Analysis of cerebral flow in patients with late life depression

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Abstract

There is growing evidence that cerebrovascular disease or risk factors may lead to late-life depression. We have investigated the relationship between response to drug treatment and vascular compliance in elderly patients with depression by analyzing flow patterns in cerebral vessels and aqueductal CSF using phase contrast magnetic resonance imaging. We find evidence for reduced vessel compliance in the more treatment-resistant patients. This lends weight to the hypothesis of a distinct subtype of depression in the elderly which has a cerebrovascular cause and different treatment requirements.

Introduction

‘Vascular depression’ [1] is characterized by MRI T2-weighted subcortical lesions [2], a late onset of first depressive episode, a reduced heritability and evidence of vascular disease or risk factors. Simpson et al. [3] report a correlation between poor response to antidepressant therapy and the presence of T2-weighted lesions in a group of elderly patients with depression. In this study we have looked for evidence of changes in vascular compliance in patients with late-life depression by analyzing flow patterns in cerebral vessels. The study forms part of a larger MRI investigation of both elderly patients with depression, who either respond (‘simple’ group) or do not respond (‘complex’ group) to conventional antidepressant drug therapy, and normal elderly volunteers (‘control’ group). Our aim has been to test the hypothesis that the patients who do not respond to conventional antidepressants have altered vessel compliance which may indicate that they are suffering from depression resulting from vascular mechanisms.

Methods

MR velocity images have been produced using a phase contrast technique, cardiac gated at 15 time points in the cardiac cycle. Blood flow into the brain has been measured by taking a single-slice image at a position perpendicular to the internal carotid and basilar arteries. CSF flow has been measured in a slice perpendicular to the cerebral aqueduct (fig 1).

Due to the relatively small size of the aqueduct we see significant point spread function effects on the flow profile. To obtain a reliable estimate of the flow at each point in the cardiac cycle we assume laminar flow and fit the flow profile at each time point to an elliptical paraboloid convolved with a sinc function. Using this technique also has the advantage that user input is minimized since accurate segmentation of the aqueduct is not required. From the results of the fit we extract the peak velocity, v_p, and area of the aqueduct, A and calculate the flow (in µL/S). The measured flow profile in the internal carotid arteries is distorted due to PSF blurring from neighbouring small vessels (see fig 1). Fitting the flow was thus impossible in this case. However, the small vessels have low absolute signal and so do not affect the modulus image which we use to define a ROI. The signal intensity from the phase difference image is averaged across this ROI and multiplied by the area to obtain the flow.

Statistical Analysis

In order to characterize the flow curves, we have extracted a number of parameters using a spline interpolation between data points and an assumption of periodicity. These include: the width of the systolic CSF flow peak in the aqueduct; the stroke volume (defined as the average of the systolic and diastolic CSF flow volumes); the width of the systolic peak for blood flow in the internal carotid and the arterial-to-aqueduct delay (defined as the time between the centre of the of the arterial peak and the centre of the aqueduct peak).

We expect a reduced vessel compliance (reduced damping) to lead to an earlier, narrower systolic CSF flow peak and a larger CSF stroke volume for the same input blood flow. The mean measured stroke volume is higher in the complex group (85±43µL) compared to the control (59±28µL) and simple (66±29µL) but this difference does not reach statistical significance (P=0.07 for the complex vs. the control). However, the diastolic CSF flow volume is significantly larger in the complex group compared to the controls (P=0.01). The actual net flow corresponding to the production of CSF is small compared to the measurement errors so we expect the systolic flow to be approximately equal to the diastolic flow over a cardiac cycle. For the control group this appears to be generally the case but for the complex patients the measured diastolic flow is greater than that during systole. The diastolic flow cannot in reality be greater than the systolic flow but at this time we do not have an explanation for this observation.

The time period of the systolic CSF flow is plotted against the arterial-to-aqueduct delay time in figure 2b. The CSF systolic peak is significantly narrower in the complex group as compared to the controls (P=0.004). This is not due to differences in the input blood flow as there is no difference in the arterial systolic peak width between the three groups and we find no correlation between the arterial and aqueduct systolic widths. The arterial-to-aqueduct delay time is 20% shorter in the complex group as compared to the controls (P=0.004). Although this difference does not quite reach significance, the trend is consistent. The results for the simple group lie between the control and complex groups and are not significantly different from either.

Discussion

CSF pulsations are driven by the pulsatile flow of blood entering the brain and are damped by compliance of the vessels and surrounding brain tissue. Both the cerebral aqueduct systolic width and the arterial-to-aqueduct delay are related to the damping of the pulsatility of the input flow and are therefore indicators of compliance. The decrease in both these measures in the complex group compared to the control group is suggestive of a decrease in this damping mechanism i.e. it may be evidence of the altered compliance that we expect with vascular disease.

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References