Correlation between cerebral blood flow and anisotropy in white matter

Andrea Federspiel[1], Sebastian Walther[1], Ariane Orosz[1], Roland Wiest[2], Stéphanie Giezendanner[1], Jennifer Andreotti[1], Simon Schwab[1], Thomas Dierks[1], and Kay Jann[1]

[1]Dept. of Psychiatric Neurophysiology, University Hospital of Psychiatry / University of Bern, Bern, Bern, Switzerland, [2]Institute of Diagnostic and Interventional Neuroradiology, University of Bern, Bern, Bern, Switzerland

Introduction: In the human brain changes in cerebral blood flow (CBF) are mostly described for gray matter (GM) but rarely for white matter (WM) [1] [2]. Non-invasive WM investigations concentrate on the microstructural organization of the WM connecting different cortical regions. Nonetheless, blood vessels that perfuse WM tissue were described by neuroanatomy. Recently, a study investigated the relationship between CBF and WM properties showing an inverse correlation (rather than a positive) between CBF and fractional anisotropy (FA) values in healthy subjects [3]. The authors propose different mechanism that may account for their finding. One of them attempts to relate CBF in WM to the axonal diameter. The authors encouraged further studies to probe for this unexpected finding [3]. Accordingly, in the present study a twofold sample was investigated in order to probe the surprising findings of Aslan et al. In the present study a rigorous treatment of partial volume was applied in order to reduce the contribution of impure tissue properties feigning the effect. Specifically, if there is a relationship between CBF in WM to the axonal diameter, then this relationship would be most prominent in the genu/splenium of the corpus callosum. We tested specifically for this hypothesis.

Methods: A total of 24 healthy subjects were included in the study (mean age: 37.4 years ± 8.5; 12 male and 12 female). All MRI scanning were performed on a 3T Siemens TRIO TIM scanner. ***Anatomical scan*** (MDEFT) [4] followed by ***ASL scan*** using pseudocontinuous ASL (pCASL) sequence [5, 6] with 8-channel head coil FOV=220 mm, matrix=64 x 64, axial slices=16, Slice thickness=7 mm, gap=1.5 mm, TE/TR[ms]=17/4000, slice-selective gradient = 6 mT/m, tagging duration τ = 700 ms and postlabeling delay (w) = 1000 ms. In total, 156 volumes were collected during ASL scan. Matlab/SPM8 was used for preprocessing of imaging data and calculation of absolute CBF maps [7]. ASL images were motion corrected and CBF was quantified using a single-compartment model (T1blood 1650ms, labeling efficiency 0.85, blood-tissue partition coefficient 0.9 [ml/g]). ***DTI scan*** was performed with a spin echo EPI using two 180° pulses (TR/TE 6500/96 ms, matrix 96x128, FOV 230x230mm, 52 slices, slice thickness 2 mm, gap 0 mm, pixel bandwidth 1396 Hz/pixel, N=2 averages). The trapezoidal diffusion sensitizing gradients were applied around the two 180° pulses at b-value of 0 s/mm^2 and at a maximal b-value of 1300 s/mm^2 along 42 non-collinear directions. All ASL and DTI slices were positioned along the AC-PC line. The calculation and diagonalization of the diffusion tensor were based on the multivariate regression approach [8]. Six independent elements of the diffusion tensor were extracted [9]. Eigenvalues and eigenvectors were determined for each voxel, and fractional anisotropy (FA) values for each voxel were computed resulting in 2D FA maps. Co-registration of the CBF and FA maps to the 3-D structural images was performed using the scanner's slice position parameters of the SE-EPI measurements and the T1-weighted anatomical measurements. CBF and FA maps were transformed into the normalized Talairach space. ***Partial Volume Estimation*** PVE was estimated in the segmented anatomical images using a "trimmed minimum covariance determinant (TMCD)" method for the estimation of the parameters of the mixed PVE model [10]. In this method, each voxel is first labeled according to the most dominant tissue type (the tissue types are gray matter, white matter and cerebro spinal fluid). Only voxels that are not prone to PVE are contained in the labeled set. The images were preprocessed as follows: i) correction of the intensity inhomogeneity and ii) classification into hard labels (WM, GM, and CSF) by a neural network classifier that was trained automatically using statistical probability of anatomy maps (SPAMs) (see [10] for more details). ***Estimation of SNR*** was performed for individual CBF and FA maps by first extracting global CBF and FA values for each subject averaged across all WM voxels [11]. For CBF values then individual SNR was defined as the ratio of the temporal mean of the WM and its standard deviation.

Results: A widespread of statistical significant negative correlations between CBF and FA values in WM was observed (Fig. 1.a). Only a cluster with 161 voxels was present after the application of Bonferroni correction [r=-0.92; p<10^{-7}] (Fig. 1.b and Fig. 2.b.). Fiber tracking from this ROI showed fiberbundles within the splenium of the corpus callosum. PVE revealed a total fraction of 12.1 % of WM voxels being prone of WM/GM and WM/CSF contamination that were removed from correlation analysis (Fig. 2.a). The effect of the rigorous PVE treatment showed improved SNR estimation on CBF and on FA values (Fig. 2.a). Significant inverse linear regression was observed for each subject (Fig.2.b).

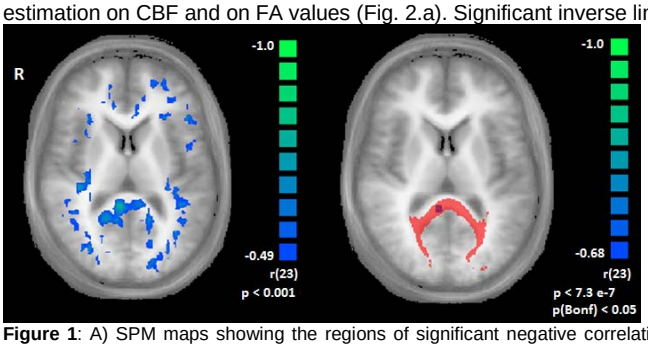

Figure 1: A) SPM maps showing the regions of significant negative correlations between CBF and FA values (z=10). B) Cluster of negative correlation (Bonferroni corrected) (blue-green) used as seed ROI for tractography, showing fiberbundles along the slpenium of the corpus callosum (red).

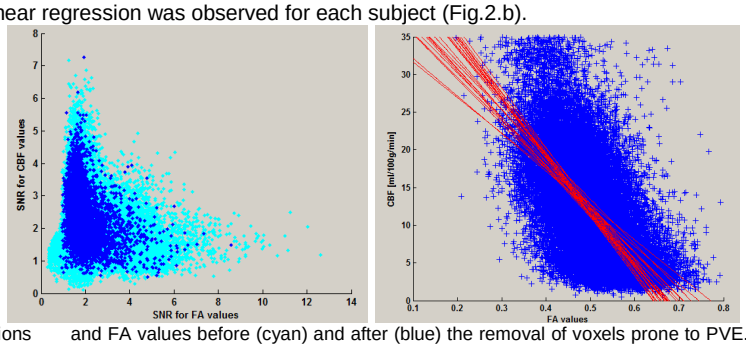

Figure 2: A) Estimation of SNR for CBF and FA values before (cyan) and after (blue) the removal of voxels prone to PVE. B) Scatterplot of CBF and FA values that were extracted from the regions with significant correlation for each subject (from Fig. 1.a). The linear regression for each subjects are shown in red solid lines.

Conclusions: The present study investigates metabolic and microstructural properties within WM in healthy controls and shows a clear significant inverse correlation between CBF and FA values. This finding is in line with previous observations [3]. The most significant negative correlation (Bonferroni corrected) was observed in the splenium of the corpus callosum. This region was described as having thin axonal diameter [12]. The values of CBF within this region are typical CBF values reported for WM [2]. Overall, the findings in the present study confirm previous findings [3], but with a larger sample. The relationship of CBF to FA in the present study cannot rule out the proposed mechanism that links CBF to averaged axonal diameter of the tracts within WM.

References: [1] van Gelderen, P., et al., Magn Reson Med, 2008. **59**(4): p. 788-95. [2] van Osch, M.J., et al., Magn Reson Med, 2009. **62**(1): p. 165-73. [3] Aslan, S., et al., Neuroimage, 2011. **56**(3): p. 1145-53. [4] Deichmann, R., et al., Neuroimage, 2004. **21**(2): p. 757-67. [5] Dai, W., et al., Magn Reson Med, 2008. **60**(6): p. 1488-97. [6] Wu, W.C., et al., Magn Reson Med, 2007. **58**(5): p. 1020-7. [7] Orosz, A., et al., Neuroimage, 2012. **61**(3): p. 599-605. [8] Basser, P.J. et al., J Magn Reson B, 1996. **111**(3): p. 209-19. [9] Basser, P.J., et al., J Magn Reson B, 1994. **103**(3): p. 247-54. [10] Tohka, J., et al., Neuroimage, 2004. **23**(1): p. 84-97. [11] Donahue, M.J., et al., J Cereb Blood Flow Metab, 2009. **29**(11): p. 1856-66. [12] Alexander, D.C., et al., Neuroimage, 2010. **52**(4): p. 1374-89.