Lawrence Honig - selected references

1 Yoshizawa, H., Vonsattel, J. P., & Honig, L. S. (2013). Early neuropsychological discriminants for Lewy body disease: an autopsy series. *Journal of Neurology, Neurosurgery and Psychiatry, 84,* 1326-1330.
Notes: OBJECTIVE: To determine which neuropsychological test measures and which symptoms at presentation might best differentiate dementia with Lewy bodies (DLB) from Alzheimer's disease (AD). METHODS: Cases were from the Columbia University Alzheimer's Disease Research Center, and included cases with pathological diagnosis of pure DLB (n=12), mixed DLB and AD (DLB+AD n=23) and pure AD (n=89) who had Clinical Dementia Rating 0, 0.5 or 1 at their first visit. Clinical symptoms and neuropsychological test measures were compared for pure DLB, DLB+AD and pure AD using univariate analysis of covariance and separate logistic regression analyses. RESULTS: Visual hallucinations, illusions and extrapyramidal tract signs were more frequent as clinical features of the early stage of pure DLB compared with AD. The pure DLB patients showed more impaired visuospatial function than pure AD or DLB+AD patients whereas memory function was more severely impaired in pure AD or DLB+AD than in pure DLB. Analysis of memory subscores suggested that failure of retrieval was the major contributor to the memory deficit of DLB. Multiple logistic regression analysis showed that visuospatial function and delayed memory recognition were independent predictors of pure DLB from pure AD and from DLB+AD. But test measures did not discriminate between DLB+AD and pure AD. CONCLUSIONS: Visuospatial function was more affected in pure DLB than in AD while memory retrieval deficit was more affected in AD than in pure DLB, in the early stages of dementia. However, DLB+AD did not show significant neuropsychological difference from pure AD
Taub Institute for Research on Alzheimer's Disease and the Aging Brain, Columbia University College of Physicians and Surgeons, , New York, NY, USA

2 Honig, L. S. & Boyd, C. D. (2013). Treatment of Alzheimer's Disease: Current Management and Experimental Therapeutics. *Curr.Transl.Geriatr.Exp.Gerontol.Rep., 2,* 174-181.
Notes: Alzheimer's disease (AD) is a major cause of morbidity in the elderly. AD affects aver 5 million persons in the United States, but because it increases in incidence in the elderly, and the "graying" population, AD is projected to increase in prevalence by many-fold over the coming decades. AD causes progressive mental impairment, resulting in the inability of persons to care for themselves. As a consequence, AD results in enormous costs to society due to both lost productivity, and required care. Thus, improved management and treatment is essential. In this review we will briefly review current understanding of the disease, including roles of beta-amyloid and tau proteins. We will then discuss current therapies in use, including the evidence for treatments with supplements, established drugs, and investigational therapeutic strategies, recently completed and ongoing

3 Honig, L. S. (2012). Translational research in neurology: dementia. *Archives of Neurology, 69,* 969-977.
Notes: Dementia disorders are characterized by clinicopathological criteria. Molecular understandings of these disorders, based on immunohistochemical studies, biochemical investigations, genetic approaches, and animal models, have resulted in advances in diagnosis. Likewise, translational research has allowed us to apply our increasing basic scientific knowledge of neurodegeneration to the rational development of new investigational therapies based on our current understanding of disease pathogenesis. This review discusses the application of translational research to both diagnosis and treatment of dementia disorders. The development of biomarkers has yielded imaging and biochemical methods that assist the physician more than ever in the diagnosis of neurodegenerative dementias, especially Alzheimer disease. New diagnostic criteria for disease are based on these molecular-based techniques. And these biomarkers are of potential use in monitoring disease activity during therapeutic trials. Translational investigations likewise have led toward new avenues in targeted dementia research. This is particularly so in the development and testing of disease-modifying treatments that might slow or deter progressive deterioration. Recent clinical trials have not

been based on empirical trials of established drugs but, rather, on trials of drugs shown, through experiments in biochemical, cell culture, and animal models, to interfere with known elements of the pathogenetic cascade of Alzheimer disease

4 Siedlecki, K. L., Honig, L. S., & Stern, Y. (2008). Exploring the structure of a neuropsychological battery across healthy elders and those with questionable dementia and Alzheimer's disease. *Neuropsychology, 22,* 400-411.
Notes: An exploratory factor analysis (EFA) and a series of confirmatory factor analyses were conducted on 17 variables designed to assess different cognitive abilities in a sample of healthy older adults. In the EFA, 4 factors emerged corresponding to language, memory, processing speed, and fluid ability constructs. The results of the confirmatory factor analyses suggested that a 5-factor model with an additional Attention factor improved the fit. The invariance of the 5-factor model was examined across 3 groups: a group of cognitively healthy older adults, a group of patients diagnosed with questionable dementia (QD), and a group of patients diagnosed with probable Alzheimer's disease (AD). Results of the invariance analysis suggest that the model may have configural invariance across the 3 groups but not metric invariance. Specifically, preliminary analyses suggest that the memory construct may represent something different in the QD and AD groups as compared to the healthy older adult group, consistent with the underlying pathology in early AD

5 Honig, L. S., Kukull, W., & Mayeux, R. (2005). Atherosclerosis and AD: analysis of data from the US National Alzheimer's Coordinating Center. *Neurology, 64,* 494-500.
Notes: BACKGROUND: Epidemiologic studies have implicated cerebrovascular disease and its antecedents as risk factors for Alzheimer disease (AD). Cerebral atherosclerosis or strokes may increase the deposition of neuritic plaques or the formation of neurofibrillary tangles. Alternatively, they may simply hasten the age at onset of disease, or increase the severity of disease symptoms. This investigation examined the association between cerebrovascular disease and the pathologic manifestations of AD in an autopsy series. METHODS: This was a cross-sectional study using data from the United States National Alzheimer's Coordinating Center database. The primary analysis included 1,054 individuals with clinical information and semiquantitative neuropathologic measurements: 921 had AD as the primary neuropathologic diagnosis and 133 were considered neuropathologically normal. RESULTS: Overall, 9% of the individuals had clinical history of stroke during life, but 33% had evidence of cerebral infarcts at postmortem. There was no association between neuritic plaques or neurofibrillary tangles, the primary neuropathologic manifestations of AD, with either clinical history of stroke or the presence of cerebral infarcts at postmortem. The authors did find a higher frequency of neuritic plaques and neurofibrillary tangles with increased amyloid angiopathy. Neither plaques nor tangles were associated with small vessel cerebrovascular disease, arteriosclerosis. However, the presence of large-vessel cerebrovascular disease, or atherosclerosis, was strongly associated with an increased frequency of neuritic plaques. CONCLUSIONS: Atherosclerotic cerebrovascular disease may have a role in the pathogenesis of Alzheimer disease, because of a strong association with frequent neuritic plaques

6 Honig, L. S. & Mayeux, R. (2001). Natural history of Alzheimer's disease. *Aging (Milano), 13,* 171-182.
Notes: Taub Institute for Research on Alzheimer's Disease and the Aging Brain, Gertrude H. Sergievsky Center, and Department of Neurology, Columbia University College of Physicians and Surgeons, New York, NY 10032-3795, USA. lh456@columbia.edu
Alzheimer's disease (AD) is the principal cause of dementia in the elderly, and affects about 15 million people worldwide. The earliest symptom is usually an insidious impairment of memory. As the disease progresses, there is increasing impairment of language and other cognitive functions. Problems occur with naming and word-finding, and later with verbal and written comprehension and expression. Visuospatial, analytic and abstract reasoning abilities, judgment, and insight become affected. Behavioral changes may include delusions, hallucinations, irritability, agitation, verbal or physical aggression, wandering, and disinhibition. Ultimately, there is loss of self-hygiene, eating, dressing, and ambulatory abilities, and

incontinence and motor dysfunction. Before diagnosis of AD, individuals may have memory complaints, which represent a period of mild cognitive impairment (MCI). Before MCI, there is a prodromal, ill-defined presymptomatic period of disease ('pre-MCI"). In this review, we particularly focus on these earliest stages. We also discuss the more advanced stages of AD, and address factors that may influence disease course. Understanding the natural history of AD will allow better targeting of the disease-modifying treatments that are on the horizon