OVS-localized ^{31}P NMR spectroscopy in the primate brain

J. Valette[1], M. Guillermier[2], P. Hantraye[1,2], V. Lebon[1]
[1]CEA-SHFJ, Orsay, France, [2]URA CEA-CNRS 2210, Orsay, France

Introduction

^{31}P NMR spectroscopy offers a unique insight into brain energy metabolism. However, ^{31}P NMR is hampered by very short transverse relaxation time T_2 of metabolites, making localization by PRESS or STEAM particularly challenging due to the dramatic signal loss during echo-time. Alternatively, localization can be performed by ISIS, but long successive adiabatic pulses are required when using a surface coil, leading again to T_2 relaxation during the pulses. In the human brain, localization may be achieved by the surface coil itself [1], but this is no longer possible for species presenting thicker muscle layers between the coil and the brain. In this work we propose a zero echo time localization technique based on Outer Volume Suppression (OVS). Efficient localization is demonstrated with a surface coil. Combination with inversion-recovery and saturation transfer allows to measure the synthesis rate of ATP in the monkey brain at 3T.

Materials and Methods

Experimental setup Experiments were performed on a whole-body 3T Bruker system equipped with gradients reaching 44mT/m. A double-tunable ^{1}H/^{31}P surface coil (Ø~4.5cm) was used. *In vivo* experiments were performed on 2 healthy macaque monkeys. Animals were anesthetized by i.v. propofol infusion and were ventilated. A 2×2×2cm^3 voxel of interest (VOI) was positioned in the brain, including a large part of the fronto-parietal cortex and the striatum.

OVS localization A BISTRO (B_1 InSensitive TRain to Obliterate signal [2]) OVS pulse train was implemented. It consisted in 15 modules repeated at increasing RF power levels. Each module consisted in 3 adiabatic double-band hyperbolic secant pulses selectively saturating 3.8cm slices in the X, Z and Y directions, around a 2×2×2cm^3 VOI. Total OVS train length was ~300ms. A 100µs broad-pulse was placed immediately after the OVS pulse train for non-selective excitation. Repetition time TR was 2.95s.

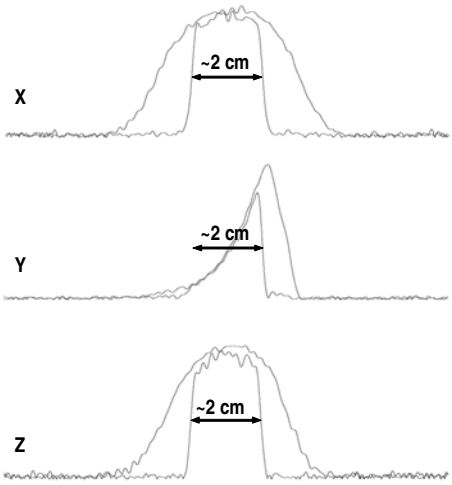

Fig. 1. Profile visualization in the ^{31}P domain on a tripolyphosphate phantom along the directions X, Z and Y with and without OVS (NT=128).

In vitro visualization of ^{31}P localization In order to calibrate OVS power and to visualize ^{31}P excitation profiles, a dedicated phantom was used (~0.1M tripolyphosphate $Na_5P_3O_{10}$ adjusted to match *in vivo* RF deposition). Readout gradients were added to the ^{31}P sequence along the X, Y and Z directions. Optimized OVS power was referenced to the ^{1}H RF power in the same VOI.

Inversion-recovery Inversion-recovery experiments were performed at long TR for full longitudinal relaxation (TR=6.4s, NT=128). Inversion was achieved with a hyperbolic secant pulse placed at a variable inversion time TI before the OVS pulse train, centered on inorganic phosphate P_i frequency. For reference at TI=0ms, the inversion pulse could also be place between the OVS pulse train and the excitation pulse.

Saturation transfer A saturation broad-pulse (t_{sat}=2s) was placed just before the OVS pulse train. The γ-ATP resonance was saturated, and the signal of inorganic phosphate P_i was compared to a control experiment with symmetric saturation [1] (NT=1024, total acquisition time for saturation and control experiment ~1h40).

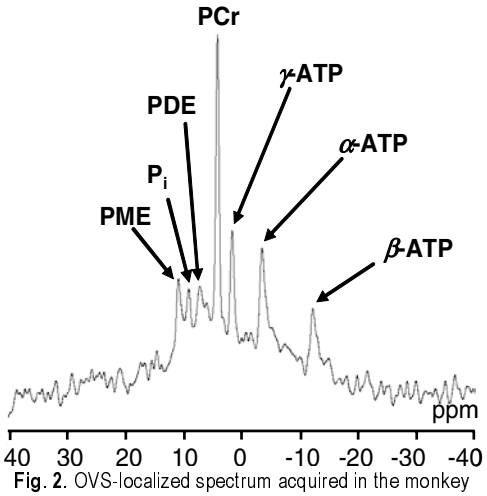

Fig. 2. OVS-localized spectrum acquired in the monkey brain (NT=256, ~12min acquisition).

Results and Discussion

^{31}P excitation profiles acquired *in vitro* along X, Y and Z are shown in Fig. 1, demonstrating excellent spatial localization with minimal signal attenuation within the VOI. An *in vivo* OVS-localized ^{31}P spectrum (~12min acquisition) is presented in Fig. 2. ATP, P_i, PCr, phosphodiesters PDE and phosphomonoesters PME are detected. The spectral pattern (high PME and PDE content relative to P_i, high ATP/PCr ratio) argues in favor of signal mainly originating from the brain, with only negligible contamination from muscle. Given the gradient strength used for OVS, maximal localization error due to chemical shift was estimated to be ~1.5mm in X and Z directions and ~1mm in the Y direction.

From the signal attenuation (peak height) measured during the inversion-recovery experiment at different TI (fig. 3), the T_1 for P_i was estimated to be ~1.5s. Saturation transfer resulted in a 13±1% attenuation of P_i signal (N=3). Although the rigorous determination of P_i→ATP unidirectional flux k_f requires measurement at different t_{sat} (progressive saturation transfer), it can be deduced from modified equations including T_1 relaxation during the OVS pulse train that this attenuation is compatible with k_f~0.1s^{-1}. Assuming that P_i concentration is about 1.3mM [1], this leads to a P_i→ATP synthesis rate of ~8µM.g^{-1}.min^{-1}. This is about 15-fold the TCA cycle rate as measured in the monkey brain under similar physiological conditions [3], supporting the idea of an efficient coupling between TCA cycle and ATP synthesis under normal conditions (the theoretical upper ratio is ~17). Note that, even in the absence of absolute quantitation of k_f, signal attenuation of P_i might still be used as an index ATP synthesis when investigating pathological conditions.

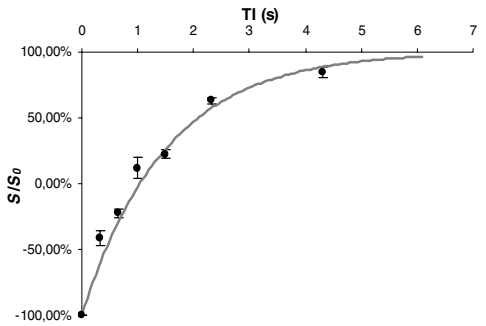

Fig. 3. P_i signal attenuation obtained by inversion-recovery (N=4 for TI=4.32s, N=2 for other TI).

Conclusion

Localization of ^{31}P signal was achieved in the monkey brain with OVS only, allowing the acquisition of ^{31}P spectrum without signal loss due to transverse relaxation. In this context, P_i signal attenuation during inversion-recovery experiment and saturation transfer experiment could be measured at 3T. Further developments include complete progressive saturation transfer experiment for accurate determination of the ATP synthesis rate.

[1] Lei H et al., PNAS 100, p.14409 (2003) ; [2] Luo Y et al., MRM 45, p.1095 (2001) ; [3] Boumezbeur F et al., MRM 52, p.33 (2004).