A Transcranial Ultrasound and Diffusion Tensor Magnetic Resonance Imaging Study of Brainstem Structural Abnormalities in Major Depressive Illness

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Introduction

It has long been recognised that virtually all empirically derived antidepressants have a common action of increasing the levels of monoamines such as serotonin and noradrenaline. The nuclei of cells synthesising these monoamines are located in the brainstem, and projection tracts such as the medial forebrain bundle reach virtually all other brain areas. Over the past decade, various studies of unipolar depressive illness have reported reduced echogenicity of the brainstem midline in unipolar depressed patients using transcranial ultrasound [1,2]. This may be consistent with a disruption of white matter tracts, including the medial forebrain bundle, and it has been suggested that the effects of such a disruption could be reversed by antidepressants. In this study we attempted to replicate these findings with 15 unipolar depressed patients and 15 controls using transcranial ultrasound imaging, and diffusion tensor magnetic resonance imaging (DT-MRI).

Subjects

Fifteen patients satisfying the DSM IV criteria for major depressive disorder, and 15 control subjects matched for age, sex and NART were recruited. All patients had an unequivocal diagnosis of recurrent unipolar major depressive illness, and were receiving a variety of medications at doses similar to that described in a previous study [1]. Medication remained at a constant level for at least two weeks prior to scanning. One subject was unable to tolerate the scanning resulting in data from 15 patients and 14 controls.

Methods

Ultrasound images were obtained from subjects using a phased array system equipped with a 2 MHz transducer. Images of the midbrain with red nucleus and rostral pontine brainstem were obtained in an axial scanning plane through a preauricular acoustic bone window [1,2]. Acquisition was standardised such that the contralateral skull surface was just visible resulting in a typical penetration depth of 14 cm. The dynamic range was 28 dB with consequent high tissue contrast. Typically, around 7 images were recorded from each subject which always included views obtained from both head sides. The objective was to record the clearest images of the midline echo from the lower midbrain. For analysis, the anonymized stored images were rated according to the semi-quantitative method described previously [1,3].

All MR imaging data were obtained using a GE Signa LX 1.5 T. Each subject underwent an axial T_2-weighted fast spin-echo (FSE) sequence to identify silent brain pathology and a T_1-weighted volume scan. This was followed by a DT-MRI protocol specifically designed to image the brainstem. Statistical pre-processing and analysis of the DT-MR images was done using SPM99. For pre-processing, T_2-weighted EP images were spatially normalised to the SPM template using an affine transformation. The T_2-weighted EP image normalisation parameters were then applied to the FA images, which were smoothed with an 8 mm isotropic gaussian filter. The null hypothesis of no difference between patient and control groups was finally tested with an independent two group *t*-test.

Results

A power analysis of the ultrasound investigation predicted that 15 subjects should provide virtual certainty of rejecting the null hypothesis. However, no difference in echogenicity of the brainstem midline of unipolar depressed patients was found. A possible trend (Cohen's d = 0.39) in the direction of previous studies was found. Whilst the echogenicity of the brainstem midline of the control group was found to be similar to previous reports, there was no reduction in the patient group. Additionally, no structural abnormality of the brainstem was identified using DT-MRI.

Conclusion

While these data do not replicate the findings of previous studies reporting a significant reduction in the echogenicity of the brainstem midline in unipolar depressed patients, the ultrasound investigation indicated that there may be a trend in this direction. Given the importance of identifying the causes of depressive illness, it is important that other groups attempt similar studies.

References

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