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REVIEW ARTICLE

Cognitive reserve in neuropsychiatry

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ABSTRACT

Background. The idea that superior cognitive function acts as a protective factor against dementia and the consequences of head injury is well established. Here we suggest the hypothesis that cognitive reserve is also important in neuropsychiatric disorders including schizophrenia, bipolar disorder and depression.

Method. We review the history of passive and active models of reserve, and apply the concept to neuropsychiatric disorders. Schizophrenia is used as an exemplar because the effects of premorbid IQ and cognitive function in this disorder have been extensively studied.

Results. Cognitive reserve may impact on neuropsychiatric disorders in three ways: by affecting the risk for developing the disorder, in the expression of symptoms within disorders, and in patients' functional outcome. Cognitive failure below a certain threshold may alone, or in combination with common psychiatric symptoms, produce neuropsychiatric syndromes.

Conclusions. Consideration of cognitive reserve may considerably improve our understanding of individual differences in the causes and consequences of neuropsychiatric disorders. For these reasons, the concept of cognitive reserve should be incorporated in future studies of neuropsychiatric disorder. It may be possible to enhance cognitive reserve through pharmacological or non-pharmacological means, such as education, neurocognitive activation or other treatment programmes.

WHAT IS COGNITIVE RESERVE?

The concept of cognitive reserve arose from the observation that there appears to be no direct relationship between the degree of brain pathology or damage and the clinical manifestation of that damage (Stern, 2002). A third factor is hypothesized to modify the relationship between pathology and clinical symptoms. This third factor has been formulated in general terms as brain reserve or brain reserve capacity (Katzman, 1993; Satz, 1993) and, in more specific terms, as neuronal reserve (Mortimer *et al.* 1981) and more recently, as cognitive reserve (Stern, 2002, 2003; Whalley *et al.* 2004). These concepts are alike to the extent that high reserve is seen as a protective factor against the development and/or expression of neurological conditions, whilst low reserve is a vulnerability factor that lowers the threshold for the symptoms, functional impairment and clinical presentation. They differ in the measures used and in assumptions regarding the neurological basis of the concept. Cognitive reserve has been investigated primarily in dementia and acute brain injury, but the concept may be applicable to broad range of neurological and psychiatric conditions.

Two broad forms of hypothesis have been suggested (Stern, 2002; Scarmeas & Stern,

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2003). The *passive* models primarily concern individual differences in brain structure, such as the number or density of neurons or synapses. Increased brain reserve, such as a higher number of healthy synapses prior to pathology, leads to an increased number of remaining available ones post pathology. If the reserve is sufficient, little or no loss of function will be seen despite pathology; if reserve is low, the threshold at which clinical manifestations occur will be reached with relatively little pathology.

In contrast, *active* models consider individual differences in the functionality of brain processes, such as the efficiency of neural processing, or the ability to recruit alternative brain networks to compensate for the effects of pathology. In its narrow sense, 'cognitive reserve' is usually taken to mean the former, referring exclusively to healthy individuals or individuals prior to the onset of brain pathology. Once pathology is suspected or known, the term 'compensation' may be more appropriate, and could also be applied to the recruitment of alternate or more extensive neural networks to compensate for the cognitive effects of normal ageing (Richards & Deary, 2005).

PASSIVE MODELS OF BRAIN RESERVE

Passive models concentrate on the 'hardware' of neural function; studies use proxy measures such as brain size or head circumference in living individuals, or, at post mortem, synaptic count and dendritic branching. Between 10% and 40% of individuals who show neuropathological markers of Alzheimer's disease (AD) during autopsy show no cognitive impairment (Mortimer, 1997). It has been reported that these non-demented subjects have larger brains and a greater number of neurons than elderly control subjects who do not show histopathological signs of AD (Katzman *et al.* 1988). As a result, many studies have considered the association between intra-cranial volume and risk for AD. One recent study followed 511 initially cognitively intact elderly patients over a mean of 6 years using magnetic resonance imaging (MRI) (den Heijer *et al.* 2006). Brain volumes were 17% smaller in those who were diagnosed with dementia within 2–3 years, and 5% smaller in those diagnosed 6 years after the initial assessment. Atrophy of the hippocampus and amygdala strongly predicted dementia, with hazard ratios of 3·0 and 2·1 respectively per standard deviation decrease in volume.

Brain reserve may also be important with respect to the severity and timing of onset of dementia, although the evidence is somewhat equivocal. Mori *et al.* (1997) assessed whole brain volume and intra-cranial volume using high-resolution MRI in 60 patients with mild to moderate AD. They found modest correlations between some cognitive functions and both whole brain and intra-cranial volume, with premorbid brain volume explaining around 8–16% of the variance in cognitive decline during AD. It has also been reported that age at onset of AD is later for patients with larger premorbid brains (Schofield *et al.* 1995), where brain reserve presumably protects against the onset of dementia. However, other groups have reported no difference in premorbid intra-cranial volume between healthy controls and dementia patients (Jenkins *et al.* 2000; Edland *et al.* 2002) and no association between premorbid brain size and age at onset (Jenkins *et al.* 2000).

ACTIVE MODELS AND COGNITIVE RESERVE

In contrast to the structural models discussed above, *active* models consider individual differences in the 'software' of brain processing, and use proxy measures of brain functionality, such as intelligence test scores and educational and occupational attainment.

A large body of epidemiological evidence has supported active models of cognitive reserve in dementia. Lower intelligence scores, and lower education and occupational attainment are all risk factors for dementia (Katzman, 1993; Stern *et al.* 1994; Snowdon *et al.* 1996; Schmand *et al.* 1997; Letenneur *et al.* 1999) although some have argued that this may reflect an ascertainment bias (Tuokko *et al.* 2003). A recent systematic review in this journal (Valenzuela & Sachdev, 2005) found an odds ratio for dementia of 0·54 in higher-reserve individuals across 22 studies involving 29 000 subjects. Highly educated individuals may also continue to benefit from cognitive reserve after the diagnosis of dementia, showing slower decline in at least some areas of cognition (Le Carret *et al.* 2005). That these findings are the result of active processes is

supported by epidemiological evidence that high levels of physical, social and intellectual activities are all protective against dementia (Kramer *et al.* 1999; Scarmeas & Stern, 2003). The 'use it or lose it' model of dementia has gained wide acceptance among both scientists and the public (Orrell & Sahakian, 1995; Melton, 2005).

Neuroimaging studies have generally supported the cognitive reserve model (Habeck *et al.* 2003; Scarmeas *et al.* 2003; Liao *et al.* 2005). Stern *et al.* (1992) used PET imaging to study patients with AD who were matched for clinical disease severity. At equal clinical severity, patients with higher levels of education showed greater parietotemporal perfusion deficit (i.e. a greater pathology) than those with lower education levels. Cabeza *et al.* (2002) compared the prefrontal cortical (PFC) activations of younger and older adults when completing two memory tasks. Younger adults were asymmetric in their recruitment of PFC regions during the source memory task relative to recall tasks, recruiting primarily from right PFC. Low-performing older adults show similar patterns of activation as the younger adults, but high-performing older adults showed more bilateral engagement of PFC regions, thereby compensating for age-related cognitive impairment.

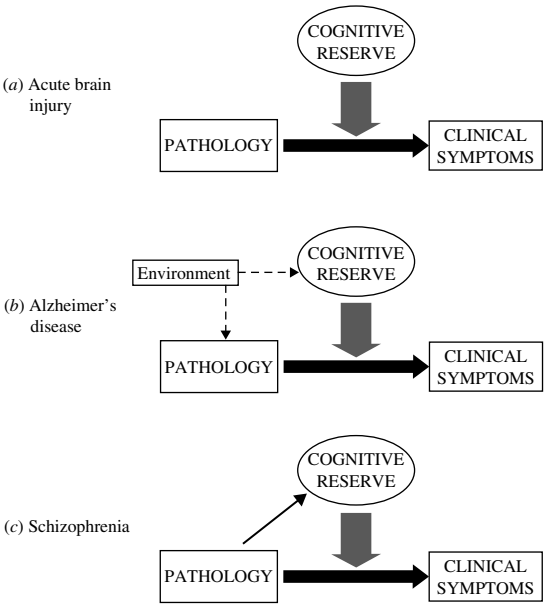

FIG. 1. Three models of cognitive reserve. (*a*) Acute brain injury: cognitive reserve mediates the expression of clinical symptoms, for any given level of pathology. (*b*) Alzheimer's disease: environmental exposures and factors such as education may mediate the risk of disease and the level of cognitive reserve. (*c*) Schizophrenia: as well as influencing symptom expression, cognitive reserve may be limited by the neurodevelopmental nature of the pathology. Note: models are not exhaustive, e.g. they exclude genetic factors.

THEORY AND APPLICATIONS OF COGNITIVE RESERVE

Whether cognitive reserve is best described by passive or active models is not yet clear. It is likely that both structural and functional factors contribute to cognitive reserve. For example, Kesler *et al.* (2003) found that both premorbid brain size and educational attainment independently decreased the magnitude of cognitive deficits following traumatic brain injury.

To some extent, passive and active models may be two sides of the same coin. In the general population, larger head circumference is associated both with higher adult IQ and with less decline in memory in old age (Gale *et al.* 2003). Individuals with more education have greater brain weight, larger neurons and increased arborization of neurons (Katzman *et al.* 1988; Mortimer, 1997). Moreover, the structure of the central nervous system is clearly sensitive to functional factors such as occupation, for example as demonstrated by changes in the topographical organization of the hippocampus in taxi drivers (Maguire *et al.* 2000).

The appropriateness of models of cognitive reserve may vary between disorders (see Fig. 1). Both passive and active concepts of reserve apply most simply to cases of acute brain injury. In these cases, pathology and reserve are independent; that is the likelihood of sustaining such an injury is largely unaffected by both structural reserve factors such as brain size and neuronal density, or by 'functional' factors such as intelligence or education. Reserve can, therefore, be indirectly inferred in acute brain injury by assessing the extent of pathology and the extent of clinical symptoms.

The role of cognitive reserve in AD is more complex than in head injury because environmental factors such diet (Luchsinger & Mayeux, 2004) and toxic exposures (Flaten, 2001) may affect the risk for disorder while others, such as education, affect the level of cognitive reserve. The degenerative nature of AD means that

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cognitive reserve is thought of primarily as a protection against the onset of dementia. This is in contrast to acute brain injury where both cognitive reserve as a protective factor, and cognitive compensation, in terms of recovery of function, are of importance.

The concept of cognitive reserve has recently been applied to a wide range of disorders including epilepsy (Oyegbile *et al.* 2004; Pai & Tsai, 2006), multiple sclerosis (Cader *et al.* 2006) and sleep apnoea-related cognitive deficits (Alchanatis *et al.* 2005). It has not been extensively investigated in neuropsychiatric conditions, but has been implicit in the large body of work assessing premorbid intelligence and risk for such disorders. This research has particularly focused on the role of intelligence in the development and outcome of schizophrenia.

COGNITIVE RESERVE AND RISK FOR SCHIZOPHRENIA

It is well established that low intelligence is a risk factor for schizophrenia. This association does not appear to be simply a consequence of the pathological process of symptomatic disease onset (Aylward *et al.* 1984). Individuals who have developed schizophrenia are more likely to have had impaired childhood educational ability scores (Jones *et al.* 1994) and prospective studies in birth cohorts (Crow *et al.* 1995; Kremen *et al.* 1998; Cannon *et al.* 2002) and conscripted populations (David *et al.* 1997; Davidson *et al.* 1999; Gunnell *et al.* 2002; Reichenberg *et al.* 2002, 2005) have consistently found lower intelligence scores in apparently healthy children and adolescents who will later develop schizophrenia.

Clearly, the neurodevelopmental nature of schizophrenia complicates the issue of cognitive reserve since the pathological process may itself affect the amount of cognitive reserve accumulated, in terms of education and occupational status as well as general intelligence. There is a small, but significant reduction in brain and intra-cranial size in patients with schizophrenia (Ward *et al.* 1996). Other markers of poor or aberrant neurodevelopment are also more common in schizophrenia, such as motor abnormalities (Jones *et al.* 1994; Walker *et al.* 1994; Isohanni *et al.* 2001) and minor physical anomalies (Green *et al.* 1989). Is there any reason then, to frame the findings in terms of cognitive reserve, such that higher intelligence is seen as protective against schizophrenia?

One reason to believe that cognitive reserve is an active process in schizophrenia is that the relationship between intelligence and schizophrenia is not restricted to the lower end of the intelligence spectrum: the risk appears to be linear over the IQ range (Jones *et al.* 1994), with individuals of average intelligence at significantly greater risk of schizophrenia than individuals with high IQ scores (Zammit *et al.* 2004). The protective effects of cognitive reserve would be expected to operate throughout the range of the intelligence spectrum in this manner. It is not clear whether this would also be expected if lowered intelligence in preschizophrenic children were simply a marker of poor neurodevelopment. For example, one model proposes subgroups of schizophrenia: a neurodevelopmental subgroup in which low premorbid IQ would be expected, plus a non-neurodevelopmental subgroup of presumably normal premorbid intelligence (Murray & Lewis, 1987; Murray *et al.* 1992). Current population-level studies do not support this model because risk for schizophrenia increases across the entire IQ range, as discussed above. Nonetheless, it remains possible that the neurodevelopmental subgroup is itself distributed over the ability range, sharing a similar decrement in ability, rather than all being below a specific threshold of reserve.

Cognitive reserve and symptom expression in schizophrenia

One interpretation of the association between intelligence and risk for schizophrenia is that cognitive capacity mediates the ability to rationalize odd experiences that could be interpreted in a delusional manner. Occasional psychotic-like experiences are common in the general population (Peters *et al.* 1999; Poulton *et al.* 2000; van Os *et al.* 2001) and healthy people who report more psychotic-like experiences show lower executive function (Krabbendam *et al.* 2005). In other words, although there is a continuum of psychotic-like experiences in the population, people of higher cognitive capacity may experience less of them, perhaps through a process of enhanced inhibition, or, alternately, use their superior executive control to dispel,

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reinterpret or rationalize these experiences. That delusions and hallucinations result from failures of cognitive control has been central to cognitive theories of schizophrenia involving aberrant self-monitoring (Frith, 1987), data-gathering biases (Garety & Freeman, 1999) and attributional biases (Baker & Morrison, 1998). Similarly, thought disorder has been proposed to result from working-memory impairments (Goldman-Rakic, 1994) although others have disputed this model (Harrow *et al*. 2004).

Cognitive reserve and functional outcome in schizophrenia

Cognitive reserve may be important not only in decreasing the risk of succumbing to schizophrenia but also in predicting outcome after its onset. Patients presenting with better cognition after the onset of psychosis have better outcomes (Green, 1996; Green *et al*. 2000), both in functional domains such as work rehabilitation (Bryson *et al*. 1998; Bell & Bryson, 2001; Gold *et al*. 2002) and in skills such as social problem-solving (Addington & Addington, 1999, 2000). Moreover, cognition appears to be a stronger predictor of functional outcome in schizophrenia than symptom levels (Velligan *et al*. 1997; McGurk *et al*. 2000; Evans *et al*. 2004).

That better post-onset cognition predicts better functioning does not necessarily support the importance of cognitive reserve, since at the time of diagnosis patients with schizophrenia show marked differences in cognitive impairment. However, patients with schizophrenia who have higher premorbid and childhood IQs probably do have better long-term outcomes (Aylward *et al*. 1984). Munro *et al*. (2002) traced patients diagnosed with schizophrenia who had received IQ assessments in childhood. They showed that social and functional outcome is better in patients with schizophrenia who had higher childhood intelligence. Interestingly, childhood IQ did not predict symptom severity. Taking symptom severity as a surrogate marker of pathology, this might indicate that individuals with high cognitive reserve have better functional outcome, despite similar levels of pathology.

There are several possible mechanisms by which increased cognitive reserve could result in better outcomes. In Munro *et al*.'s (2002) study, service utilization was greater in the higher-IQ patients. Joyce *et al*. (2002) found that duration of untreated psychosis in first-episode patients was shorter in patients with intact executive function. In addition, higher IQ has been associated with better insight into illness (David *et al*. 1995). Cognitive reserve may, therefore, moderate the impact of psychosis on patients' lives as well as protecting them from initially developing the disorder. This mechanism may be similar to that described in the general population, where people with higher intelligence and educational level live longer, even when indices of social deprivation have been controlled for (Hart *et al*. 2003).

COGNITIVE RESERVE AND NEUROPSYCHIATRIC DISORDERS

The role of cognitive reserve in neuropsychiatric disorders is more complicated than in acute or degenerative conditions because of two factors. First, cognitive reserve and pathology cannot be assumed to be independent, because, as discussed above, neurodevelopmental pathology may itself interfere with the accumulation of cognitive reserve. As a result, there are substantial methodological problems in assessing cognitive reserve in a disorder such as schizophrenia where substantial cognitive impairments are often present by the time of first onset (Saykin *et al*. 1994; Bilder *et al*. 2000). However, results from recent first-episode psychosis studies suggest that at least some cognitive impairments can be dissociated from premorbid IQ by first onset of psychotic symptoms (Barnett *et al*. 2005).

In addition, disorders that affect early brain development offer the possibility of substantial compensatory change via mechanisms of brain plasticity. Such compensation might confound the relationship between cognitive reserve and outcome. Separating the effects of aberrant development from the determinants of measures of reserve, such as intelligence, is therefore complex. Moreover, both diagnosis and cognitive reserve may be impacted on by environmental (such as years of education) as well as genetic factors (Stern, 2002; Lee, 2003). Large, longitudinal studies are needed in order to address this issue. While such studies have been fruitful in elucidating the genetic and

environmental antecedents of cognitive decline in normal ageing and in dementia (Deary *et al.* 2002; Scarmeas & Stern, 2003), further attempts are needed if such progress is to be made for disorders that are rarer and potentially more complex in course.

Despite these methodological challenges, further research into cognitive reserve in psychiatric disorders is possible because the concept of cognitive reserve makes a series of specific predictions regarding the incidence and heterogeneity of psychiatric disorders.

First, at any given level of symptoms, an individual with higher cognitive reserve will have a higher degree of neural abnormality or pathology compared to an individual with lower cognitive reserve. Therefore, in order to meet diagnostic criteria for a psychiatric disorder, an individual with high cognitive reserve has greater neural abnormality. This predicts that population studies would find that the incidence of a psychiatric disorder is higher in individuals with low cognitive reserve. While this has been demonstrated in schizophrenia, far less research has been conducted in other disorders such as depression and bipolar disorder.

In a longitudinal population-based study, Zammit *et al.* (2004) reported that low premorbid intelligence is associated with a higher risk of depression severe enough to warrant hospital admission. Education does not appear to protect against neuropsychological impairments in late-life depression (Bhalla *et al.* 2005) but a study of memory loss following electroconvulsive therapy for depression found reduced memory loss in patients with higher cognitive reserve, as estimated by educational and occupational attainment (Legendre *et al.* 2003).

There is limited evidence for a role of cognitive reserve in bipolar disorder. In contrast to schizophrenia, a number of longitudinal studies have reported no differences in childhood intelligence between controls and individuals who will later develop bipolar disorder (e.g. Cannon *et al.* 2002; Reichenberg *et al.* 2002), suggesting that risk for bipolar disorder is not affected by cognitive reserve. However, Donaldson *et al.* (2003) found higher IQ in bipolar I patients who had a family history of affective disorder, compared with patients with no family history. This may be compatible with a cognitive reserve model in that high cognitive reserve may protect people with no strong genetic liability from the development of symptoms, resulting in lower IQ in patients with no family history than in those with a genetic vulnerability. The relative paucity of evidence for cognitive reserve in bipolar disorder may reflect a generally lesser role for cognition in the development of bipolar disorder when compared with schizophrenia. For example, cognition during remission remains relatively intact in bipolar disorder (Quraishi & Frangou, 2002).

The cognitive reserve hypothesis also suggests that in a patient population, the severity of symptoms for any given level of pathology would be greater for those individuals with low cognitive reserve. In the absence of any well-established pathological markers of psychiatric disease, such a hypothesis is usually investigated by examining the relationship between indices of cognitive reserve and symptom severity. For example, high premorbid intelligence has been associated with lower symptoms in an elderly cohort with depression (Evans & Katona, 1993). This logic is problematic in neuropsychiatric disorders because the absence of an association may merely indicate that the sample contains a variety of degrees of pathological severity. Thus, if the high-cognitive-reserve individuals have more extensive pathology than those with low cognitive reserve, no relationship between the reserve and symptom severity would be noted. In disorders where the extent of pathology is directly quantifiable, the relationship between cognitive reserve and symptomatic consequences can more easily be tested. For example, a recent study in individuals who survived moderate to severe head injury found that those with higher premorbid intelligence appeared to be more resilient to depression post-head injury, irrespective of lesion location (Salmond *et al.* in press). This study demonstrates that cognitive reserve may also prove important in protecting against non-cognitive consequences of brain insult.

Cognitive reserve in the diagnosis of neuropsychiatric disorders

When an individual meets criteria for a psychiatric diagnosis, the presenting features usually include both cognitive failure and psychiatric symptoms (APA, 1994). However, the relative causal roles of these two features are currently

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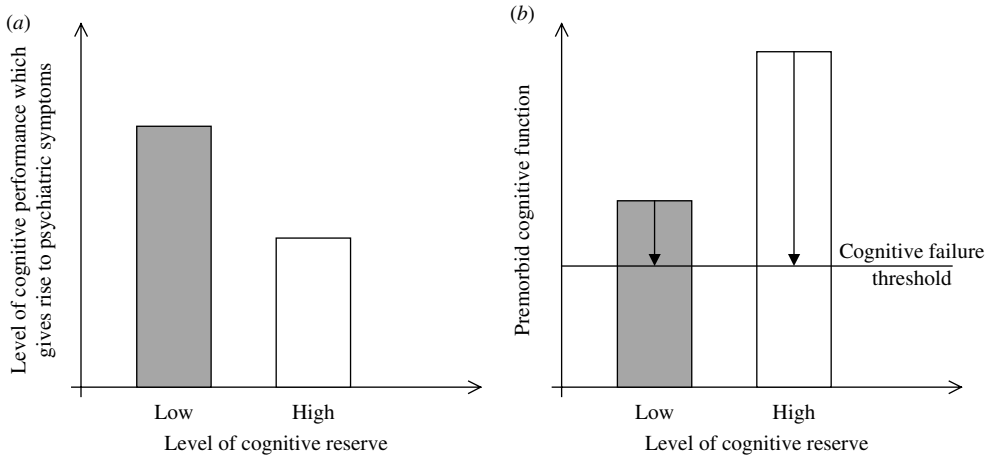

FIG. 2. Cognitive reserve and cognitive failure in neuropsychiatric disorders. (*a*) Level of cognitive performance giving rise to psychiatric symptoms. (*b*) Deterioration in cognitive reserve prior to reaching the threshold. ↓, Degree of deterioration required to give rise to psychiatric symptoms.

poorly understood. The role of cognitive failure, in particular, is important to our understanding of the role of cognitive reserve in psychiatric disorders.

It is possible that cognitive failure is a key cause in psychiatric disorders. For example, cognitive failure below a certain threshold may result in a cognitive endophenotype, which in turn may give rise to the secondary phenomenon of psychiatric symptoms. In such a model, cognitive reserve may have a protective role via two potential mechanisms. Those individuals with high cognitive reserves may have a higher cognitive failure threshold than individuals with low cognitive reserve (see Fig. 2*a*). Alternatively the threshold may remain fixed between individuals, but individuals with high cognitive reserve (and high premorbid functioning) must deteriorate more prior to reaching the threshold (see Fig. 2*b*). However, it should be highlighted that cognitive failure alone is unlikely to be sufficient to induce a psychiatric disorder. For example, not all individuals with learning disability go on to be diagnosed with a psychiatric disorder (Moss *et al.* 2000) and although the incidence of dementia is significantly increased in Down's syndrome (Holland *et al.* 2000) it is not clear that this is the case in other forms of learning disability (Zigman *et al.* 2004).

Alternatively, it may be that it is the combination of cognitive failure and psychiatric symptoms that causes the psychiatric syndrome, leading to diagnosis. Such an explanation is consistent with findings that suggest that psychiatric symptoms are common in non-clinical samples. For example, delusions have a similar range of severity in psychotic and healthy samples (Peters *et al.* 1999). This suggests that it is the combination of psychiatric symptoms and cognitive failure that leads individuals to seek medical attention. High cognitive reserve would increase an individual's resilience to cognitive failure and psychiatric symptoms, potentially via the individual exerting control over these thoughts or 'symptoms'. As with the previous model, this might act through increasing the level of cognitive failure and/or psychiatric symptoms required to produce a psychiatric syndrome (Fig. 3*a*) or through the greater deterioration required to meet the fixed threshold level (Fig. 3*b*).

It is currently not possible to unravel the relative roles of cognitive failure and psychiatric symptoms in psychiatric disorders. Moreover, the associations may differ in different disorders. However, recent advances in cognitive enhancement (e.g. Turner *et al.* 2004) have demonstrated that it is possible to improve cognition in psychiatric patients. By extending these trials to chronic studies, it will be possible to investigate whether cognitive enhancement results in a reduction of psychiatric symptoms (as suggested by the first model) or whether the

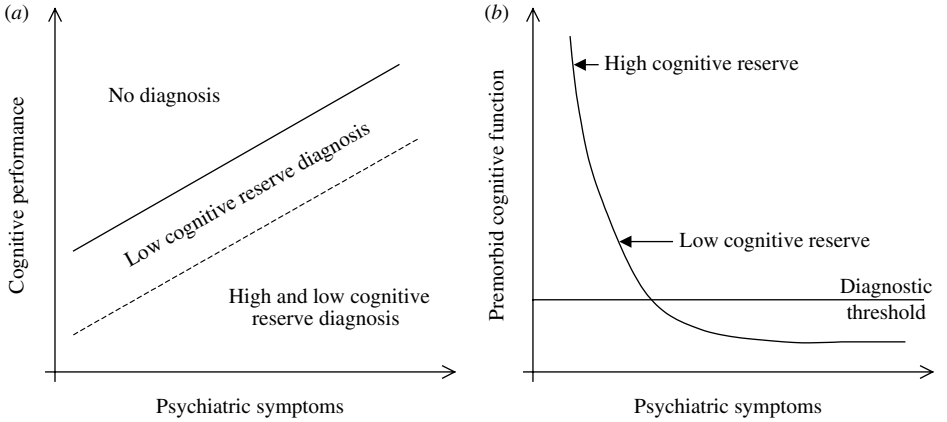

FIG. 3. Cognitive reserve and neuropsychiatric diagnoses. (*a*) Increase in the level of cognitive failure and/or psychiatric symptoms necessary to produce a psychiatric syndrome. (*b*) Deterioration required to meet the fixed threshold level. —, Low reserve diagnostic threshold; ---, high reserve diagnostic threshold.

individuals continue to suffer psychiatric symptoms (as might be predicted by the second model).

Mechanisms of cognitive reserve in neuropsychiatric disorders

The neural basis of cognitive reserve is currently poorly understood. Imaging studies have revealed differential neural activation according to cognitive reserve when performing cognitive tasks (Habeck *et al.* 2003; Scarmeas & Stern, 2003; Stern *et al.* 2003). However, it is unclear whether these distributed patterns are specific to the particular task investigated or if they are more generalizable. Indeed, since cognitive reserve was developed as an explanation for the apparent lack of relationship between neural abnormality and outcome, it is perhaps unlikely that the mechanisms underlying cognitive reserve can be attributed to particular regions, systems or neurotransmitters, at least at the resolution of current techniques. Moreover, the neural basis of cognitive reserve may, by definition, change with age since it may involve the recruitment of alternative neural regions and networks in compensating for age-related cognitive decline (Cabeza *et al.* 2002; Scarmeas *et al.* 2004; Stern *et al.* 2005).

Cognitive reserve may also affect the nature, as well as magnitude of symptoms including cognitive deficit. Le Carret *et al.* (2005) showed that among AD patients with similar global impairments, individuals with higher levels of education experienced greater deficits in abstract thinking, while those with less education experienced greater deficits in memory and attention. The authors suggest that even after the diagnosis of dementia, high cognitive reserve may help protect memory and attentional processes.

Perhaps one potential mechanism for the concept of cognitive reserve is suggested by the recent finding that inactivation of the ventromedial PFC in rats eliminates the influence of cognitive control on serotonergic activity and stress-related behaviour (Amat *et al.* 2005; Robbins, 2005). It is, therefore, possible that cognitive reserve buffers the impact of stress (or other neural or environmental insult), potentially through neuromodulation of the serotonin system. We would predict that the integrity of frontal lobe function would be particularly critical in this mechanism since it is the most plausible 'site' of general intelligence (Duncan *et al.* 2000). Such modulation is unlikely to be detectable using conventional imaging techniques. However, this hypothesis could be examined using psychopharmacological manipulations in a functional imaging paradigm.

CONCLUSIONS

The concept of cognitive reserve has significantly helped understanding of the consequences of both acute brain injury and degenerative disorders, especially Alzheimer's. It may now

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prove useful in furthering our understanding of the risks, expression and outcomes of neuropsychiatric disorders. There is evidence to suggest that cognitive reserve may be a resilience factor in at least some neuropsychiatric disorders. Further work, particularly epidemiological studies, is urgently required to enhance our understanding of the importance of cognitive reserve in neuropsychiatry.

Increasing understanding of cognitive reserve has potential benefits across a wide range of disorders. Since both education and participation in challenging activities help protect against dementia, they may be potentially useful interventions to increase resilience in those at risk of cognitive impairment (Orrell & Sahakian, 1995). Post-onset, neurocognitive rehabilitation programmes, such as those used in schizophrenia (Wykes *et al*. 1999), may be helpful in other disorders where cognition plays a role in functional and clinical outcome by promoting brain compensation. Such amelioration of cognitive deficits, or improvement of cognitive resilience (Erickson *et al*. 2005), may also provide a means of testing hypotheses about the consequences of cognitive reserve. Manipulating levels of cognitive reserve through neurocognitive activation may provide further insights about the processes of both optimal and sub-optimal brain function.

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DECLARATION OF INTEREST

None.

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