Reserve in mild cognitive impairment – new approaches

Akademisk avhandling

som för avläggande av medicine doktorsexamen

vid Sahlgrenska akademin vid Göteborgs universitet

kommer att offentligen försvaras vid Psykologiska institutionen

lokal F1 – Göteborg fredagen den 16 april 2010 kl.09:00

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Avhandlingen baseras på följande delarbeten:


Gothenburg 2010

UNIVERSITY OF GOTHENBURG
Reserve in mild cognitive impairment – new approaches

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The concept of reserve stems from the observation that premorbid factors, e.g. education, result in variation in the response to any kind of brain pathology. As subjects with higher reserve tolerate more neuropathology, symptomatic expression of pathology is delayed. It is thus predicted that neuropathology should be more pronounced in those with higher reserve as compared to those with lower at the same level of clinical severity. Most research within the reserve paradigm has been conducted on patients with established diagnoses, mainly Alzheimer’s disease, but knowledge on the modifying effects of reserve in preclinical, Mild Cognitive Impairment (MCI), and early phases of dementia is limited.

The main purpose was to investigate if use of cerebrospinal fluid (CSF) biomarkers, would enable studies of reserve in earlier phases. Specifically, the 42 amino acid form of beta-amyloid (abeta42), mirroring amyloid plaques depositions, and CSF total tau (t-tau), reflecting axonal degeneration, were used as surrogate measures for neuropathology. Another purpose was to explore if patients with higher reserve diverge from patients with intermediate and lower reserve in terms of CSF pathology, and cognitive functioning in various disease phases. As premorbid intelligence Quotient (IQ), cognitive functioning prior to manifest disease, may be a better proxy for reserve than education, the final objective was to construct a test for assessment of premorbid IQ in Swedish.

In summary, we found that patients with higher reserve were distinguishable from those with intermediate and lower reserve with regards to abeta42 pathology, but not clinical manifestations. The incongruence between pathology and clinical outcome indicates compensation for neuropathology. We also found that abeta42 may be sensitive to disease progress when taking level of reserve into account. Patients with higher reserve with stable MCI had lower concentrations of CSF t-tau, but comparable abeta42 concentrations. This finding may either indicate a true protective effect for education, or suggests that higher education promotes cognitive stimulation resulting in better axonal integrity. Also, a test for assessment of premorbid IQ, NART-SWE, was successfully constructed and found to have satisfactory psychometric properties. The results of these studies may contribute to earlier identification, and consequentially treatment of patients with higher reserve at risk for dementia.