Reserve in mild cognitive impairment – new approaches

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av

Sindre Rolstad

Leg.psykolog

Fakultetsopponent

Professor Yaakov Stern

Columbia University College of Physicians and Surgeons, NY, USA

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I. Rolstad S, Nordlund A, Eckerström C, Gustavsson MH, Zetterberg H & Wallin A. **Biomarkers in Relation to Cognitive Reserve in Patients with Mild Cognitive Impairment – Proof of Concept.** Dementia and Geriatric Cognitive Disorders. 2009;27(2):194-200.

II. Rolstad S, Nordlund A, Eckerström C, Gustavsson MH, Zetterberg H & Wallin A. **Cognitive reserve in relation to Abeta42 in patients converting from MCI to dementia - a follow-up report.** Dementia and Geriatric Cognitive Disorders. 2009; 28 (2):110-115.

III. Rolstad S, Nordlund A, Eckerström C, Gustavsson MH, Blennow K,Olesen PJ, Zetterberg H & Wallin A. **High education may offer protection against axonal degeneration in patients with MCI.** Journal of Alzheimer's disease. (in press)

IV. Rolstad S, Nordlund A, Eckerström C, Gustavsson MH, Zetterberg H & Wallin A. **The Swedish National Adult Reading Test (NART-SWE): a test of premorbid IQ. Scandinavian Journal of Psychology.** 2008 Dec;49(6):577-582.

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UNIVERSITY OF GOTHENBURG

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Sindre Rolstad
Section of Psychiatry and Neurochemistry, Institute of Neuroscience and Physiology,
Sahlgrenska Academy at Göteborg University,
Gothenburg, Sweden, 2010

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.