Afina W. Lemstra - selected publications

1 van der Flier, W. M., Pijnenburg, Y. A., Prins, N., Lemstra, A. W., Bouwman, F. H., Teunissen, C. E. et al. (2014). Optimizing patient care and research: the Amsterdam Dementia Cohort. *Journal of Alzheimers Disease, 41,* 313-327.
Notes: Since its opening in 2000, patient care and research go hand in hand at the Alzheimer center of the VU University Medical Center, both organized in such a way that they mutually strengthen each other. Our mission is to give patients a voice by lifting the stigma on dementia, to find new diagnostic and treatment strategies, and, ultimately, to cure diseases that cause dementia. Our healthcare pathway is uniquely designed to accommodate all necessary investigations for the diagnostic work-up of dementia in one day (one-stop shop). A second unique feature is that research has been fully integrated in the healthcare pathway. The resulting Amsterdam Dementia Cohort now includes over 4000 patients, and for the majority of these, we have MRI, EEG, blood (serum, plasma), DNA, and CSF available. The Amsterdam Dementia Cohort forms the basis of much of our research, which focuses on four major research lines: 1) variability in manifestation, 2) early diagnosis, 3) vascular factors, and 4) interventions. By answering research questions closely related to clinical practice, the results of our research can be looped back to improve clinical work-up for our patients

2 Smits, L. L., Liedorp, M., Koene, T., Roos-Reuling, I. E., Lemstra, A. W., Scheltens, P. et al. (2011). EEG abnormalities are associated with different cognitive profiles in Alzheimer's disease. *Dementia and Geriatric Cognitive Disorders, 31,* 1-6.
Notes: OBJECTIVE: Our purpose was to investigate associations between different cognitive profiles and their underlying functional brain changes as measured by electroencephalogram (EEG) in Alzheimer's disease (AD). METHODS: EEG was obtained and neuropsychological performance assessed in 254 patients with AD. The EEGs were visually assessed for the presence of focal and/or diffuse abnormalities. Multivariate analysis of variance for repeated measures was performed with presence of focal and/or diffuse abnormalities as between-subjects factor and neuropsychological tests as within-subject factor. Age, sex and education were entered as covariates. RESULTS: Twenty-eight percent of the patients had a normal EEG, 32% had focal abnormalities, 14% diffuse abnormalities and 26% had both focal and diffuse abnormalities. Patients with a normal EEG presented with a cognitive profile in which memory was mostly impaired. Patients with focal and diffuse EEG abnormalities presented with a nonmemory profile. CONCLUSION: These results illustrate that specific types of EEG abnormalities are associated with different cognitive profiles in AD, providing biological support in terms of brain functioning for variability in cognitive impairment

3 Lemstra, A. W., Kuiper, R. B., Schmand, B., & van Gool, W. A. (2008). Identification of responders to rivastigmine: a prospective cohort study. *Dementia and Geriatric Cognitive Disorders, 25,* 60-66.
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BACKGROUND: Although the overall effects of cholinesterase inhibitors (CEIs) are limited, there could be a subpopulation of patients who experience unequivocal benefit. This study aimed to describe a clinical profile based on a combination of specific neuropsychological test scores and clinical symptoms associated with a favourable response to rivastigmine. METHODS: A prospective cohort study was conducted in 53 patients who started rivastigmine treatment. Neuropsychological evaluation was performed at baseline and 6 months of treatment. Patients were labelled responders and non-responders based on change scores after 6 months in 3 clinical domains: cognition, activities of daily living and behaviour. RESULTS: After 6 months 19 responders and 15 non-responders were identified. Variability in reaction time and Continuous Performance Test (CPT) scores differed significantly at baseline between groups. A previously defined cluster of 4 items of the Neuropsychiatric Inventory was correlated with therapeutic response. CONCLUSION: These findings suggest that patients who respond well to CEI therapy can be identified by deficits in attention, combined with a cluster of behavioural symptoms, including hallucinations, apathy, anxiety and psychomotor

disturbances. This may constitute the clinical profile of cholinergic deficiency. Further prospective studies in larger populations are warranted to investigate whether this profile can be used to select patients who will benefit from CEIs.

4 Lemstra, A. W., Richard, E., & van Gool, W. A. (2007). Cholinesterase inhibitors in dementia: yes, no, or maybe? *Age and Ageing, 36,* 625-627.

5 Lemstra, A. W., Eikelenboom, P., & van Gool, W. A. (2003). The cholinergic deficiency syndrome and its therapeutic implications. *Gerontology, 49,* 55-60.
Notes: Cholinesterase inhibitors are licensed for treatment of dementia in Alzheimer's disease. However, the effects of these drugs on the cognitive symptoms of dementia are very small. We suggest that symptoms like impairment of attention and concentration, anxiety, restlessness and hallucinations, delineate a specific central cholinergic deficiency syndrome (CDS), that may be a much better target for such treatment. Changes in the quantitative electroencephalogram, muscarinic subtype radioimaging and serum anticholinergic activity may potentially help to diagnose the CDS. CDS is suggested to occur in various neurodegenerative diseases like Alzheimer's disease, Lewy body dementia and Parkinson's disease and to respond well to cholinesterase inhibitor therapy