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Neuropsychology in the Diagnosis of Alzheimer's Disease: Connecting Biology and Clinical Expression

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The diagnostic landscape of Alzheimer's disease (AD) is undergoing a fundamental transformation. Contemporary criteria increasingly define AD biologically, using amyloid and tau biomarkers, including validated cerebrospinal fluid, positron emission tomography, and emerging blood-based biomarkers. Yet this evolution should not diminish the role of neuropsychology. Neuropsychology provides the essential bridge between biological disease and its clinical cognitive and functional expression.

Neuropsychological assessment offers a multidimensional characterization of cognition that cannot be derived from biomarkers. Assessment of episodic memory, executive functions, language, visuospatial abilities, attention, and processing speed can identify the patient's cognitive phenotype and help distinguish the amnestic presentation commonly associated with AD from patterns suggesting alternative or additional neuropathologies. Contemporary diagnostic approach recommendations incorporate neuropsychological assessment within a broader clinical diagnostic process that includes history, examination, laboratory studies, imaging, and biomarkers.

Neuropsychology also contributes importantly to clinical staging. The presence of AD pathology does not establish the severity of cognitive or functional impairment. It is important to distinguish biological staging from clinical staging, ranging from asymptomatic biomarker-positive disease through progressive cognitive impairment, mild cognitive impairment, and levels of dementia. Neuropsychological examination can quantify objective clinical impairment in cognition and function, document decline from estimated premorbid abilities, and provide a baseline against which subsequent progression and/or treatment-related change can be evaluated.

Equally important, neuropsychology helps interpret cognitive findings within the individual patient's context. Education, premorbid cognitive ability, culture and language, psychiatric symptoms, sleep, medications, sensory limitations, vascular disease, and other comorbidities may influence cognitive performance. A biomarker result therefore requires clinical interpretation rather than existing independently of the patient.

The biomarker era should therefore consequently be viewed as an evolution—not a displacement—of neuropsychology's role. Biomarkers increasingly answer the question, "Is Alzheimer's disease pathology present?" Neuropsychology addresses the complementary clinical questions raised: "How is the disease affecting cognition? How severe is the clinical syndrome? What are its functional consequences? And how is the patient changing over time?"

In an era of increasingly early diagnosis and of disease-modifying treatment, these neuropsychological questions remain indispensable to patient-centered clinical care.

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