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Commentary: Sensitive and Specific pre-clinical identification of Alzheimer's disease: A key to novel intervention development

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Early detection of preclinical Alzheimer's disease is clearly critical to development of effective interventions. By the time the clinical symptoms manifest, much of the neuropathological damage is already present. Hope for truly effective treatments rests in being able to intervene early in the pathological process, before the cascade of damage is well-underway (Cummings, Doody, & Clark, 2007).

Over the past two decades, there substantial evidence pointing to episodic memory tests as a sensitive measure to identify those in the very earliest stages of Alzheimer's disease(Bondi et al., 2008). Of note, contemporary episodic memory tests are essentially modified forms of some of the most enduring measures in existence. For example, the Rey Auditory Verbal Learning Test (RAVLT), a list learning task which remains widely used and is also the precursor to the popular California Verbal Learning Test (CLVT) was initially introduced in the early 1900s by Édouard Claparède (Boake, 2000). But there remains a need to identify high-risk people even earlier in the process of pathological change. For example, data from the well-publicized "Nun study" indicated that an index of "idea density" (number of ideas expressed per 10 words) in autobiographies written at age 18-32 predicted subsequent risk of development of cognitive impairment or dementia approximately six decades later (Riley, Snowdon, Desrosiers, & Markesbery, 2005). Such findings raise the possibility that there are subtle forms of subclinical neuropathology present decades before the emergence of mild cognitive impairment or dementia.

The need to identify people in the earliest stages of Alzheimer's disease is not one that is going to be solved by a single test, biomarker, or other index. It is likely to require a complex formulation of neurocognitive performance, identification of genetic, lifestyle, environmental, and other risk factors. Nonetheless, because neurocognitive testing remains one of the key measures that can be reliably administered in the context of routine clinical care, a part of the solution is likely to continue the search for very early cognitive markers of dementia risk. In this regard, the paper provided by Loewenstein and colleagues in this issue is of particular interest and potential value.