Memory Impairment and Awareness of Memory Deficits in Early-Stage Alzheimer’s Disease

MASARU MIMURA

Department of Neuropsychiatry, Showa University School of Medicine, Tokyo

In addition to their memory impairment, individuals with Alzheimer’s disease (AD) often suffer from deficits in self-awareness. Awareness of memory deficits or metamemory is a multifaceted function, comprising on-line self-monitoring, generalized self-beliefs of memory efficacy, and generalized knowledge about memory functions. Awareness of memory problems in early-stage AD is a matter of clinical importance from a humanistic point of view, because higher levels of awareness may be associated with better future outcomes. Current methods of measuring awareness tend to fall into two categories, i.e., to introduce a questionnaire assessing patient/caregiver discrepancies; or to ask a patient to prospectively predict or retrospectively postdict their own memory performances. Characteristics of each measure as well as relationship between the two measures were discussed.

For the performance prediction/postdiction paradigm, we used recognition memory of auditory verbal learning tests and awareness of memory deficits were examined in 24 individuals with early-stage AD. In addition to their significantly impaired recognition memory, individuals with AD displayed underawareness of memory deficits even at this early stage. They retrospectively overestimated memory performance after actual performance, but appeared to benefit from feedback and displayed intact on-line awareness of memory dysfunction, leading to normal prediction of the second session. However, individuals with AD again failed to retrospectively incorporate incidents of memory failure into generalized self-belief systems. Brain/behavior correlational analyses suggest that the prefrontal cortex and posterior dorsomedial regions including the precuneus may be involved in self-awareness.

Keywords: awareness; dementia; SPECT; frontal lobe; precuneus.

© 2008 Tohoku University Medical Press
about cognitive functions (Metcalfe and Shimamura 1994). Their unawareness may vary across domains (Kotler-Cope and Camp 1995). Individuals with AD may deny or underestimate deficits in memory (for review, see Kasniak and Zak 1996), functional ability (Green et al. 1993; Vasterling et al. 1995), or mood (Vasterling et al. 1995). Amongst such wide range of various cognitive domains, unawareness of memory is most frequently observed in AD individuals and also is most rigorously investigated by clinical researchers who are interested in humanistic aspects of dementia.

Awareness of memory problems in individuals with early-stage AD is a matter of clinical importance, because higher levels of awareness may be associated with better future outcomes. For example, Tabert et al. (2002) found that in people with mild cognitive impairment (MCI) (Petersen 2004), as an intervening or transitional stage between normal aging and early dementia, lack of awareness of functional deficits was predictive of a future diagnosis of AD. These findings have led to increasing empirical attention devoted to understanding awareness of deficit in early-stage AD, to facilitate prediction of long-term outcomes.

**Questionnaire discrepancy method**

Various measures have been devised and refined to evaluate awareness of memory deficit. Current methods of measuring awareness tend to fall into two categories: to introduce a questionnaire assessing patient/caregiver discrepancies; or to ask a patient to prospectively predict or retrospectively postdict their own memory performances. In the questionnaire discrepancy method, patients and caregivers answer questions about the memory function of the patient. Using this questionnaire discrepancy method, patients with AD or MCI often underestimate their memory dysfunction as compared with caregiver reports (Reisberg et al. 1985; McGlynn and Kaszniak 1991; Albert et al. 1999; Vogel et al. 2004).

Correa et al. (1996) proposed that AD individuals’ underestimation of their own memory deficits observed in the questionnaire discrepancy experiment depends on generalized self-efficacy beliefs. However, caution should be paid for interpretation of the results because the questionnaire discrepancy method relies on caregiver judgments as gold standards. Assessment of patients’ memory activities could be biased by any problems on caregivers’ side including their personality, depression and anxiety, physical status and patient-caregiver relationships.

**Prediction/postdiction method**

In the prediction/postdiction method, patients estimate their own performance before or after actually performing a memory task provided by the experimenter. More specifically, participants estimate the number of errors they would make or had made before and after performing a recognition task. Such performance prediction/postdiction requires integrated on-line processes to monitor ongoing memory performance and to use feedback. Deficit of awareness is indexed by differences between self-estimation and actual own performance, usually as overestimation. Although most studies using the prediction/postdiction method focused on the patients’ own memory performances, a few studies also investigated in AD individuals’ estimation of other person’s memory activities. AD individuals’ overestimation in prediction/postdiction may not be limited to their own performances. Duke et al. (2002) found that individuals with AD overestimated not only their own memory performances, but also those of spouses and of fictional, memory-disordered individuals observed on videotape.

The medial temporal lobe structures including the hippocampus and parahippocampus are known to be essential for the formation of recognition memory; that is, the capacity to judge a recently encountered item as familiar. Previous studies concerning recognition memory in AD have also addressed the aspect of prediction on memory monitoring. For example, Moulin et al. (2000) examined the accuracy of judgment-of-learning (JOL), in which predictions are made about the likelihood of subsequent recollection of recently studied items in AD. The results suggest that AD individuals experience difficulty predict-
ing the likelihood of remembering studied items. Similarly, Souchay et al. (2002) assessed another metacognitive index, feeling-of-knowing (FOK), in which predictions are made about the likelihood of subsequent recognition of non-recalled information. Compared to healthy elderly adults, individuals with AD exhibit impaired accuracy of FOK. Souchay et al. (2002) argued that episodic memory may represent a more important factor than executive function in explaining accuracy of FOK in AD.

Since such previous studies regarding JOL or FOK have only addressed the predictive aspects of memory monitoring, we investigated both predictive and retrospective monitoring within the same AD individuals (Mimura and Yano 2006). We explored awareness of memory deficits in 24 individuals with early-stage AD (mean age, 75.8 ± 7.6 years; mean Mini-Mental State Examination [MMSE] score, 22.3 ± 3.8; mean duration of illness, 2.7 ± 2.1 years) using a prediction-postdiction method in the recognition paradigm. The study was accepted by the Ethics Committee of Showa University School of Medicine and the overall protocol is illustrated in Fig. 1. The Auditory Verbal Learning Test (AVLT) was used to examine recognition, with participants making predictions and postdictions of performance in the AVLT. Each participant was given a 15-item list of words to study, then received a recognition trial with 15 distractors. Following completion of the first session, participants were instructed to provide a retrospective estimation (i.e., postdiction, post 1) of task performance. Feedback of actual performance was subsequently given by the experimenter (actual 1), and participants were then instructed to provide a prospective prediction for the second session (pre 2). After the second session was over, participants were again instructed to provide a subjective postdiction (post 2). Finally, feedback of actual performance in the second session was given by the experimenter (actual 2).

Individuals with AD displayed impaired recognition memory of auditory verbal learning tests. In addition, underawareness of memory deficits was also marked even at this early stage. In contrast to healthy control participants, postdiction of Session 1 in AD did not reflect their actual performance (Fig. 2). However, AD participants’ prediction of Session 2 appeared to be based on the immediately preceding feedback from Session 1 actual performance, as with healthy participants (Fig. 3). In fact, AD participants displayed better prediction actual performance for Session 2 than healthy control participants. Nonetheless, AD

![Fig. 1. Outline of the experiment protocol to examine recognition memory and awareness of memory (cited from Mimura and Yano, 2006 with permission). Two sessions of recognition of the Auditory Verbal Learning Test were given to a participant. For postdiction sessions 1 and 2, participants were asked to guess the number of omission and commission errors. Following questions and answers for postdiction, feedback regarding actual performance was given for omission and commission errors. A question regarding prediction for the second session was subsequently given in the same fashion.](image-url)
participants’ postdiction of Session 2 was again unrelated to actual performance in Session 2. Postdiction of Session 2 was highly correlated with the feedback provided for Session 1 in healthy participants, but not in AD participants. The findings of awareness deficits in AD are summarized in Table 1. Individuals with AD retrospectively overestimated their memory performance after actual performance, but appeared to benefit from feedback and displayed intact on-line awareness of memory dysfunction, leading to normal prediction of the second session. However, such on-line awareness was transient, and feedback given by the experimenter did not improve AD participants’ postdiction in Session 2.

Our study demonstrated underawareness of deficits in individuals with AD, using the performance prediction / postdiction paradigm. As was
Awareness of Memory Deficits in Alzheimer’s Disease

Table 1. Summary of awareness in individuals with Alzheimer’s disease (AD)

- Retrospectively overestimate their performance of immediately-past memory events.
- Outside feedback is effective and display intact on-line awareness of their memory dysfunction, leading to normal prediction of the near-future events.
- However, such on-line awareness is transient.
- Feedback given from outside do not improve their postdiction for future events.

discussed by Kaszniak and Zak (1996), this paradigm involves on-line monitoring in addition to generalized self-beliefs. The impaired awareness of memory deficits among participants with AD was indicated by a remarkably optimistic postdiction for recognition performance, even at the early stage of AD. This tendency to overestimate performance may be related to inflated, generalized beliefs concerning the current state of their memory ability in individuals with AD. However, participants with AD appeared to benefit from immediate feedback and displayed intact immediate awareness of memory deficits, resulting in normal predictive estimation. Some preserved on-line ability to assess memory functioning was apparent. However, incidents of memory failure were not successfully incorporated into generalized self-belief systems.

Agnew and Morris (1998) proposed a model to explain underawareness in AD, and described two patterns of impairment. According to their model, incoming information concerning an event of memory failure enters the short-term memory, then proceeds to long-term memory (Fig. 4). The event is then compared, using mnemonic comparators within the central executive system, with the semantic personal knowledge base (PKB). In cases of mismatch detected by the comparator, the PKB is updated, and information from the PKB is directed back into conscious awareness. In one pattern of deficit, patients with AD were able to perceive and detect memory failure in an online fashion, using links between episodic memory and conscious awareness, but PKBs remained impaired. For the second pattern of deficit, patients with AD and impaired executive functioning or on-line monitoring display executive anosognosic deficits, because these individuals are unable to perceive incidents of memory failure due to faulty memory comparators. The degenerative process of AD affects not only memory ability, but also other higher cortical functions, including executive processes, thus making both types of unawareness plausible in AD. Since participants with AD in the present study failed to

![Fig. 4. Schematic model to explain underawareness proposed by Agnew and Morris (1998). Two patterns of deficit may occur in patients with Alzheimer’s disease (AD); In pattern (1), patients with AD are able to perceive and detect memory failure in an online fashion, but personal knowledge base remains impaired. In pattern (2), patients with AD are impaired in executive functioning or on-line monitoring, thereby showing faulty memory comparators.](image-url)
retrospectively estimate memory failure, but prospectively estimated memory based on immediate feedback, the current results partially support the first pattern of deficit in AD.

**Relation between questionnaire discrepancy and prediction/postdiction**

Although individuals with AD may display underawareness in both paradigms, previous studies have documented modest correlations between questionnaire discrepancies and prediction/postdiction. Between-method correlations have been reported to be small but positive. Accordingly, the questionnaire discrepancy and performance prediction/postdiction are hypothesized to emphasize different aspects of self-awareness (Correa et al. 1996; Duke et al. 2002). These two methods seem most likely to rely on various overlapping cognitive processes involved in awareness, but to differing extents. As was mentioned earlier, the questionnaire discrepancy method appears to be dependent on generalized memory self-efficacy beliefs, whereas the prediction/postdiction method requires monitoring of ongoing memory performance in addition to self-efficacy beliefs and memory knowledge (Kaszniak and Zak 1996).

Only a few studies have incorporated both questionnaire discrepancy and prediction/postdiction methods of examining underawareness in the same AD individuals. However, prior research by Kaszniak and colleagues (McGlynn and Kaszniak 1991; Kaszniak and Zak 1996) has demonstrated that different components of self-awareness, particularly generalized self-efficacy beliefs versus on-line monitoring ability, contribute to observations of underawareness in AD.

Recently, Clare and colleague (Clare et al. 2002, 2004) developed two new scales for evaluating awareness in individuals with AD, i.e., the Memory Awareness Rating Scale (MARS) for those with mild impairment, and MARS-Adjusted (MARSA) (Hardy et al. 2006) for those with more advanced impairments. Both MARS and MARSA were devised to include two measures of the questionnaire discrepancy and the performance prediction/postdiction.

**Toward a neural substrate for awareness**

The neural substrate for self-awareness include a variety of brain regions, and are, of course, difficult to determine. Since self-monitoring is supposed to be deeply dependent on the prefrontal lobes, previous neuropsychological and neuroimaging studies have naturally found that underawareness is associated with frontal dysfunction (Mangone et al. 1991; Reed et al. 1993; Lopez et al. 1994; Michon et al. 1994; Starkstein et al. 1995, 1997; Ott et al. 1996). Specifically, the prediction/postdictions method is thought to require on-line processes dependent on frontal lobe integrity (Correa et al. 1996). Based on associations found between underawareness of deficit and deficient frontal lobe functioning, individuals with frontal impairment would be unable to monitor their ongoing memory performances and therefore would fail to significantly adjust estimations of self-performance from prediction to postdiction trials. In addition, similar to findings observed in focal brain damaged patients with anosognosia, dysfunctions in the right posterior brain regions have also been implicated in unawareness in AD (Mangone et al. 1991; Ott et al. 1996).

We utilized single photon emission computed tomography (SPECT) to investigate whether regional cerebral blood flow (rCBF) correlated with participant processing of awareness of memory deficits. In our above mentioned study of prediction/postdiction paradigm (Mimura and Yano 2006), we tried to identify the brain regions for self-awareness that were dissociable from those areas responsible for recognition memory itself. Our results on brain/behavior correlational analyses between awareness indices and voxel-based rCBF suggest that both the prefrontal cortex and the posterior dorsomedial regions including the precuneus may be involved in self-awareness. Fig. 5 shows areas displaying positive correlations with comparative awareness indices in AD [(hit – false alarm) \_post \_1 \_ - \_ (hit – false alarm) \_actual \_1]. Significant clusters were obtained with peak Talairach coordinates at the medial aspect of the frontal lobe, the inferior frontal gyrus and the
Awareness of Memory Deficits in Alzheimer’s Disease

It has been implicated that the frontal and parietal cortices contribute to awareness (Rees and Lavie 2001). Specifically, recent studies have shown the precuneus, angular gyri, anterior cingulate gyri and adjacent structures to be highly metabolically active in support of resting consciousness. Indications of a role for the precuneus in notions of the self have been identified (Ruby and Decety 2001; Vogeley et al. 2001). Kjaer et al. (2002) proposed that these regions constitute a functional network of reflective self-awareness, thought to represent a core function of consciousness. Kircher et al. (2002) used fMRI and found differential activation for intentional self-processing in the left precuneus, with functional neuroanatomical correlates in areas previously implicated in the awareness of one’s own state. Of note, brain/behavior correlational analyses in our study only provide indirect evidence for the neural bases of recognition and awareness. Future activation studies comparing prediction / postdiction of cognitive activities in the self and others will facilitate our understanding of the brain substrates of self-awareness in AD.

Fig. 5. Areas showing positive correlations with awareness performance. Left side is shown on the right. The medial aspect of the frontal lobe, the inferior frontal gyrus and the posterior dorsomedial regions including the right precuneus (arrows) showed significant correlations with comparative awareness indices (cited from Mimura and Yano, 2006 with permission).
References


