Increased resting state connectivity between left and right hemispheres with increasing age

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Introduction: There has recently been much interest in using fMRI to explore the neural bases of cognitive decline in older age in order to better understand the functional and structural changes that accompany it. In particular, an increase in bilateral activation has been seen with increasing age[2] with various theories being posited as to why this occurs[3-4]. In this study we aim to investigate in which areas the BOLD signal relating to a cognitive Stroop task is significantly correlated with age, and whether resting-state connectivity is altered between these key regions. We hypothesize that functional connectivity will increase between bilateral regions as they are recruited to the task, despite known structural deficits[5].

Methods: Data acquisition: After obtaining informed consent, 40 healthy volunteers (age 20 – 76, 20 male and 20 female) took part in this experiment (approved by the University of Liverpool research ethics committee). Scanning was carried out on a 3 T Siemens Trio system using a QUIPSSII Arterial Spin Labeling (ASL) sequence with gradient echo EPI signal collection. The ASL data formed part of another study; however the underlying gradient echo EPI images, with BOLD signal contrast, were used for the purpose of this study. Acquisition parameters were as follows: TR 2.13s, TI_1 0.7s, TI_2 1.4s, TE 25ms. A total of 12 slices (3.5mm thickness and 3.5 mm isotropic resolution) were acquired covering the parietal, motor and frontal cortices, in addition to a 1mm isotropic MPRAGE structural image.

Task: The task used for this experiment was a colour-word Stroop task. Participants were presented with one word (in white text) at the bottom of the screen and were asked to determine whether the *meaning* of this word matched the text colour of the word above it. Stimuli were self-paced with a minimum time of 2 s between stimuli. Responses were measured using a two-button response box, each button being assigned to a particular response (match/non-match). A run time of 8 mins consisted of 8 active blocks (30 s each) interspersed with 30 s fixation cross periods to act as a baseline measure. The mean accuracy and response time to the Stroop stimuli were calculated for each subject. In addition, an 11 minute scan was collected during periods of breathing either air or oxygen (2 periods of 3 minutes), which was required for a separate study. Resting state data was extracted from the 4 periods of 2 minutes, during which equilibrium was reached.

Image analysis: Analysis was performed in BrainVoyager. Preprocessing included slice-time correction, volume realignment, coregistration to the T_1-weighted image and transformation into Talaraich space along with spatial and temporal smoothing. A multi-subject General Linear Model (GLM) was used to determine the regions activated by the Stroop paradigm, using a threshold of $p<0.05$ (corrected for false detection rate). Within each region the fitted beta-weights from the GLM, which relate to the BOLD amplitude, were recorded. Multiple regression was used to determine if age, accuracy or response time (to the Stroop task) were significant predictors of BOLD signal.

For analysis of resting state connectivity, data was pre-processed in a similar way but without any temporal smoothing. Partial correlation was performed on the time course data between bilateral regions, taking into account signal from both a white matter region and a ventricular region, in order to remove spurious global effects for example due to movement[6]. Correlation coefficients from each 2 minute period of rest were averaged and multiple regression was used to determine where age, accuracy or response time (to the Stroop task) were significant predictors of the correlation coefficient.

Results and Discussion: Eleven regions of activation were identified, including bilateral inferior (BA40)/superior (BA7) parietal lobule and middle frontal gyrus (MFG [BA9]), supporting earlier findings[1]. Three of these regions showed a negative BOLD signal, in the anterior cingulate (BA32), precuneus (PC [BA31]) and medial frontal gyrus (MeFG [BA9]). The BOLD response was found to significantly increase with age in the right MFG (Fig 1a), causing a reduction in laterality (as confirmed by a measure of laterality index), concurring with other studies [2]. A significant reduction in the BOLD response with increased task accuracy was also found in the right MFG (Fig 1b), suggesting that increased BOLD with age may not necessarily be benefitting task performance. Two regions (PC & MeFG) of negative BOLD showed significantly more negative signal with increased task accuracy, suggesting that these regions need to be inhibited for accurate task performance. When considering the group of older adults (age 40+), functional connectivity between bilateral MFG was found to increase with both age and accuracy (Fig.1c-d), which suggests that increased connectivity may improve performance. Importantly, there was no significant relationship between connectivity measures and the BOLD response, suggesting that increased connectivity may reflect a separate process by which task performance can be maintained with increasing age. This research demonstrates age-related differences in BOLD response during a Stroop task, building upon the findings of previous studies, and suggests that alterations in functional connectivity with age may play an important part in performance.

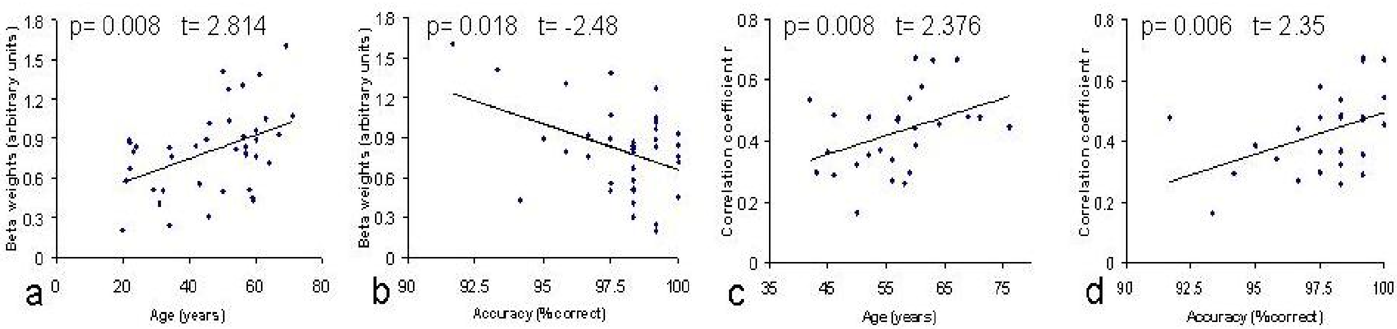

Fig. 1. MR scatterplots showing correlations between variables from right MFG. Correlations between age (a) and accuracy (b) against beta weights. Correlations between age (c) and accuracy (d) against connectivity correlation coefficients from subjects aged 40+ between L/R MFG.

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