ASL OPTIMIZATION FOR HIPPOCAMPUS PHYSOSTIGMINE CHALLENGE PERFUSION STUDY

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Introduction

The cholinesterase inhibitor physostigmine (PHY) has different effects on cerebral blood flow (CBF) between normal healthy controls and patients with neurodegenerative disorders [1]. The hippocampus is involved in many brain diseases, such as Alzheimer's disease and Gulf War Syndrome [2]. Therefore, the response of hippocampus to PHY challenge has diagnostic and prognostic potential. The purpose of this study is to determine proper post-bolus delay time for PHY challenge perfusion study using ASL. This optimization was achieved by performing multiple inversion perfusion studies with fixed labeling time but varied post-bolus delay times for sessions with both saline infusion and PHY infusion.

Materials and Methods

Six normal healthy subjects took part in this study, three male (54 ± 2 years) and three female (42 ± 17 years). ASL optimization studies were performed in two sessions 2 days apart: the first session with the infusion of saline as a placebo and the second session with the infusion of PHY. At each session, subjects received about 40 minutes intravenous infusion before the MRI scans, and the infusion was continued during the MRI session. The infusion rate of PHY is 1.0 mg/hour. To counteract the peripheral autonomic effects (nausea) of PHY, 0.3 mg of glycopyrrolate was injected IV over one minute prior to beginning MRI scans.

The study was conducted on a Siemens 3T TIM Trio scanner using a modified FAIR [3] sequence with Q2TIPS [4] using the following parameters: TR/TE = 3200/9.2 ms, FOV = 230 x 230 mm^2, matrix size = 66 x 66, resolution = 3.5 x 3.5 mm^2, 16 imaging slices, slice thickness = 3.5 mm with 20% gap, 110 measurements, iPAT GRAPPA factor = 2 with 24 reference lines using CP mode, partial Fourier (PF) = 7/8, ascending acquisition order, temporal bolus width (TI_1) = 0.6 s, post-bolus delay time = {0, 400, 800, 1000, 1200, 1400, 1600, 2000} ms, inferior saturation number/pulse interval/slab size= 20/25 ms/20 mm. Hippocampus ROIs were generated from high-resolution MPRAGE anatomic images using FIRST from the FSL package, and co-registered to ASL series. Siemens' Auto-align technique was used to ensure consistent imaging slice position across sessions. The single blood compartment model was used for CBF quantification [5].

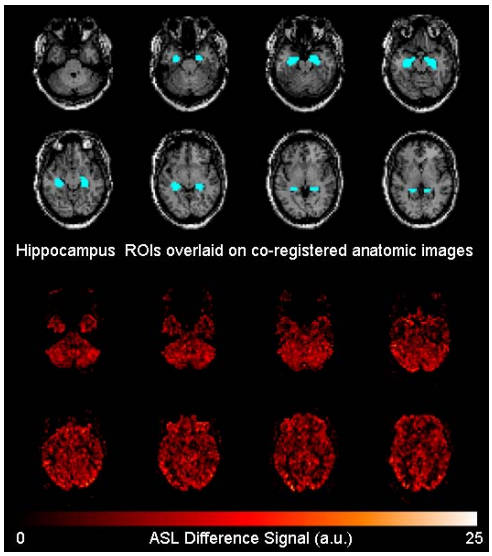

Fig. 1 Hippocampus ROIs (top) and perfusion-weighted imaging maps at 1.2 s post-bolus delay time (bottom)

Results and Discussion

Figure 1 shows the segmented hippocampus ROIs overlaid on co-registered high-resolution anatomic images and perfusion-weighted imaging maps at 1.2 s delay from one typical subject. Figure 2 presents the inter-subject variability of CBF measurements from both saline and PHY sessions as a function of post-bolus delay. Relative hippocampus CBF changes between the PHY session and the saline session are displayed for five different delay times in Figure 3. In Figure 4, hippocampus CBF measurements from two sessions are shown for five post-bolus delay times. At delay times of 1.0 s and 1.2 s, CBF measurements have much lower inter-subject variability. CBF measurements from the PHY session have larger inter-subject variability, which may be due to the subject-dependent effects from PHY. At shorter (<1.0 s) and longer (> 1.4 s) delay times, the results indicate that the hippocampus region has increased CBF level with PHY, while at delay times ranging from 1.0 s to 1.4 s, CBF decreases with PHY, reaching the lowest level around 1.2 s (about 5% decrease). To minimize inter-subject variability and increase the sensitivity of ASL for the detection of significant differences between normal healthy controls and patients, it is suggested that the post-bolus delay that gives the lowest inter-subject variability should be used. This study indicates that different delay times may give different trends of CBF changes upon PHY challenge, which may be due to the different stages of the delivery of labeled blood to brain tissue.

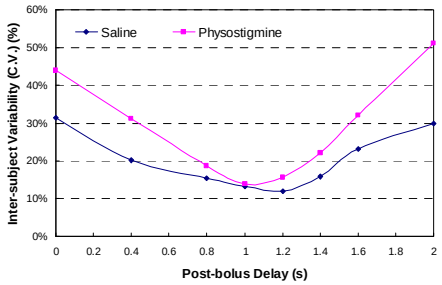

Fig. 2 Inter-subject variability of hippocampus CBF measurements (C.V.: coefficient of variance)

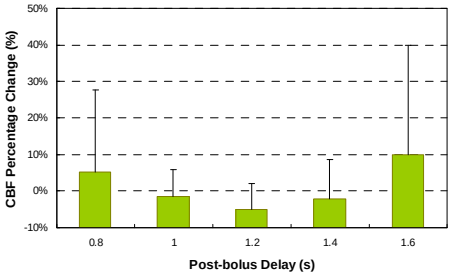

Fig. 3 Hippocampus CBF changes due to PHY. CBF percentage change = (CBF_{phy} – CBF_{saline})/ CBF_{saline} * 100

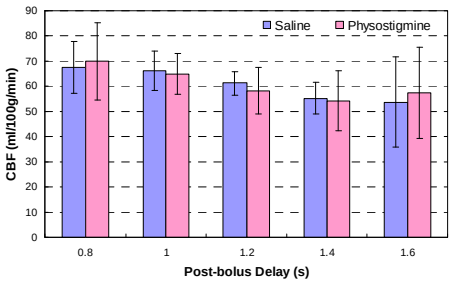

Fig. 4 Hippocampus CBF measurements from perfusion studies with the infusion of saline or physostigmine

Conclusions

Post-bolus delay times equal to 1.0 s or 1.2 s give lower inter-subject variability of hippocampus CBF measurements for perfusion studies with both saline and PHY challenge. Hippocampus CBF measurements at post-bolus delay equal to 1.2 s showed the largest decrease in CBF with PHY infusion.

Acknowledgements

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