Schizophrenia impact on perfusion parameters: a dynamic susceptibility contrast magnetic resonance imaging study.

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INTRODUCTION.

Dynamic Susceptibility Contrast Magnetic Resonance Imaging (DSC-MRI) allows to quantify several perfusion parameters, such as Cerebral Blood Flow (CBF) Volume (CBV), Mean Transit Time (MTT) and Time To Peak (TTP). Cerebral perfusion has been already studied in schizophrenia :abnormalities of CBF [1,2] and CBV [3] have been observed, suggesting that a disruption of the brain microvascular system may occur in subjects affected by schizophrenia [4]. However, cerebral perfusion is also influenced by several physiologic parameters, not necessarily connected to the pathology, such as age [5,6].In this study, we performed a DSC-MRI analysis to study the role of the demographic information on perfusion parameter estimates between patients with schizophrenia and normal control subjects.

MATERIALS AND METHODS.

Data set: 39 patients with schizophrenia (mean age and SD 37±11 years) and 27 normal controls (mean age and SD 45±10 years) were studied. The following demographic variables were collected for each subject: age, length of illness, gender, handedness, smoker/non smoker, alcoholic abuse, drug abuse, school attendance, BPRS negative and positive symptoms. The MRI image acquisition was performed with a gradient echo EPI (on a 1,5T Siemens Magneton Symphony Maestro class, Syngo MR 2002B; TR=2160ms, TE=47ms, FOV=230x230 mm, 5mm slice thickness). The bolus dose was 0.1mmol/Kg of Gd-DTPA, at a rate of 2.5 ml/s in the right antecubital vein. *DSC-MRI quantification:* the CBF maps have been obtained from DSC-MRI images by deconvolution between a manually selected arterial input function, AIF(t) and tissue concentration, C(t). Deconvolution was performed using the block-circulant Singular Value Decomposition as in [7]. The CBV maps were computed using the relation in [8] $CBV=\int C(t)dt/\int AIF(t)dt$. The MTT was computed as the ratio between CBV and CBF. Finally, TTP was computed as the time interval from the tracer arrival time to the moment of the maximum concentration. A Region Of Interest (ROI) was manually drawn on the frontal cortex in each hemisphere and the mean CBF, CBV, MTT and TTP values were evaluated in each ROI. *Statistical Analysis:* the best predictor model was computed in each ROI for each perfusion parameter following a stepwise procedure. All demographic variables were considered as potential predictors. At each step, a linear model including all predictors was computed. Then, the least significant predictor was excluded and a new linear model was computed until all predictors were excluded. Finally, the best predictor model was selected on the basis of the F-statistic and on p-value.

	Left CBF	Right CBF	Right CBV	Right CBV
Model Statistics	F= 2.56 p= 0.06	F= 2.09 p= 0.11	F= 2.75 p= 0.05	F=2.04 p=0.11
Predictor	Estimate ±SD	Estimate ±SD	Estimate ±SD	Estimate ±SD
Intercept	0.29 ±0.05*	0.29 ±0.05*	0.982 ±0.16*	1.002 ± 0.17*
Group	-0.07 ±0.03*	-0.07 ±0.03*	-0.262 ±0.10*	-0.256 ± 0.11*
Age	-0.002 ±0.0010*	-0.002 ±0.0011*	-0.006 ±0.003	-0.006 ± 0.004
Length of illness	0.004 ±0.0014*	0.004 ±0.0015*	0.013 ±0.005*	0.011 ±0.005*

Table 1: Estimate of the predictor model parameters computed for the CBF and CBV. (*:statistical significance of the predictor in the model).

RESULTS.

The models for CBF, CBV, MTT and TTP both in the left and right ROIs were estimated independently from each other, and *No significant models* were obtained for MTT and TTP, whereas the best model for CBF and CBV contains the same predictors (i.e. group, age, length of illness). Table 1 reports the best model statistics and the coefficient value for each predictor. The intercept coefficient represents the amount of the predicted perfusion parameter that it is not predictable using the other predictors. Group is a class-based predictor and its coefficient represent the impact of the secondary class on the predicted perfusion parameter with respect to the primary class. In our study, the primary class for group includes the normal subjects, whereas the secondary class contains the patients. Therefore, a negative value for the group coefficient indicates that the predicted perfusion parameter decreases in the patients with respect to the normal subjects. On the other hand, age and length of illness are numeric predictors, this means that their coefficient must be multiplied by the value of the predictors to compute their impact on the predicted perfusion parameter. Finally, a T-test was performed for each predictor to compare the performance of the predictor model with and without the predictor. Statistical significant predictors (i.e. $p<0.05$) are pointed out in Table 1 with a asterisk next to the coefficient estimate. Noticeably, predictor age appears not to be a significant predictor for CBV, bilaterally (i.e. $p=0.08$ for the left CBV and $p=0.12$ for the right CBV). However, models estimated without the predictor age performed worse than the models containing it.

DISCUSSION.

This study shows that differences (i.e. between-subject variability) in CBF and CBV are partially explained by an age difference between subjects and/or by a difference in the subject health conditions. In particular, negative coefficients for covariate age indicate that CBF decreases when age increases, as already reported in [5,6]. The reduction effects of age on CBV, even if present, do not overpass the statistical significance. Moreover, the covariate group presents negative coefficients in the models, thus suggesting that a perfusion and a blood volume decrease is present in patients with respect to control subjects. This agrees with the recent theories, which include a perfusion disease as a possible cause of schizophrenia. The positive model coefficients for the length of illness covariate suggest a recovery from the pathological perfusion deficit as the length of the illness increases. Particular attention is necessary to comment this finding and different hypotheses can explain it. For example, the positive coefficients for length of illness covariate may indicate that the CBF and CBV age-induced decrease is less evident in patients than in control subjects. Alternatively, the pharmacological treatment may be involved. Of course, an in-depth study is necessary to investigate the drug effects and verify this theory. However, length of illness coefficients are very small if compared to the group ones, thus the recovery in perfusion parameters is very small if compared to the decrease due to the pathology.

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