



The Concept of Cognitive Reserve: A Catalyst for Research

Yaakov Stern*

Cognitive Neuroscience Division, Departments of Neurology and Psychiatry, Taub Institute for Research in Alzheimer's Disease and the Aging Brain, College of Physicians and Surgeons of Columbia University, New York, NY, USA

This special issue assembles articles which define, explore, and utilize the concept of cognitive reserve. This powerful concept has been applied to a wide range of research, ranging from epidemiologic to imaging studies. Thus, the selected articles make use of the cognitive reserve concept in diverse ways. In order to place them in context, I begin this introduction with a brief theoretical review. Much of this based on a recent paper (Stern, 2002).

RESERVE

The concept of reserve has been proposed to account the repeated observation that, across individuals, there is not a direct relationship between the severity of the factor that disrupts performance (such as degree of brain pathology or brain damage) and the degree of disruption in performance. One idea is that the variability that naturally exists across individuals in cognitive reserve (CR) might be translated into differential susceptibility to factors that disrupt performance. A related idea is that there may be individual differences in how people compensate once pathology disrupts the brain networks that normally underlie performance.

The threshold model, critically reviewed by Satz (1993), and suggested by many others, is a well-articulated model of how reserve may operate. The threshold model revolves around the

construct of “brain reserve capacity” (BRC). This is a hypothetical construct, but concrete examples of brain reserve capacity might include brain size or synapse count. The model recognizes that there are individual differences in BRC. It also presupposes that there is a critical threshold of BRC such that specific clinical or functional deficits emerge once BRC is depleted past this threshold. This formulation begins to account for the disjunction between the extent of pathology and the extent of clinical change. If 2 patients have different amounts of BRC, a lesion of a particular size may exceed the threshold of brain damage sufficient to produce a clinical deficit in patient but not the other. Thus, more BRC can be considered protective factor, while less BRC would impart vulnerability.

There are also more active models of CR which suggests that the brain actively attempts to compensate for the challenge represented by brain damage. The active model of reserve focuses more on the mode in which tasks are processed as opposed to differences in underlying physiologic differences. Thus *cognitive reserve* could take the form of using brain networks or cognitive paradigms that are more efficient or flexible, and thus less susceptible to disruption. This type of reserve is a normal process used by healthy individuals when coping with task demands as well as individuals with brain damage. In essence, an individual who uses a brain network more efficiently, or is more capable of calling up

*Supported by NIA grant AG 14671.

Address correspondence to: Yaakov Stern, 630 West 168th Street, P&S Box 16, New York, NY 10032, USA. Tel.: +1-212-305-9194. Fax: +1-212-305-2426. E-mail: ys11@columbia.edu

Accepted for publication: December 15, 2002.

alternate brain networks or cognitive strategies in response to increased demand may have more cognitive reserve and might maintain effective performance longer in the face of brain pathology.

Individual variability in CR can stem from innate or genetic differences or from life experiences, such as education, occupational experience or leisure activities. The neural substrates underlying task performance refer to the both the basic neural hardware, such as the number of synapses, and to the neural networks that underlie task performance.

The concept of cognitive reserve provides a ready explanation for why many studies have demonstrated that higher levels of educational and occupational attainment, or of intelligence, and are good predictors of which individuals can sustain greater brain damage before demonstrating functional deficit. Rather than positing that these individuals' brains are grossly anatomically different than those with less reserve (e.g., they have more synapses), the cognitive reserve hypothesis posits that they process tasks in a more efficient manner.

COMPENSATION

I have suggested that the term cognitive reserve be limited to the variability seen in nonbrain damaged individuals. The term compensation has been used quite often in recent functional imaging studies that compare a control group to a group that is expected to have some level of neural disruption, such young versus old, or healthy elders versus Alzheimer's disease. Often, any group difference in these types of studies is interpreted as compensation on the part of the more impaired group. I suggest that the term compensation be reserved for a specific response to brain dysfunction or damage. In this usage, the term compensation implies an attempt to maximize performance in the face of brain damage by using brain structures or networks not engaged when the brain is not damaged.

If compensation truly represents a change that is induced by brain damage, then it

might be important to distinguish between compensation and cognitive reserve. Disentangling compensation and reserve presents a specific experimental design problem. This distinction has not been commonly used in the reserve literature.

Because compensation was not treated extensively in my earlier review of the concept of reserve, I briefly review several points about the application of the term compensation in the context of functional imaging studies. My definition of compensation does not speak to whether the use of compensatory networks allows an individual to maintain optimal function. Again, there is a range of possibilities in this regard. Optimally these changed patterns of activation either help maintain effective function in the face of disruption to normally used brain networks, or are associated with relatively better performance in the individuals who use them. However, in some cases compensatory changes may simply allow some degree of function, even if it is less effective than "normal" function. Thus, the role of compensatory networks is variable, and may differ as a function of task and degree of pathologic disruption. This requires careful exploration in each case. Correlation with task performance can help to determine whether a compensatory network provides behavioral benefits.

The large majority of studies of compensation in aging have not considered functional connectivity across brain regions, but a few published studies have suggested pathology-related changes in connectivity (Cabeza, McIntosh, Tulving, Nyberg, & Grady, 1997; Grady et al., 1995; Stern et al., 2000; McIntosh et al., 1999). A major advantage of considering connectivity is that age-related reorganization should not be limited to one particular brain area. Thus, studies that focus on one region of interest, even if that region is implicated in task performance, may not provide the degree of information required to fully evaluate functional reorganization. Reorganization of the networks subserving various cognitive functions may take place in response to brain pathology, with specific brain regions displaying different interactions with other brain areas and there-

fore having different roles within cognitive networks.

As with cognitive reserve, the reserve hypothesis would posit that there is inter-individual variability in the ability to compensate effectively. Again, individuals with higher levels of education or higher IQ might be able to compensate more effectively. We have observed situations where elder subjects with less CR showed more utilization of a compensatory network. We also predict situations where high CR will be associated with greater use of a compensatory network. This emphasis on individual variability has been lacking in many studies. Evaluating individual variability, coupled with the flexibility of our analytic approaches, provides a framework for delineating compensatory networks.

In summary, I suggest that the term compensation be used to denote alternate recruitment in a population with a condition that can disrupt normal cognitive function. This alternate recruitment is considered compensatory in that it is adopted as a consequence of this disruption. In some cases differential use of this compensatory network is associated with improved performance, while in other cases it may be associated with best possible maintenance of function in the face of age-related neural changes. There are individual differences in compensation across normal aging, and the individuals with greater cognitive reserve should also have more adaptive compensation.

THIS SPECIAL ISSUE

This issue assembles a body of work which defines, explores and utilizes the concept of cognitive reserve. I have attempted to gather together a diverse set of research approaches ranging from genetics to neurogenesis, and from neuroepidemiology to neuroimaging.

Lee reviews the genetic basis for cognitive performance and how this might interact with the concept of cognitive reserve. Since a potentially substantial proportion of variability in cognitive abilities can be genetically determined, this is a fitting place to begin the special issue.

This is followed by Richards and Sacker, who set the stage for a comprehensive consideration of the factors that can contribute to cognitive reserve. They use data from the British 1946 birth cohort. This prospective birth cohort study has followed a representative sample of the UK general population since their birth in 1946, and has repeatedly obtained demographic, medical and psychological information on its members through midlife. They used path analysis to assess the relative contribution of paternal occupation, childhood cognition, educational attainment and adult occupation to the NART, a word reading task that has been used as a proxy for cognitive reserve. They showed independent paths from childhood cognition, educational attainment and adult occupation to cognitive reserve, with that from childhood cognition the strongest, and that from adult occupation the weakest. This prospective study elegantly demonstrates that cognitive reserve is malleable, and that both genetic (childhood IQ) and experiential components contribute to it.

The next series of articles evaluate the potential influence of lifetime activities, including physical leisure and cognitively stimulating activities on cognitive reserve, and explore their influence on specific outcomes. Scarmeas reviews his and other's studies evaluating the relationship between elders' engagement in leisure activities and two outcomes: cognitive decline in normal aging, and the incidence or severity of Alzheimer's disease. He uses two research approaches, epidemiologic and neuroimaging. Of note are the findings suggesting that differential engagement in leisure activities during aging may modulate reserve against the clinical expression of AD pathology. Wilson et al. review their epidemiologic research in this area, and describe an assessment scale for quantifying lifetime participation in cognitively stimulating activities. Dik et al. present data from 1,241 prospectively followed elders regarding the association between early life physical activity and cognition in aging. Their findings suggest a positive association between regular physical activity early in life and level of information processing speed at older age in men, but not in women.

The following series of articles incorporate a series of proxies that have been used for cognitive reserve in three different settings. Farinpour et al. followed a cohort of HIV positive individuals, using onset of AIDS, dementia and mortality as outcomes. Lower Shipley IQ estimates were associated with a more rapid disease progression (to AIDS and dementia) and shortened survival. Somatic symptoms of depression were associated with shortened survival. In addition, age, IQ, and somatic symptoms of depression had an additive effect, with an increase in the number of risk factors associated with accelerated disease progression and shortened time to death. Mortimer et al. report data from the Nun Study, using the diagnosis of dementia as an outcome. They used education as a proxy measure for reserve, and also looked at head size, which has been associated with reserve against dementia in several studies. Sisters whose head circumferences were in the highest tertile and those with high educational attainment had the lowest probability of being demented. Among those with head circumference in the low or middle tertile, the likelihood of dementia was significantly higher for individuals with low education. However, in those with head circumferences in the highest tertile, there was no difference between individuals with low versus high education in the frequency of dementia. This interesting interaction suggests that protective role of education is more readily detected when an individual is at increased risk for dementia. Finally, Manly et al. followed 136 nondemented elders, and looked at decline in memory performance over time. After accounting for age at baseline and years of education, they found that elders with low levels of literacy had a steeper decline in both immediate and delayed recall of a word list over time as compared to high literacy elders. These findings suggest that literacy may be an important measure of cognitive reserve, or that literacy itself provides reserve.

Two papers provide examples of how the concept of reserve can be applied to functional imaging studies. Stern et al. report data from an fMRI study of healthy young adults where two versions of a nonverbal memory test were administered. They evaluated the relationship

between variability across subjects in task-related activation and an estimate of subjects' cognitive reserve. During both the study and test phases of the recognition memory task they noted areas where there were significant correlations between the NART score and change in activation from the easier to the more difficult memory task. These correlations support the idea that neural processing may differ across individuals as a function of CR. This imaging study establishes an approach to investigating the neural substrates of reserve. Friedman provides a thoughtful review of event related potential data that shed light on the concept of compensation.

Finally, Kozorovitskiy and Gould provide an insightful review on the topic of adult neurogenesis and its potential for being a compensatory mechanism for brain damage. Theoretical treatments of cognitive reserve and compensation have traditionally emphasized mechanisms for coping with brain damage. These approaches typically view the brain as a resource that can be depleted or damaged, and do not incorporate recent information about neurogenesis in the mature brain. This review points to the future, where compensation may not simply be adaptation of alternate brain networks, but regeneration of underlying brain circuitry.

The diversity of the articles in this special issue highlights the utility and flexibility of the concept of cognitive reserve for understanding how the brain copes with challenge and pathology. The cognitive reserve model has been applied to many other settings not covered in this special issue, including schizophrenia and traumatic brain injury. Hopefully this issue will encourage further exploration of this concept in diverse research domains.

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