Background: Patients with Alzheimer’s Disease (AD) show remarkably intact very-long-term memory. However, they seem to base their remote memories on factual knowledge (i.e. semantic memory) and less on an actual re-experience of the episode. This shift is probably related to structural decline of the hippocampus, and leads to the hypothesis that AD patients will attempt to compensate by activating for instance the left inferior frontal gyrus (LIFG; semantic processing) and the ventromedial prefrontal cortex (vmPFC; interacts with hippocampus during consolidation). Methods: Using fMRI, we investigated 22 healthy elderly control subjects (aged 69.6 ± 8.6, MMSE 29.0 ± 1.1) and 21 patients with early stage probable AD (aged 72.4 ± 7.1, MMSE 25.1 ± 3.2), according to the research criteria by Dubois (Lancet Neurology 2007). Matched Autobiographical and Semantic (world knowledge) statements (true:false = 3:1) were visually presented to the subjects, who indicated if the statements were true (button press). Autobiographical statements were derived from an interview occurring >6 weeks before scanning. Memories were transcribed and scored, according to the Autobiographical Interview Scoring Manual (Levine et al, Psychology and Aging 2002). Results: While reported memories were of similar length, AD patients reported less episodic details (F(1,41) = 17.70, P<0.001), and more semantic details than healthy elderly (F(1,41) = 13.15, P<0.005). During fMRI, performance on the Autobiographical (F(1,41) = 15.89, P < 0.001) and the Semantic (F(1,41) = 21.88, P < 0.001) condition was lower for the AD patients. All subjects activate a network involved in autobiographical retrieval during fMRI, when we contrast autobiographical versus semantic memory (A > S). Controlling the data for performance, AD patients showed enhanced activity in LIFG, vmPFC, right precuneus and left lingual gyrus compared to healthy elderly. Also, AD patients had smaller hippocampi (t(40) = 2.02, P < 0.05). Moreover, activation of LIFG and vmPFC was significantly negatively correlated with hippocampal volume in the AD patients only (r = -0.40, P < 0.05 and r = -0.37, P < 0.05), indicating the linking function of the hippocampus is moved to the vmPFC (like in consolidation), and patients rely more on semantic processing. Conclusions: AD patients attempt to compensate for their hippocampal damage/ autobiographical memory impairment by relying more on the vmPFC as a linking node and by increasing semantic processing.