



<b>Title</b>	<b>The effect of normal and abnormal ageing on prospective memory showed increased cognitive conflict: a functional MRI study</b>
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## The effect of normal and abnormal ageing on prospective memory showed increased cognitive conflict: a functional MRI study

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**Introduction:** Prospective memory (PM) is memory for planned intention, which needs to be executed appropriately in the future. PM task is usually embedded in ongoing activities. The neural correlates of PM have not been elucidated. To date, no functional imaging study has been conducted to examine the relevant functional change of PM during the processes of ageing and dementia.

**Methods:** Twelve patients with mild AD, 12 age-matched old adults, and 11 young adults were recruited. A laboratory event-based PM paradigm was revised and applied to this study. It was block-designed. Basically, there were three conditions conducted sequentially: baseline ongoing condition, no-go condition, and PM condition. Each condition had four alternations of 42s activation and 18s rest, which lasted for 4 minutes. The fMRI study was conducted with a 3T Philips MRI scanner in MRI centre of the University of Hong Kong. Three conditions were scanned separately. TR=2000 ms, TE=40 ms, FOV: 230×230×128 mm, temporal resolution: 1.8×1.8×4 mm, flip angle: 90°, slice thickness=4 mm. The data were processed by standard procedure of statistic parametric mapping (SPM8).

**Results:** Behavioural data showed that accuracy of three groups in three conditions were all higher than 90%. fMRI results showed that the activation of brain during task performance were larger in old adults and AD patients than in the young adults, including supplementary motor area, precentral and postcentral gyrus, inferior parietal lobe. PM task activates a similar network of bilateral, especially left inferior frontal lobe, angular gyrus and inferior temporal gyrus among three groups.

**Conclusion:** There is obvious compensation of the old adults and AD patients when performing PM task, although PM task activates a similar brain network for action observation and execution among the groups. Interestingly, PM-specific activations in frontal lobe of young, old adults and patients with AD demonstrate a rostral-caudal activation. This may imply increasing cognitive conflict among the three groups.

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## Fibroblast growth factor 21 promotes glucose uptake through transactivation of glucose transporter-1 gene in adipocytes

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**Introduction:** Fibroblast growth factor-21 (FGF-21) is a liver-secreted hormone with multiple beneficial effects on obesity-related disorders. Recent studies indicated that FGF-21 induces glucose uptake through a pathway independent of insulin in adipocytes. However, the molecular mechanism underlying this FGF-21 action remains elusive. Our study aimed to investigate the signalling transduction pathway by which FGF-21 upregulates glucose transporter (GLUT)1 in adipocyte.

**Method:** 3T3-L1 adipocytes were stimulated with recombinant FGF-21 and the mRNA level of GLUT1 was quantified by real-time PCR. The activity of the protein kinases Erk1/2 was assessed by Western blotting against phospho-Erk1/2. The transcriptional activity of the GLUT1 promoter was measured by the luciferase reporter assay and chromatin immunoprecipitation (ChIP) was performed to evaluate the association of the transcription factors with the promoter. Suppression of Erk1/2 was achieved by its pharmacological inhibitor PD98059.

**Results:** FGF-21 induced GLUT1 expression through transcriptional activation. This effect was mediated by Erk1/2, which promoted the recruitment of Ets-like protein 1 (Elk-1) and serum response factor (SRF) to the highly conserved E-Twenty Six (ETS) and Serum Response Element (SRE) binding motifs located within the distal region of the GLUT1 promoter. Furthermore, FGF-21-evoked phosphorylation of Erk1/2, transcriptional activation of the GLUT1 gene and induction of glucose uptake were markedly attenuated in the diet-induced obese mice.

**Conclusion:** FGF-21 induces GLUT1 expression through Erk1/2, which in turn activates SRE/ETS signalling cascade to enhance glucose uptake in adipocytes. The present findings suggest that FGF-21 signalling pathway may represent an appealing therapeutic target for the treatment of obesity-related metabolic diseases.

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