Determining Ischemic Thresholds for Gray and White Matter in Stroke Penumbra

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Introduction

A major goal of magnetic resonance perfusion-weighted imaging (PWI) is to identify the tissue at risk of infarction that may be salvaged with treatment in acute ischemic stroke. Studies suggest that gray (GM) and white matter (WM) have different ischemic thresholds.[1] Human MR studies, however, have not assessed this to date. We have applied a novel method[2] to derive GM and WM quantitative cerebral blood flow (CBF) values from different ischemic compartments. This study confirms that GM and WM have different ischemic thresholds and suggests that attempts to identify the penumbra via CBF should take tissue type into account.

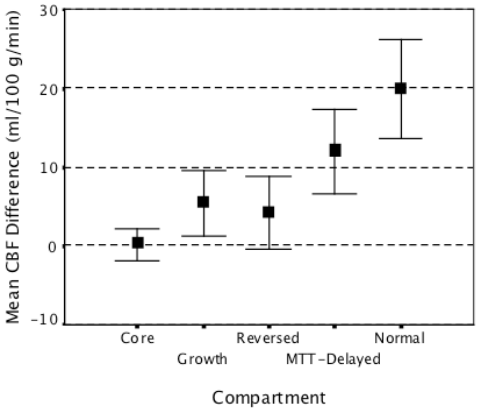
Methods

Ten patients were scanned at 3.0 T (Signa, GE Medical Systems, Waukesha, WI) less than 6 hrs from stroke onset (baseline) and at 1 month (follow-up). At baseline, diffusion-weighted imaging (DWI) and PWI were performed. As well, we acquired an inversion recovery, spin-echo, EPI sequence (IRSEPI) (TR/TE/TI= 12000/17/400 ms) that was designed to maximize contrast between GM and WM. At follow-up, DWI and fluid attenuated inversion recovery (FLAIR) imaging were performed. All images were registered to the initial PWI. CBF and mean transit time (MTT) maps were made following semi-automatic arterial input function selection[3] and deconvolution by singular value decomposition. Computer-assisted segmentation derived the initial and final lesions on baseline and follow-up DWI and FLAIR images. Our stroke model consisted of 5 compartments: 1) *core infarct* (identified as lesion on both the baseline and follow-up images), 2) *growth region* (or penumbra, identified as lesion only at follow-up, not at baseline), 3) *reversed region* (lesion at baseline but not follow-up), 4) *MTT-delayed region* (regions with delayed MTT compared to the surrounding tissue but excluding the core, growth and reversed regions), and 5) *normal* (all other tissue). The IRSEPI images were segmented into GM, WM and cerebrospinal fluid by a K-means algorithm.[4] The resulting segmented image was used to separate each compartment from the stroke model into GM and WM. The means of the median CBF values from each patient were calculated for each compartment in GM and WM. Paired t-tests were performed on the median GM and WM CBF values in each compartment and the differences between GM and WM for each compartment were calculated along with their 95% confidence intervals (CI). A receiver operator characteristics (ROC) analysis was done on all voxels within the four non-normal compartments to evaluate the sensitivity and specificity of CBF thresholds for identifying voxels that infarcted. The ROC analysis was performed on GM and WM separately.

Table 1. Means and standard deviations of CBF values in GM and WM in each compartment

Compartment	Tissue	CBF (ml/100 g/min) Mean (SD)
Core	GM	11.9 (3.9)
	WM	11.6 (6.4)
Growth	GM	17.7 (7.7)
	WM	12.2 (4.1)
Reversed	GM	17.4 (8.9)
	WM	13.6 (6.9)
MTT-Delayed	GM	28.1 (11.5)
	WM	16.0 (6.3)
Normal	GM	39.3 (15.1)
	WM	19.4 (7.2)

Figure 1. Mean CBF difference between GM and WM (and 95% CI) in each compartment. CBF in GM and WM are significantly different in the compartments where the CI does not cross zero



Results

The means of the median CBF values are shown in Table 1 and the mean differences between GM and WM CBF are shown in Figure 1 along with the 95% CI for each compartment. There was a significant difference between CBF of GM and WM in the growth ($p = 0.02$), MTT-delayed ($p < 0.01$) and normal ($p < 0.01$) compartments. The difference in the reversed compartment neared significance ($p = 0.07$) and there was no difference in the core ($p = 0.7$). In the growth, or penumbral region, GM CBF was a mean of 5.5 ml/100 g/min higher than WM (95% CI: 1.3-9.6 ml/100 g/min). ROC analysis indicated that the optimal CBF thresholds for predicting tissue infarction based on maximizing the Youden index (sensitivity + specificity - 1) are 19 and 15 ml/100 g/min for GM and WM respectively. The sensitivity and specificity at these thresholds were 73% for both GM and WM, shown in Table 2.

Table 2. Optimal CBF thresholds for identifying infarcting GM and WM based on ROC analysis

Tissue	CBF (ml/100 g/min)	Sens (%)	Spec (%)
GM	19	72.8	73.5
WM	15	72.6	72.5

Conclusions

Penumbral GM and WM have significantly different CBF. In addition, ROC analysis indicates that there are different optimal CBF thresholds for predicting infarcting tissue in GM and WM. These results demonstrate that GM and WM have different ischemic thresholds in humans. Attempts to identify salvageable tissue via CBF should therefore take tissue type into consideration.

References

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