## Cognitive Reserve: An important emerging construct for quality-of-life research

Aims: The concept of cognitive reserve is emerging as increasingly relevant in research on neurological disorders and aging populations. Comprised of both pre-morbid childhood enrichment activities (passive reserve) and current leisure and educational stimulation (active reserve), it has been shown to have prognostic significance in predicting better disease trajectories in people with Alzheimer's disease, multiple sclerosis (MS), and the elderly. Our aim is to introduce this relevant construct to quality-of-life (QOL) researchers, and to describe recent empirical investigations implemented by our group related to the measurement of cognitive reserve, patterns of relationships between passive and active reserve and health and well-being outcomes, and the cognitive appraisal processes underlying these relationships.

**Methods:** Cross-sectional data (n=1142) were drawn from the North American Research Committee on MS (NARCOMS) Registry, from whom additional survey data were collected. Cognitive reserve was measured using the Stern and Sole-Padulles measures, the O\*NET occupational classification system, and the Godin Leisure-Time Exercise Questionnaire. PROs were assessed using generic (SF -12v2, Perceived Deficits Questionnaire, Ryff Psychological Well-Being, Diener Satisfaction with Life Scale) and disease-specific (Patient-Determined Disease Steps, Performance Scales) measures. Psychometric analysis created unidimensional cognitive reserve subscales. Regression models examined relationships between cognitive reserve, demographic characteristics, and PROs. Using the QOL Appraisal Profile (QOLAP), we assessed how MS patients conceptualize their experiences and how that impacts how they report their QOL. Multivariate analysis of variance compared groups within sets of appraisal parameters, and t-tests or chi-square tests were used to compare mean item responses within appraisal parameters for continuous or dichotomous variables, respectively.

Results: The cognitive reserve measures assessed distinct but related constructs. Individuals with high cognitive reserve were more likely to report lower levels of perceived disability and perceived cognitive deficits, and higher levels of physical health, mental health, and well-being. Both active and passive reserve are associated with better outcomes, independent of demographic factors, and these associations apply to both generic and disease-specific outcomes. People high in passive or active reserve report different conceptualizations of QOL, different types of goals, and considering different types of experiences and standards of comparison in responding to QOL questionnaires, as compared to low-reserve individuals. Although item response patterns were slightly different between passive and active indicators, they generally reflect a tendency in high-reserve individuals to emphasize the positive, focus on aspects of their life that are more controllable, and less based in fantasy.

**Conclusions:** Adaptation and compensation in the face of changing pathology may be better understood by considering the concept of cognitive reserve. Individuals with high passive and/or active reserve are healthier and experience higher levels of well-being. Cognitive appraisal processes underlying self-report affect the interpretation of patient-reported outcomes. These processes are relevant to resilience and adaptability, and may relate to how cognitive reserve protects against disability in MS. MS patients high in cognitive reserve differ in their cognitive appraisals from their low reserve counterparts. These appraisal metrics may predict disease course and other important clinical outcomes in MS patients.