Cognitive reserve and appraisal in multiple sclerosis

Carolyn E. Schwartz[a,b,*], Erin Snook[c], Brian Quaranto[a], Ralph H.B. Benedict[d], Bruce D. Rapkin[e], Timothy Vollmer[f,g]

[a]DeltaQuest Foundation, Inc., Concord, MA, USA
[b]Departments of Medicine and Orthopaedic Surgery, Tufts University Medical School, Boston, MA, USA
[c]Department of Kinesiology, University of Massachusetts Amherst, Amherst, MA, USA
[d]Department of Neurology, The Jacobs Neurological Institute, School of Medicine and Biomedical Sciences, University of Buffalo, Buffalo, NY, USA
[e]Department of Epidemiology and Population Health, Division of Community Collaboration & Implementation Science, Albert Einstein College of Medicine, Bronx, NY, USA
[f]Department of Neurology, University of Colorado Denver, Denver, CO, USA
[g]Rocky Mountain Multiple Sclerosis Center, Aurora, CO, USA

Abstract

Background: 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 multiple sclerosis (MS).

Objectives: To describe how passive and active indicators of cognitive reserve relate to QOL appraisal processes in MS.

Methods: Cross-sectional data (*n*=860) 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. Using the quality of life appraisal profile (QOLAP), we assessed how MS patients conceptualize their experiences and how that impacts how they report their quality of life. Multivariate analysis of variance was used to compare 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: 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.

*Corresponding author at: DeltaQuest Foundation, Inc. 31, Mitchell Road, Concord, MA 01742, USA. Tel.: +1 978 758 1553.
 E-mail address:* carolyn.schwartz@deltaquest.org (C.E. Schwartz).

Conclusions: 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.

1. Introduction

Cognitive reserve is an intriguing construct that has been studied in neurologic diseases, brain injury, and aging (Stern, 2007). Originally motivated by the repeated observation of poor correspondence between brain pathology and clinical presentation(Stern, 2007), the concept of cognitive reserve has broad implications for understanding resilience in the face of neurological disease. In the context of multiple sclerosis (MS), cognitive reserve may buffer patients against the long-term cognitive effects of the disease(Arnett, 2010) and possibly even for the transition from relapsing-remitting to progressive disease course.

Cognitive reserve theory (Stern, 2007) posits that there are two components of reserve: *passive and active.* Whereas passive reserve reflects past and premorbid indicators of brain reserve (e.g., IQ, educational and occupational attainment, childhood enrichment activities, etc.), active reserve reflects current enriching activities that keep the brain active and fit (e.g., stimulating leisure and cultural activities, exercise, etc.). Recent work by our group has documented consistent and substantial relationships between both reserve components and patient-reported outcomes (Schwartz et al., in press). Individuals with high passive and/or active reserve appear to be healthier and experience higher levels of well-being (Schwartz et al., in press). From the literature on cognitive reserve, Richards and Deary (2005) have proposed a Life Course Model of Cognitive Reserve that posits four types of influences on the clinical expression of disease. Pre-morbid cognitive ability and other influencing factors (genes, education, lifestyle behaviors) indirectly influence disease expression and central nervous system lesions; other factors (e.g., cultural norms) directly influence disease progression. The Richards and Deary model provides a useful theoretical starting point for thinking about cognitive reserve. It accommodates important complexities. Later exposure and behaviors are linked to early determinants (i.e., exposure and behaviors), and patterns of risk and protection are likely to accumulate over the life course (Richards et al., 2007; Kuh and Ben-Shlomo, 1997; Kuh and Cooper, 1992).

There is a growing body of research that suggests that the QOL appraisal processes underlying self-report affect the interpretation of patient-reported outcomes across a range of medical conditions. *Cognitive appraisal processes* underlie patient response to surveys or questionnaires (Tourangeau et al., 2000). These mental steps that people go through when they answer questions on a survey have implications for accurately interpreting survey responses (Tourangeau et al., 2000). Indeed, part of questionnaire development involves cognitive interviewing to understand what thoughts and feelings are evoked by specific questions to ensure that they are those intended (Willis, 2005). Even when developers follow the current doctrine about best practices for questionnaire design (NIH, 1996), however, other patient factors come into play that yield clinically relevant differences in the underlying appraisal processes. There is, for example, evidence that better adaptation to chronic illness is characterized by using specific patterns of QOL appraisal processes. For example, HIV/AIDS patients who reported better mental health than would be expected based on overt health status used appraisal strategies such as avoiding to think about things that are disappointing, worrisome, or difficult (Bobinski and Lipinski, 2009). The cognitive processes underlying patient response to patient-reported outcome measures have also been found to change over time in cancer patients, and to be affected by treatment side-effects (Taminiau-Bloem et al., 2010). These findings suggest that QOL appraisal processes are relevant to resilience and adaptability. It is possible that such changes in appraisal may be indicative of cognitive flexibility, which may be adaptive in some circumstances (Schwartz et al., 1998) but maladaptive in others (Schwartz and Daltroy, 1999).

1.1. Theoretical model

The theoretical model underlying our work is an integration of a useful theory from the cognitive reserve research arena – the abovementioned Richards and Deary cognitive reserve model (Richards and Deary, 2005) – and the appraisal and response shift theory of Sprangers and Schwartz (1999)) and Rapkin and Schwartz (2004)). The response shift model posits that a health (see Fig. 1). Response shift theory provides a useful way to think about how cognitive reserve may impact clinical presentation in MS. The response shift theoretical model (Rapkin and Schwartz, 2004) posits that a health state change (*catalyst*) causes an individual to utilize cognitive, behavioral, and emotion-focused coping strategies (*mechanisms*), and that stable characteristics of the individual (*antecedents*) determine the selection of these strategies. The Richards and Deary conceptualization of cognitive reserve fits into antecedents in our model. This interaction of antecedents and mechanisms yields appraisal processes, which influence perceived QOL. There are four specific appraisal processes of note in this model: (1) *Frame of Reference*: What life domains are relevant to an individual's QOL mean?; (2) *Sampling of Experience*: What experiences does the individual consider pertinent within these domains?; (3) *Standards of Comparison*: What points of reference does the individual use to evaluate these experiences?; and (4) *Combinatory Algorithm*: What is the relative importance attributed to these different evaluations in forming an overall QOL rating?. These appraisal processes determine perceived QOL, both immediately and over time as this *iterative process* repeats itself in a feedback loop. Appraisal measures have been used to
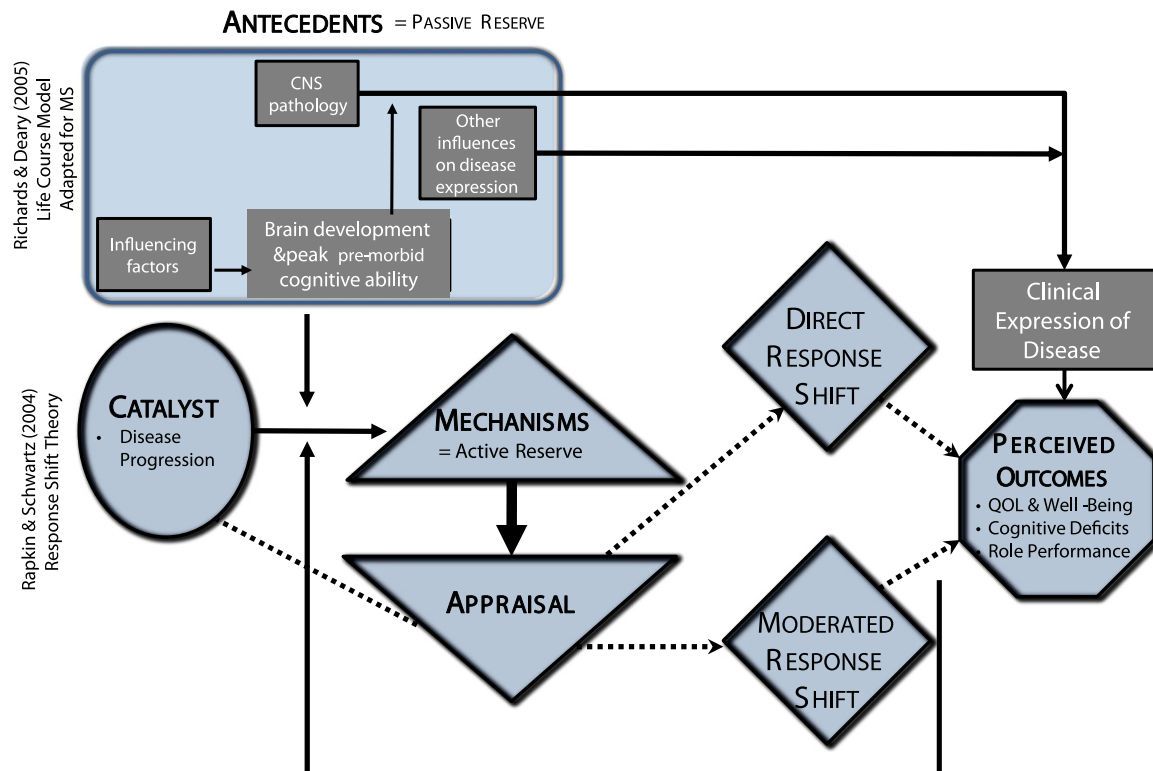
Fig. 1 A theoretical model of cognitive reserve and appraisal.*A theoretical model of cognitive reserve and appraisal*. The theoretical model underlying our work is an integration of a useful theory from the cognitive reserve research arena – the Richards and Deary Life Course Model of Cognitive Reserve (Richards and Deary, 2005) – and response shift theory of Sprangers and Schwartz (1999) and Rapkin and Schwartz (2004). The response shift model posits that a health state change (*catalyst*) causes an individual to utilize cognitive, behavioral, and emotion-focused coping strategies (*mechanisms*), and that stable characteristics of the individual (*antecedents*) determine the selection of these strategies. The Richards and Deary conceptualization of cognitive reserve fits into antecedents in our model. This interaction of antecedents and mechanisms yields appraisal processes, which determine perceived QOL, both immediately and over time as this iterative process repeats itself in a feedback loop. QOL response shift is inferred when changes in appraisal explain the discrepancy between expected and observed QOL (Rapkin and Schwartz, 2004).

understand instances when ratings of QOL differ appreciably from expected values—for example, when an individual's QOL ratings remain stable or even improve despite worsening health status. Changes in appraisal that explain discrepancies between expected and observed ratings of QOL are referred to as "response shifts" (Rapkin and Schwartz, 2004). Changes in appraisal can either affect QOL ratings directly (*Direct Response Shift*) or can affect QOL ratings by attenuating the impact of "catalysts" such as worsening health status (*Moderated Response Shift*).

The purpose of the present work is to investigate how passive and active cognitive reserve influence the appraisal process. It is expected that appraisal processes will differ in high versus low cognitive-reserve groups, and that these differences will be distinct for passive versus active reserve. Note that in our theoretical model, passive cognitive reserve would be considered a background or "antecedent" construct, while active cognitive reserve would function as a "mechanism" that directly determines current appraisal. Thus, these two components may not be identical in the appraisal processes they evoke. For example, active and passive reserve could affect appraisal independently, active reserve could mediate the influence of passive reserve, or the two aspects of reserve could interact in a synergistic manner.

2. Material and methods

2.1. Sample and design

This project involved secondary analysis of cross-sectional data from 860 people who provided data in an add-on survey to the North American Research Committee on Multiple Sclerosis (NARCOMS) registry. This self-report registry includes over 36,000 individuals of age 18 or over, reporting clinician-diagnosed MS. Bi-annual survey updates using either paper or secure web-based survey forms capture data on demographics, disease characteristics, disability, treatments and access to healthcare providers. Potential candidates for the study were selected from those NARCOMS registry participants who completed the latest two semi-annual update surveys online, and resided in the United States. These NARCOMS participants were sent an invitation to participate voluntarily in this add-on survey after they completed the Fall and Spring 2010 semi-annual updates.

2.2. Procedure

An email notification describing the study was sent to a randomly-selected subset of eligible patients. This email

included a unique identifier that was linkable to the NARCOMS data base by NARCOMS staff, and a link to a web-based set of questionnaires designed for this study. The survey engine is SurveyGizmo.com (http://www.survey gizmo.comwww.surveygizmo.com), a user-friendly and HIPAA-compliant interface for collecting data in a secure environment. The SurveyGizmo questionnaire began with an online consent form and the measures described below. Data from the NARCOMS Fall Update and the SurveyGizmo data were then linked by the NARCOMS Coordinating Center using the NARCOMS unique identifier to preserve the inability to identify any individual respondent, and data were de-identified prior to data analysis. The project was reviewed and approved by the institutional review boards associated with NARCOMS at the time of data collection (the Western IRB, Olympia, WA) and DeltaQuest Foundation (the New England IRB, Newton, MA).

2.3. Measures

Cognitive reserve was operationalized utilizing measures of both passive and active reserve. *Passive reserve* was measured using the Sole-Padulles Passive Reserve measure of childhood cultural and educational enrichment (Sole-Padulles et al., 2009), which includes respondent's education level, parents' education levels, and childhood participation in music, the arts, and social activities. *Active reserve* was measured by the Stern Leisure Activities measure of *current* hobbies and leisure activities (Scarmeas et al., 2001). These measures are both unidimensional and showed reasonable-to-good internal consistency reliability (α reliability=0.72 and 0.58 for the Stern and Sole-Padulles measures, respectively)(Schwartz et al., in press). Note that such moderate reliability is actually desirable on measures such as these which tally activities rather than traits; for example, individuals who took music lessons may or may not have taken dance or drawing.

Cognitive appraisal processes were assessed using the QOL Appraisal Profile (Rapkin and Schwartz, 2004). This measure includes open-ended (i.e., qualitative) and multiple choice questions to assess the four appraisal parameters described above. The open-ended data were coded by at least two trained coders, and inter-rater agreement was moderately high (mean kappa 0.65). For this analysis, we conservatively used only those codes on which both raters agreed to reduce random variation in the data. This approach reduced the number of different QOL themes attributed different individuals. *Frame of Reference* was assessed using open-ended text items that asked participants to describe what QOL means to them at this time, as well as what their goals were at this time. The *QOL Definition* text data were coded according to a standardized protocol (Rapkin et al., 2011) with themes originally derived from an extensive sorting procedure (Bobinski and Lipinski, 2009). QOL Definition themes were coded as "0" if not relevant to the individual's written text response, and "1" if they were reflected in the individual's written text response. The *Goal Delineation* data were derived from seven open-ended questions that asked the individual to indicate concerns that were most important to their current life satisfaction, specifically: (1) What are the main things you want to accomplish? (2) What are the main problems that you want to solve? (3) What situations do you want to prevent or avoid? (4) What things do you want to keep the same as they are now? (5) What things do you want to accept as they are? (6) What demands and responsibilities do you want to let go of or reduce? (7) Of the things that you just mentioned, which ones did you think about the most when filling out this questionnaire? Goal themes were rated on a series of items describing goal content, such interpersonal involvement, roles, mood states, and health-relevance. For each of an individual's goal statements, items were coded as "0" if not relevant to the individual's written text response, and "1" if they were reflected in the individual's written text response, and the seven goal items were summed, resulting in scores that ranged from 0 to 7 for each of the goal theme codes. Sampling of Experience (14 items, each ranging from 0 to 4), Standards of Comparison (8 items, each ranging from 0 to 4), and Combinatory Algorithm (16 items each ranging from 1 to 3) were assessed with close-ended Likert-scales.

2.4. Statistical analysis

This is primarily a descriptive analysis, seeking to characterize differences in appraisal by cognitive reserve. We started by creating empirical cut-points at the top and bottom tertiles of the cognitive reserve scales, because these measures are relatively uncharacterized. We then examined patterns of relationships with QOL appraisal items by comparing average appraisal scores between the groups highest and lowest in passive and active reserve. Prior to interpreting individual item differences, we tested omnibus group differences using Multivariate Analysis of Variance (MANOVA) models within sets of appraisal parameters. Mean item responses within appraisal parameters were then compared by group using t-statistics for Likert-scaled items and multi-item sum scores; chi-squared statistics were used for dichotomous variables. A Type I error rate of $\alpha < 0.05$ was used to determine if group differences were notable. Fig. 2 illustrates how high and low scores in the active and passive measures correspond to one another. Although they are moderately correlated ($r=0.31$, $p<0.00001$), they do not always converge. This supports the view that cognitive reserve is a multi-dimensional construct comprised of both passive and active reserve components, and further, that analyses should consider passive and active reserve separately. We thus compared top and bottom scorers on the passive and active reserve measures by mean scores for items within each appraisal parameter.

3. Results

3.1. Sample

Table 1 shows the sample demographic characteristics. Participants in the study sample had a mean age of 54 years, and 74% of the participants were female, which is consistent with the gender distribution in MS (Matthews, 1991). Less than half of the sample was employed, with a median annual household income between $50,000 and $100,000 in the whole sample. Ninety-seven percent of
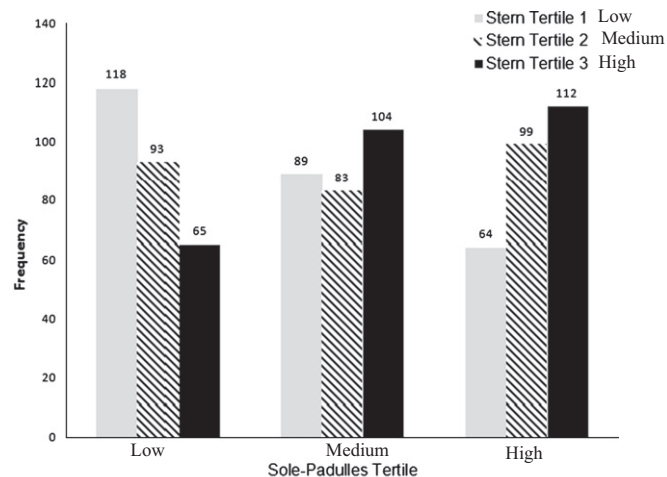
Fig. 2 *A comparison of passive and active cognitive reserve groupings.* Low and high scores in the passive and active reserve measures correspond to one another. They do not always converge, however, although they are moderately correlated ($r=0.31$, $p<0.00001$). This finding supports a hypothesis that cognitive reserve is a multi-dimensional construct comprised of unidimensional active and passive reserve indices.

participants reported living in a private home. In terms of health risks, 59% endorsed drinking alcohol monthly or less, and 88% were non-smokers. The median body mass index characterized the sample as overweight (body mass index of 25-29.9), with 30% in the overweight category (over 25) and 29% in the obese category (over 30).

3.2. Cognitive reserve and appraisal

3.2.1. Differences in frame of reference
MANOVA models comparing QOL Definition codes were significant for passive and active reserve (Lawley-Hotelling Trace=0.0554 and 0.0839, $p<0.03$ and 0.0001 for passive and active reserve, respectively), but the Goal Codes would not converge due to multicollinearity. Item analysis for comparisons of Frame of Reference themes for are shown separately for passive (Table 2) and active (Table 3) cognitive reserve patient groupings (Supplemental Tables S1a-S5b show all comparisons done). *In thinking about what QOL means to them*, individuals with high passive cognitive reserve were more likely to mention family/friends, making a contribution, and personal growth, less likely to mention independence, and were more likely to reference both self and others. In thinking about what QOL means to them, individuals with high active cognitive reserve were also more likely to mention family/friends and making a contribution, and were more likely to reference both self and others. Additionally they were more likely to mention reminiscence, and less likely to mention problems or to give a non-answer. They were also less likely to define QOL both by what it is and what it is not.

In defining goals to which they aspire, individuals with high passive cognitive reserve were more likely to mention goals related to legal and crime/safety concerns, leisure activities, and work, and less likely to give a non-answer. Individuals with high active cognitive reserve were also more likely to mention goals related to leisure activities and were less likely to give a non-answer, but additionally were more likely to mention goals related to community

involvement, education, interpersonal relationships, religious/spirituality, and social/altruistic concerns.

3.2.2. Differences in sampling of experience
MANOVA models comparing Sampling of Experience for passive and active reserve were statistically significant (Lawley-Hotelling Trace=0.0468 and 0.2086, $p<0.04$ and 0.00001 for passive and active reserve, respectively). The results of the comparisons of Sampling of Experience are also shown separately for passive (Table 2) and active (Table 3) cognitive reserve patient groupings. In answering the standardized QOL questionnaires, individuals high in passive reserve were more likely to balance the positive with the negative, less likely to take into account what their doctor told them about their health, and less likely to try not to complain too much. Individuals high in active reserve were also more likely to balance the positive with the negative, but they also tended to emphasize the positive, to think about the future, and to consider relationships with family and friends. They were less likely to think about the worst moments, to focus on their MS, or to try to communicate the seriousness of the situation.

3.2.3. Differences in standards of comparison
MANOVA models comparing Standards of Comparison for passive and active reserve were statistically significant (Lawley-Hotelling Trace=0.0444 and 0.1524, $p<0.003$ and 0.00001 for passive and active reserve, respectively). The results of the comparisons of Standards of Comparison are also shown separately for passive (Table 2) and active (Table 3) cognitive reserve patient groupings. In answering the standardized QOL questionnaires, individuals with high passive reserve were less likely to compare themselves to a time before they had their MS, and more likely to think about the kind of life they are really working for. Individuals with high active cognitive reserve were also less likely to compare themselves to a time before they had their MS and were more likely to focus on the kind of life they were really working for. Additionally, they were less likely to compare

Table 1 Sample demographic characteristics.

Variable	N=860 (%)
Gender: % female	74.27
Mean age (sd)	54.58 (9.24)
Marital	
Never married	8.92
Married	70.07
Divorced	11.27
Widowed	3.87
Separated	1.41
Cohabitation/domestic partner	4.46
Employment status	
Full-time	24.24
Part-time	13.35
Not employed	62.41
Annual income	
Less than $15,000	6.10
$15,001-30,000	12.68
$30,001-50,000	14.08
$50,001-100,000	30.40
Over $100,000	20.07
Do not wish to answer	16.67
Income change in past six months	
Yes	20.84
No	74.59
Do not wish to answer	4.57
If income changed, how?	
Increased	28.09
Decreased	66.29
Lost all income	5.62
Residence status	
Private home	96.71
Private home with home health aid	2.70
Assisted living	0.23
Nursing home	0.35
Mean body mass index (sd)	27.44 (6.67)
% underweight (BMI<18.5)	2.93
% normal weight (BMI 18.5-25)	37.91
% overweight (25.1-30)	30.40
% obese (>30)	28.76
Alcohol use	
Never	32.51
Monthly or less	26.64
2-4 times per month	18.31
2-3 times per week	11.62
4 or more times a week	10.92
Smoking	
No, not at all.	88.26
Yes, some days.	3.64
Yes, every day	8.10

themselves to people whose health does not limit in any way, doctor predictions, or their ideal health.

3.2.4. Differences in combinatory algorithm

In contrast to the other appraisal parameters, there were no differences in how people with high and low passive or active cognitive reserve weighed different aspects of a situation to derive their answers (Lawley-Hotelling Trace=0.0375 and 0.0202, p=0.22 and 0.79 for passive and active reserve, respectively; data on individual items shown in Supplemental Tables S5a and S5b).

3.2.5. Overall differences in appraisal

To assess overall passive versus active group differences in appraisal, we summed across comparisons (statistically significant versus null result) by group (passive versus active cognitive reserve) across all of the appraisal parameters. We found that there were more statistically significant differences between low and high active cognitive reserve (14 as compared to 26) individuals than between the passive cognitive reserve groupings (X^2=4.82, p<0.03).

4. Discussion

Our findings suggest that there are differences in QOL appraisal processes between people high in passive or active reserve as compared to people low in passive or active reserve. Generally speaking, those high in either type of cognitive reserve report different conceptualizations of QOL, different types of goals, and answer QOL questionnaires considering different types of experiences and standards of comparison. They tend to emphasize the positive, focus on aspects of their life that are more controllable, and less based in fantasy. Further, those high in active cognitive reserve evidenced more differences as compared to low active reserve than their passive reserve counterparts. This finding suggests that although premorbid differences can influence appraisal and predispose one to appraisal processes that seem more positive, there are even more notable differences in a similar direction related to current engagement in intellectually and other stimulating activities that maintain brain health. These findings may have important implications for the benefits of retaining activities to the extent that one is able. It is notable, for example, that the appraisal processes endorsed were generally more positive and focused on controllable factors in one's life.

These appraisal differences suggest possible differences in coping and personality, and are reminiscent of work by Folkman and others suggesting that adaptive coping is characterized by problem-focused coping that emphasizes aspects that are controllable rather than uncontrollable (Folkman and Lazarus, 1980; Shapiro et al., 1996). These findings are also consistent with the literature on the self-complexity that suggests that people whose goals and life activities have multiple roles are buffered from stress (Linville, 1987). Finally, these findings are reminiscent of work that suggests that altruistic attitudes and behaviors are associated with better health and well-being outcomes (Schwartz, 2007, 2003, 2012, 2009). While primarily descriptive, these findings provide a useful foundation for further research on the role of cognitive reserve in one's selection of appraisal processes. The relationships between these two sets of variables may provide a key to understanding how cognitive reserve buffers against disability.

Table 2   Differences in low vs. high passive cognitive reserve as measured by Sole Padulles childhood enrichment measure.

	Bottom tertile (N=276)		Top tertile (N=275)			
Quality of life definition	(%)	Standard error	(%)	Standard error	chi2	p
Family/friends	32.6	0.028	41.6	0.030	4.77	0.029
Independence	35.1	0.029	26.6	0.027	4.65	0.031
Contribution	9.4	0.018	19.3	0.024	11.01	0.001
Personal growth	3.3	0.011	7.3	0.016	4.49	0.034
Self vs. others-self	53.6	0.030	45.6	0.030	3.98	0.046
Others	0	–	0%	–		
Both	35.1	0.029	43.1	0.030		
Goal codes	Mean	SD	Mean	SD	t	p
Non-answer	1.75	1.59	1.41	1.46	2.62	0.009
Legal and crime/safety concerns	0.00	0.00	0.01	0.12	−2.02	0.044
Leisure activities	0.08	0.30	0.16	0.41	−2.39	0.017
Work and unemployment	0.32	0.68	0.56	0.85	−3.63	0.000
Sampling of experience	Mean	SD	Mean	SD	t	p
Balance positives with the negatives?	2.47	1.04	2.65	1.01	−2.06	0.040
Take into account what your doctor has told you about your health?	2.14	1.12	1.94	1.25	1.97	0.049
Try not to complain too much?	2.86	1.04	2.65	1.15	2.30	0.022
Standards of comparison	Mean	SD	Mean	SD	t	p
The kind of life that you are really working for?	2.18	1.02	2.40	1.07	−2.42	0.016
A time in your past before you had your MS?	2.06	1.21	1.82	1.24	2.30	0.022

4.1. Limitations

The limitations of the present work should be acknowledged. First, an inherent limitation to using cross-sectional data to evaluate relationships is that it is not appropriate to infer causality with such data. In other words, it is possible that people with high cognitive reserve use more positive and constructive appraisals in considering QOL because they have better health and well-being. It is equally possible that they have better health and well-being because they use more positive appraisal processes. Since the present study is cross-sectional and correlational, we cannot tease apart cause and effect. These results can primarily serve for generating hypotheses. Future planned work will evaluate patterns between appraisal and cognitive reserve over time. Second, the analyses are descriptive and many comparisons were computed. There is thus an elevated Type I error rate. A third caveat of this work is that the cut-offs used to define low and high groupings were sample-specific (i.e., low and high tertiles). Although it is possible that other studies using these measures in different MS samples would derive different empirical cut-points, we believe that the relatively large sample size of this study and the relatively simple analytic approaches used reduce the chance that the groups we identified are not representative of MS patients with different levels of reserve. Further, the clear differences between top and bottom tertiles on these measures have intuitive meaning and are thus relatively interpretable. Nonetheless, the robustness of the findings would need to be tested in other independent samples.

4.2. Clinical implications

As we move forward as MS researchers on the basis of this presented scientific work as well as previous work done by our group (Schwartz et al., in press), we can capitalize on the potential buffering effects of passive and active cognitive reserve. If cognitive reserve predicts better clinical outcomes and more adaptive ways of thinking about one's current situation, then the implications for intervention are far-reaching. If passive cognitive reserve is clinically meaningful, the promotion of childhood enrichment activities could extend not only to the management of pediatric MS but also to wellness programs for all children that include this broad range of enrichment activities. If active cognitive reserve is supported by our findings, then clinical programs could promote active reserve activities for all patients, regardless of level of disability. These activities would include not only exercise, but also cultural, intellectual, and social stimulation activities. Based on the results of the present study, cognitive reserve might be encouraged by cognitive behavioral interventions that teach different ways of thinking about one's current situation. Further, clinical trials of new pharmacotherapy agents might be designed differently on the basis of our research, such that any disease-modifying agent would be combined with an active

Table 3 Differences in low vs. high active cognitive reserve as measured by Stern Leisure activities measure.

Quality of life definition	Bottom tertile (N=276)		Top tertile (N=275)		chi2	p
	(%)	Standard error	(%)	Standard error		
Family/friends	30.1	0.027	48.2	0.030	19.75	0.000
Problems	6.3	0.014	2.1	0.009	6.18	0.013
Contribution	10.5	0.018	17.6	0.023	5.98	0.014
Reminiscence	0.3	0.003	2.8	0.010	5.58	0.018
Non answer	13.6	0.020	5.3	0.013	11.60	0.001
Self vs. others-self	54.2	0.030	42.6	0.029	12.25	0.000
Others	0	–	0	–		
Both	31.8	0.028	47.2	0.030		
Is vs. not—is	71.7	0.027	88.0	0.019	10.11	0.001
Not	0	–	0	–		
Both	4.5	0.012	0.7	0.005		
Goal codes	Mean	SD	Mean	SD	t	p
Non-answer	1.86	1.583	1.380	1.413	3.82	0.000
Community involvement	0.04	0.193	0.165	0.450	−4.39	0.000
Education	0.02	0.131	0.060	0.279	−2.32	0.020
Interpersonal relationships	1.38	1.278	1.810	1.416	−3.79	0.000
Leisure activities	0.10	0.342	0.180	0.436	−2.49	0.013
Religious/spirituality	0.05	0.291	0.187	0.598	−3.41	0.001
Societal and altruistic concerns	0.02	0.144	0.130	0.498	−3.57	0.000
Sampling of experience	Mean	SD	Mean	SD	t	p
Find yourself thinking about the worst moments?	1.80	1.09	1.25	0.95	6.36	0.000
Emphasize the positive as much as possible?	2.60	0.98	3.10	0.84	−6.54	0.000
Balance positives with the negatives?	2.42	1.05	2.74	1.06	−3.70	0.000
Think about the future?	2.44	1.05	2.68	1.01	−2.73	0.007
Focus on your MS?	2.51	1.09	2.17	1.06	3.79	0.000
Consider your relationships with family and friends?	3.00	0.88	3.34	0.82	−4.80	0.000
Try to communicate the seriousness of your situation?	2.26	1.16	1.96	1.06	3.16	0.002
Standards of comparison	Mean	SD	Mean	SD	t	p
People whose health does not limit in any way?	2.17	1.29	1.74	1.19	4.08	0.000
The things your doctor told you would happen?	1.24	1.12	0.99	1.01	2.86	0.004
Your ideal; your dream of perfect health?	2.23	1.24	1.95	1.16	2.79	0.006
The kind of life that you are really working for?	2.19	1.09	2.45	1.08	−2.87	0.004
A time in your past before you had your MS?	2.27	1.21	1.64	1.23	6.18	0.000

cognitive reserve intervention to capitalize on the synergism of brain stimulation with biological agent. Finally, it is possible that as we learn more about cognitive reserve, our understanding of the natural history of MS may change as it is examined through the lens of this construct.

5. Conclusions

We believe that the concepts of passive and active cognitive reserve have great potential to elucidate the course of MS and factors that generate individual resilience. By considering past resources and current indices of reserve separately, this concept can address a complex, multifactorial pathway toward health and disease in MS. Future research should address the possible additive and/or synergistic ways these two distinct components of cognitive reserve work together to influence individual function and well-being in the face of MS. Such research may well uncover promising approaches for behavioral and psychosocial interventions that can help patients maintain active reserve as long as possible (Schwartz, 1999).

Conflict of interest statement

Acknowledgements

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.msard.2012.07.006

References

Arnett PA. Does cognitive reserve apply to multiple sclerosis? Neurology 2010;74:1934–5.

Bobinski J, Lipinski M. [EORTC risk tables—a new diagnostic tool in urology]. Pol Merkur Lekarski 2009;27:524–8.

Folkman S, Lazarus RS. An analysis of coping in a middle-aged community sample. Journal of health & social behavior 1980;21:219–39.

Kuh D, Ben-Shlomo Y. A life course approach to chronic disease epidemiology.Oxford, UK: Oxford University Press; 1997.

Kuh D, Cooper C. Physical activity at 36 years: patterns and childhood predictors in a longitudinal study. Journal of Epidemiology and Community Health 1992:114–9.

Linville PW. Self-complexity as a cognitive buffer against stress-related illness and depression. Journal of Personality and Social Psychology 1987;52:663–76.

Matthews WB. McAlpine's multiple sclerosis.2nd ed. New York: Churchill Livingstone; 1991.

NIH, The science of self-report: implications for research and practice, Bethesda, MD, Nov. 7–8, 1996. Office of Behavioral & Social Sciences Research, National Institute of Health, 1996.

Richards M, Deary IJ. A life course approach to cognitive reserve: a model for cognitive aging and development? Annals of Neurology 2005;58:612–22.

Richards M, Sacker A, Deary IJ. Lifetime antecedents of cognitive reserve. In: Stern Y, editor. Cognitive reserve theory and applications. New York, NY: Taylor & Francis; 2007. p. 37–52.

Rapkin BD, Schwartz CE. Toward a theoretical model of quality-of-life appraisal: Implications of findings from studies of response shift. Health QualLife Outcomes 2004;2:14.

Rapkin BA, Ryniker L, Morgenstern B, Schwartz CE. User manual for the quality of life appraisal profile.Concord, MA: DeltaQuest Foundation, Inc; 2011.

Stern Y. The concept of cognitive reserve: a catalyst for research. In: Stern Y, editor. Cognitive reserve theory and application. New York, NY: Taylor & Francis; 2007. p. 1–4.

Schwartz CE, Snook EM, Quaranto BR, Benedict RHB, Vollmer T. Cognitive reserve and patient-reported outcomes. Multiple Sclerosis Journal 2012.

Schwartz CE, Peng CK, Lester N, Daltroy LH, Goldberger AL. Self-reported coping behavior in health and disease: assessment with a card sort game. Behavioral Medicine 1998;24:41–4.

Schwartz CE, Daltroy LH. Learning from unreliability: the importance of inconsistency in coping dynamics. Social Science and Medicine 1999;48:619–31.

Sprangers MA, Schwartz CE. Integrating response shift into health-related quality of life research: a theoretical model. Social Science & Medicine 1999;48:1507–15.

Sole-Padulles C, Bartres-Faz D, Junque C, et al. Brain structure and function related to cognitive reserve variables in normal aging, mild cognitive impairment and Alzheimer's disease. Neurobiology of Aging 2009;30:1114–24.

Scarmeas N, Levy G, Tang M-X, Manly J, Stern Y. Influence of leisure activity on the incidence of Alzheimer's disease. Neurology 2001;57:2236–42.

Shapiro Jr DH, Schwartz CE, Astin JA. Controlling ourselves, controlling our world. Psychology's role in understanding positive and negative consequences of seeking and gaining control. American Psychologist 1996;51:1213–30.

Schwartz CE. Altruism and subjective well-being: conceptual model and empirical support. In: Post SG, editor. Altruism & health: perspectives from empirical research. Oxford, United Kingdom: Oxford University Press; 2007. p. 33–42.

Schwartz CE, Meisenhelder JB, Ma Y, Reed G. Altruistic social interest behaviors are associated with better mental health. Psychosomatic Medicine 2003;65:778–85.

Schwartz CE, Quaranto B, Bode R, Finkelstein JA, Glazer PA and Sprangers MAG Doing good, feeling good, and having more: resources mediate the health benefits of altruism differently for males and females with lumbar spine disorders. Applied Research in Quality of Life, http://dx.doi.org/10.1007/s11482-012-9165-y, in press.

Schwartz CE, Keyl P, Bode R, Marcum J. Helping others shows differential benefits on health and well-being for male and female teens. Journal of Happiness Studies 2009;10:431–48.

Schwartz CE. Teaching coping skills enhances quality of life more than peer support: results of a randomized trial with multiple sclerosis patients. Health Psychology 1999;18:211–20.

Tourangeau R, Rips LJ, Rasinski K. The psychology of survey response.New York: Cambridge University Press; 2000.

Taminiau-Bloem EF, van Zuuren FJ, Koeneman MA, et al. A 'short walk' is longer before radiotherapy than afterwards: a qualitative study questionning the baseline and follow-up design. Health and Quality of Life Outcomes 2010;8:69.

Willis GB. Cognitive interviewing.Thousand Oaks, CA: Sage Publications; 2005. 335.