Evaluation of the PET-radioligand [^{11}C]DASB in dogs

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Introduction

Over the years, [^{11}C]DASB has been put forward as the radiotracer of choice to image the serotonin transporter availability in the brain. Despite the frequent use in human and small animal studies, its use in dogs has not been validated yet.

Objectives

This abstract presents an evaluation of *in vivo* imaging data obtained in dogs with the radioligand [^{11}C]DASB and PET, where different quantification methods were assessed.

Materials and methods

Five male adult (4-8 years) dogs were included in the study and were scanned in a combined Gemini PET/CT imaging system. After conducting a low dose CT survey for attenuation correction, dynamic emission recordings in list mode were initiated on bolus-injection of 290 ± 60 MBq [^{11}C]DASB. Emission data were reconstructed as 34 frames of increasing duration (6 x 10, 8 x 30, 5 x 120, 15 x 300 s). During the 90 minutes PET scan, arterial whole blood was sampled manually at 26 time points with increasing intervals and, after centrifuging the blood samples (5 min, 5200 rpm), plasma activity was measured using a NaI(Tl) scintillation detector. For each dog the parent compound fraction was measured at 4 – 9 time points using a validated SPE method described by Ginovart et al,2001.

After the scan, each PET image was coregistered with an MR image, which was taken prior to the study and was used for anatomical information in order to manually draw 20 ROIs. For each ROI, the distribution volume (V_T), obtained via the one- and two- tissue compartment model (1-TC, 2-TC) and the Logan graphical analysis, was calculated and the goodness-of-fit was evaluated via the standard error coefficient of variation (%SE) and the Akaike Information Criterion (AIC, Akaike, 1974). V_T's of the preferred model were used to calculate binding potentials (BP_{ND}) using the cerebellum (vermis excluded) as a reference region. Finally, these BP_{ND}'s could then be compared with those obtained via three tissue reference methods: SRTM2, MRTM2 and the Logan noninvasive model.

Results and discussion

The averaged metabolite data from all dogs could be interpolated by fitting a Hill function to the fraction data in order to derive the metabolite-corrected plasma input functions. Volumes of distribution were compared between the 1 and 2-TC model and, based on %SE and AIC, the 2-TC model was preferred in respectively 60 and 66% of the brain regions. Both the 1-TC model and the Logan graphical analysis significantly underestimated the distributions volumes (p-value respectively 0,002 and 0,015), especially in high-binding regions such as the raphe nucleus, the hypothalamus and the thalamus. When comparing the BP_{ND}'s, calculated via the 2-TC model, with those obtained via the tissue reference methods, similar fits were observed in all the models, however the best correlation was obtained using the MRTM2 model (Y= 0,9133 X + 0,052; R^2: 0,96).

Conclusion

The MRTM2 can be put forward as the tissue reference method of choice in order to avoid invasive 2-TC compartment modeling, however small underestimations of binding potentials in high-binding regions must be taken into account.

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