Interhemispheric Visual Integration in Alzheimer's Disease: Decrease of FMRI BOLD Response in VP/V4 Areas

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BACKGROUND

Early Alzheimer's disease (AD) mainly affects learning and memory and the majority of AD research has focused on these deficits but several other cognitive skills are impaired with the development of the disease. Verbal skills worsen next, then orientation and visuo-spatial skills are affected. Thus, in newly diagnosed AD patients we planned to investigate higher-order visual areas to detect their malfunction before the appearance of clinical signs. We choose a paradigm that addresses visual integration functions that(as we have shown in a previous fMRI experiment (Knyazeva 2006)) are associated with activation (BOLD fMRI) in areas of the basal occipito-temporal cortex. This cortex is involved in the higher order cognitive functions that suffer in AD.

METHODS

Fifteen patients (mean age 68.8 yrs, CDR:0.5-1, FAST:3-4) and 15 age-matched controls were successfully scanned in a 3 Tesla Philips scanner. Functional MRI images were acquired EPI gradient echo T2* weighted sequence (FA 90, TE 30, matrix size 128X128, FoV 256, 16 slices, 5mm thick, acquisition time 1.1 s) with a TR = 3s. Subjects viewed bilateral sinusoidal black-and-white gratings with a spatial frequency of 0.5Hz and drifting with a temporal frequency of 2 Hz. The stimuli either obeyed Gestalt grouping rules (iso-oriented collinear gratings, IG) or violated them (orthogonally-oriented (OG)). The stimulus conditions were alternated with background in a balanced-randomized order 6 times 15 s each. Preprocessing, single subject analysis and group statistics were conducted on SPM5. All group maps were thresholded for peak height at $p < 0.01$ and at $k > 30$ for spatial extent.

RESULTS

In contrast to differently oriented and moving OG, IG stimulus consists of identical halves fusible into a single image. The fMRI experiments showed that both stimulus conditions (IG or OG) were associated with extensive activation of striate and extrastriate areas compared to the background (equiluminant gray screen) in both groups.

Our previous experiments showed that, in adults, bilateral IG compared to OG, induced BOLD increase within VP/V4 areas. This increase reflects an interhemispheric integration process (Knyazeva et al. 2006a,b). In this study we replicated these results in an older control group showing that there are no main age-related changes in activation for this particular paradigm. In controls, the IG vs. OG contrasts revealed higher BOLD signal in ventral extrastriate cortex and centered bilaterally on the lingual gyrus (Fig 1 top row).

In AD patients, the same contrast showed the involvement of the same cortical regions but characterized by a reduction of their activation level (Fig 1 bottom row). In particular, the activation in the right lingual gyrus showed a significant decrease both in intensity and in extent ($P < 0.01$).

CONCLUSION

The interhemispheric integration has already been shown as highly dependent from the myelination level of cortico-cortical connection. As the BOLD activation increases with the myelination level during development (Fornari, 2007), it can be reduced by neurodegenerative diseases affecting the white matter integrity.

Although AD patients seem to have unaffected activations for early visual processing and they do not show deficits for basic visual functions in the early stages of their disease, they show already significant changes in the activity of the extrastriate cortex during specific higher-level processing. This is supported by the substantial decrease of BOLD activation in VP/V4 areas involved in the interhemispheric integration process.

We can conclude that specific activation of areas involved in interhemispheric visual integration seems to be reduced at the early stages of AD and we can suggest that this decrease is probably due to an already decreased myelination of cortico-cortical connections involved in spatial integration.
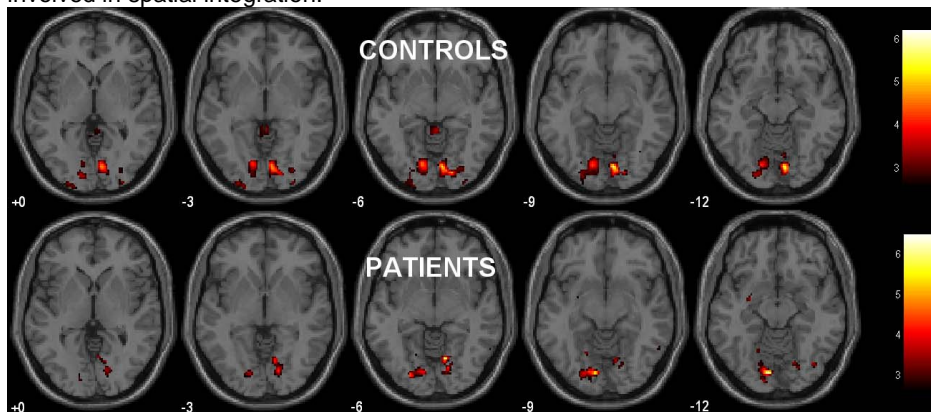

Fig.1 IG vs OG BOLD response ($P < 0.01$) in controls (top row) and AD patients (bottom row). Hot-scale represents T-values.

References:
Fornari E et al. 2007 Myelination shapes functional activity in the developing brain. Neuroimage 38, 511-518
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