). For quantification purposes the standard uptake value weighted by the glucose level ($\mathrm{SUV_{GL}}$) was calculated as follows,

$$\mathrm{SUV_{GL}} = \lambda \frac{WG}{D}, \tag{1}$$

where λ is the pixel activity in μCi, W is the body weight in g, G is the glucose level before the scan in mg/dL, and D is the injected dose in μCi.

III. Results

The reconstruction of a single frame 60 minutes post injection in the asleep and awake scans is shown in figure 2. The time activity curves (TACs) for two ROIs for two rats are shown in figure 3. During the awake scan the markers on the rats' heads were not always visible to the motion tracker; at these times the corresponding list-mode events were discarded.

Therefore, on average, 85% of the measured events could be used. The calculation of the effective frame duration accounted for this.

IV. Discussion & Conclusion

The effect of isoflurane on the uptake of FDG in the rat brain has been studied by comparing the scans of fully awake rats to those of asleep rats. In these preliminary results, an increased uptake at steady-state in awake rats is observed, with an accompanying increase in the time taken to reach the steady-state. A variation of the uptake in different regions is also observed. Further rat studies are being conducted to confirm and further quantify this effect.

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