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 with various theories being posited as to why this occurs. 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.

**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 Labelling (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, TI1 0.7s, TI2 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 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 task) were recorded. Multiple regression was used to determine if age, accuracy or response time (to the Stroop task) were significant predictors of BOLD signal.

**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. 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), concluding with other studies. 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 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.

**References:**