

Neuropsychological Evaluation in Clinical Practice: Case Interpretation and Treatment

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QUESTIONS

Questions 1–3 refer to the following case.

An 83-year-old right-handed man is referred for an initial neuropsychological evaluation by his primary care physician (PCP) to address concerns about progressive cognitive difficulties. When asked, the patient denies experiencing any cognitive problems. In contrast, his wife, who is present for the clinical interview, describes a 4- to 5-month history of gradually progressive cognitive difficulties. As examples of these problems, she states that she must repeat things more often and in general feels that her husband does not “remember like he used to.” She has managed his medication for the 3 months prior to the evaluation because of concern that he would forget to take them on his own. The patient continues to drive without reported difficulty and has never gotten lost while driving in a familiar area, yet his wife notes that she is no longer comfortable with him driving long distances because he seems to be a less conscientious driver than in the past. The patient reports feeling less interested in doing things he used to enjoy, such as woodworking, although he continues to be interested in reading and visits local libraries daily. The patient describes his mood as “pretty neutral,” but he recently had a prolonged grief reaction after a close family member passed away. His wife describes a mild increase in anxiety and irritability. A recent note from his PCP indicates that the patient was passive and withdrawn and that content of speech was somewhat “empty.” The patient denies difficulty with sleep and reports no change in appetite. Medical history is significant for hypertension, rheumatoid arthritis, and a head injury as a child with a very brief loss of consciousness and no significant post-traumatic amnesia.

The patient’s PCP recommended that he undergo brain magnetic resonance imaging prior to neuropsychological evaluation. Results indicate generalized parenchymal and proportional bilateral mesial temporal lobe volume loss, although there is no regional cortical volume loss to strongly suggest a specific dementia or other neurodegenerative process. In addition, scat-

tered T2/FLAIR hyperintensities in the periventricular and subcortical white matter are noted and felt to be nonspecific, although they are most likely consistent with chronic small ischemic vessel disease.

The patient received a bachelor’s degree in engineering and a master’s degree in business administration and reportedly was always a good student. Family history is significant for cognitive difficulties in his father beginning in his 80s, with no formal diagnosis of dementia. His mother lived to age 98 years and was reportedly very sharp, even in her later years. A maternal aunt lived to 100 years of age, without any significant memory difficulties. The patient has no siblings, and he and his wife have no children.

1. All of the following are goals that should be addressed in the initial neuropsychological evaluation of this patient EXCEPT:

- (A) Assessment of the patient’s cognitive status across a range of domains in order to determine areas of strength and weakness
- (B) Assistance in addressing questions pertaining to differential diagnosis
- (C) Monitoring cognitive status over time through repeat neuropsychological evaluations
- (D) Providing recommendations regarding possible treatments and interventions that can help patients and their families.

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2. Given this patient's history, what is the least likely cause of his cognitive difficulties?

- (A) Alzheimer's disease
- (B) Depression
- (C) Traumatic brain injury
- (D) Vascular dementia

3. Given the patient's history and presenting complaint, which part of the family history is most important to consider when determining etiology?

- (A) The patient's father had cognitive difficulties in his 80s
- (B) The patient's mother lived to 98 years of age and was reportedly "very sharp," even in her later years
- (C) The patient had a maternal aunt who lived to 100 years of age without any significant memory difficulties
- (D) The patient has no siblings
- (E) The patient and his wife have no children

Questions 4 and 5 refer to the patient's neuropsychological test results.

During testing, behavioral observations reveal a mildly flat affect with some anxiety. The patient becomes more relaxed as the assessment progresses, and he is cooperative and motivated throughout the evaluation. His speech is fluent and sensible. Given his full level of effort and motivation, the test results are considered a valid indicator of his functioning at that time.

Premorbid intellectual functioning is estimated to be within the superior range based on his educational and occupational attainment and other demographic variables, and this is consistent with the results of a task of oral word reading. The patient's performance on the Mini-Mental State Examination¹ (24/30) falls within the impaired range, with errors on orientation and recall of 3 words that he had successfully encoded. More detailed neuropsychological evaluation reveals average to above average performance on measures of attention, working memory, executive functioning, and confrontation naming, suggesting intact ability within these domains. In contrast to his superior intellect and intact functioning within most domains, the patient exhibits significant difficulties on tests within the domain of memory. He has difficulty learning a 12-item word list presented across 3 repeated learning trials and exhibits impaired performance on the delayed recall condition, remembering none of the words that had been presented. The additional structure of a recognition task does not

improve performance. Although he endorses 10 correct items, he makes an increased number of false-positive responses (ie, incorrectly endorsing distracter words as having been previously heard). On a second memory measure providing increased structure in the form of a short narrative, he also performs below expectations on immediate, delayed, and recognition trials. Memory for visual material is slightly better, with immediate recall for visual designs falling within the average range, but he displays the same pattern of impaired retention over time, with no improvement during a recognition trial. Moreover, on a memory measure that has been found to be highly sensitive to dementia (Free and Cued Recall²), the patient performs worse than expected, with free recall of pictured objects introduced with semantic cues to enhance learning falling 18 points below normal cut-off. Although his performance improves somewhat when he is provided with cues to aid in retrieval, he continues to perform below expectations (12 points below normal cutoff). Overall, memory performance suggests reduced new learning and impaired retention of information over time. In addition to the patient's marked memory impairment, his performance on semantic fluency measures also falls below expectations and is significantly weaker than his performance on a letter fluency measure. In contrast to his difficulty accessing semantic information on the category fluency measure, performance on a confrontation naming task is intact. On mood inventories, the patient endorses minimal symptoms of anxiety and mild symptoms of depression. His wife's responses on rating scales pertaining to executive functioning behaviors indicate significant difficulty with emotional control, significant apathy, and mild difficulties initiating behavior.

References

1. Folstein MF, Folstein SE, McHugh PR. "Mini-mental state." A practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res* 1975;12:189-98.
2. Grober E, Lipton RB, Hall C, Crystal H. Memory impairment on free and cued selective reminding predicts dementia. *Neurology* 2000;54:827-32.

4. Which etiology is most consistent with this patient's pattern of memory performance on this neuropsychological evaluation?

- (A) Alzheimer's disease
- (B) Depression
- (C) Traumatic brain injury
- (D) Vascular dementia

5. All of the following should be recommended in this case EXCEPT:

- (A) Psychoeducation surrounding his diagnosis of early Alzheimer's disease
- (B) Reevaluation in 1 year to monitor the patient's cognitive status using the initial findings as a baseline to which future performance can be compared
- (C) Referral back to his physician for a benzodiazepine to treat the patient's reported increase in anxiety
- (D) Referral back to his physician for possible pharmacological treatment (cholinesterase inhibitor) given his diagnosis of early Alzheimer's disease
- (E) Strategies to enhance memory (eg, keeping reminder lists, maintaining an uncluttered and organized environment, using a calendar or daily minder, and repeating information when it is presented to him to effectively help with encoding) given the report of memory difficulties

ANSWERS

1. The correct answer is (C) monitoring cognitive status over time through repeat neuropsychological evaluations. In clinical practice, the goals of a neuropsychological evaluation include: (1) assessment of a patient's cognitive status across a range of domains in order to determine areas of strength and weakness, (2) assistance in addressing questions pertaining to differential diagnosis, (3) monitoring cognitive status over time through repeat neuropsychological evaluations, and (4) providing recommendations regarding possible treatments and interventions that can help patients and their families. The neuropsychologist accomplishes these goals using both qualitative observation and quantitative data obtained by administration of standardized tests.¹ For this patient, it will be important for the neuropsychologist to assess his cognitive status across a range of domains, assist in addressing questions pertaining to differential diagnosis, and provide recommendations regarding beneficial treatments and interventions. However, as this is the patient's initial neuropsychological evaluation, prior data with which to monitor functioning over time are not available, and thus this goal cannot be addressed in the present evaluation. Given the patient's age, presenting complaint of memory loss, and history, a follow-up neuropsychological evaluation will likely be beneficial, and monitoring the patient over time will be addressed at the reevaluation.

Reference

1. Lezak M, Howieson DB, Loring DW. Neuropsychological assessment. New York: Oxford University Press; 2004.

2. The correct answer is (C) traumatic brain injury.

Traumatic brain injury is the least likely etiology because the patient's only history of head injury was "brief" and in childhood and the patient denied experiencing any changes in behavior or cognition at that time. A "very brief" loss of consciousness with no posttraumatic amnesia would likely not have resulted in significant cognitive deficits, and any minor cognitive deficits would have resolved in an injury of such minor severity. An individual suffering from depression, vascular cognitive impairment, or early stage Alzheimer's disease would be much more likely to present with the types of cognitive complaints and minor functional decline described here. In addition, depression is a diagnostic consideration given reported grief over the recent loss of a family member, which coincided with onset of reported memory difficulties. Certain behavioral features such as anhedonia are also potentially related to depression. Alzheimer's disease is a consideration due to his age, paternal history of cognitive difficulties, lack of insight into cognitive decline, and memory concerns, as reported by both the patient's PCP and wife. Finally, a vascular dementia is a consideration due to his history of hypertension.

3. The correct answer is (A) the patient's father had cognitive difficulties in his 80s.

In light of the patient's age, history, and presenting memory complaints, a dementing illness is an important consideration in this evaluation. Family history is crucial when considering a dementia syndrome because most dementias have some genetic component, particularly Alzheimer's disease.¹ Furthermore, a first-degree family history of Alzheimer's disease and the apolipoprotein E epsilon4 allele (APOE4) are risk factors for Alzheimer's disease that may impact brain function prior to onset of clinical symptoms.² Because of this strong genetic component, it would be most important to consider his father's history of cognitive difficulties beginning in his 80s, which suggests a neurodegenerative disorder even though no formal diagnosis was made. It would be important to further investigate when the patient's father's memory difficulties began and whether they were progressive. The fact that his mother and maternal aunt lived well into late life with no cognitive

difficulties is not relevant, and there is no indication that preserved cognition in family members is a prognostic indicator for dementia. Therefore, when determining an etiology of dementia it is less important to consider whether the patient had family members who did not suffer from dementia, but it is essential to consider if there is a significant family history of cognitive difficulties or dementia. The fact that the patient does not have siblings or children has no impact on this etiologic consideration.

References

1. Mendez MF, Underwood KL, Zander BA, et al. Risk factors in Alzheimer's disease: a clinicopathologic study. *Neurology* 1992;42:770–5.
2. Xu G, McLaren DG, Ries ML, et al. The influence of parental history of Alzheimer's disease and apolipoprotein E epsilon4 on the BOLD signal during recognition memory. *Brain* 2009;132(Pt 2):383–91.

- 4. The correct answer is (A) Alzheimer's disease.** Testing results indicate that the patient's cognitive difficulties are primarily confined to the domain of memory and are characterized by rapid forgetting of information with little to no benefit from structure or a recognition format. He also exhibits mild difficulty accessing information from semantic memory as seen by reduced semantic fluency, which contrasts with his intact phonemic fluency. The patient's verbal reasoning, visuospatial abilities, working memory, attention, and executive functioning all fall at or above the average range. Given the pattern of cognitive performance and the described difficulties with higher order activities of daily living (including driving and independently managing his medications), results of the evaluation support a diagnosis of early Alzheimer's disease. Although the patient's history indicated possible depression, the pattern of rapid forgetting with intact attentional capacity is more consistent with the pattern of findings associated with temporolimbic involvement, as is seen in Alzheimer's disease. Results are also not consistent with more frontally mediated or subcortical memory difficulties as would be expected in a vascular dementia. Specifically, the patient's memory difficulty is characterized by impaired encoding and consolidation of information associated with temporolimbic processes; patients with frontosubcortical pathology have strategic memory difficulties that may reduce new learning and retrieval but do not grossly impair retention of learned material. The patient's intact attention, working memory, ab-

stract reasoning, ability to shift set, and better phonemic than category fluency performances are also inconsistent with a frontally mediated process. As discussed in question 2, the patient's history is not consistent with dysfunction secondary to traumatic brain injury.

- 5. The correct answer is (C) a referral back to his physician for a benzodiazepine to treat the patient's reported increase in anxiety.** It is certainly important to address the patient's psychiatric symptoms, as they may have played a role in exacerbating cognitive difficulties. However, a benzodiazepine would not be an appropriate recommendation because benzodiazepines are one of the most common causes of drug-induced dementia and have been shown to impair immediate and delayed memory and psychomotor performance in the elderly.^{1–3} These side effects would clearly be detrimental to an individual suffering from early Alzheimer's disease; therefore, it would be more effective to suggest an antidepressant, particularly given this patient's presentation and history of a recent grief reaction following the death of a close family member.

Recommendations that were offered to the patient and his wife included a referral back to his physician for initiation of a cholinesterase inhibitor for pharmacologic management of cognitive difficulties. The patient and his wife were also provided with psychoeducation surrounding the diagnosis of Alzheimer's disease during feedback and were given information for local resources that provide programming in an effort to help them further their understanding of the disease and the services available to them. In addition, strategies to enhance memory were provided, such as keeping reminder lists, maintaining an uncluttered and organized environment, using a calendar or daily minder, and repeating information when it is presented to the patient to help him with encoding. A reevaluation in 1 year was recommended to monitor the patient's cognitive status and modify recommendations, using the initial findings as a baseline to which future performance could be compared.

References

1. Starr JM, Whalley LJ. Drug-induced dementia. Incidence, management and prevention. *Drug Saf* 1994;11:310–7.
2. Tune LE, Bylsma FW. Benzodiazepine-induced and anticholinergic-induced delirium in the elderly. *Int Psychogeriatr* 1991;3:397–408.
3. Reifler BV. Pre-dementia. *J Am Geriatr Soc* 1997;45:776–7.