THE EFFECT OF EDUCATIONAL ATTAINMENT ON COGNITIVE PERFORMANCE AND RECOVERY IN PATIENTS WITH SUBARACHNOID HEMORRHAGE (SAH).

by

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Abstract

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Adviser: Professor Joan C. Borod

Subarachnoid hemorrhage (SAH) is a sudden and catastrophic event with a high initial mortality rate and lasting cognitive deficits in many patients. Previous studies have investigated numerous disease-related factors and demographic variables in an attempt to identify predictors of cognitive and functional outcome after SAH. However, the effect of educational attainment on cognitive outcome in SAH patients has been largely unexplored. The cognitive reserve model suggests that variables such as education and IQ may moderate the effects of brain injury or disease severity on cognitive functioning. The current study examined the effect of educational attainment on cognitive outcome at 3 months after subarachnoid hemorrhage (SAH) and on recovery of cognitive functioning from 3 to 12 months after SAH. Data were collected from SAH patients (N=113) with a wide range of education levels (0 to 20 years) who were prospectively enrolled in the Columbia University SAH Outcome Project in the Department of Neurology. Seven cognitive domains were examined: attention/concentration, language, verbal memory, visuospatial skills, visual memory, psychomotor speed, and executive functions. After controlling for the influence of age, gender, SAH severity, and specific SAH-related complications, education emerged as a significant predictor of outcome in all domains of cognitive functioning at 3 months post SAH. Education also moderated the relationship between SAH severity and language scores, such that in participants with a lower level of education, the presence of severe SAH was significantly associated with lower performance on language measures. Conversely, in participants with a high level of education, there was no significant association between severity of SAH and language scores. When the impact of educational attainment on recovery of cognitive functioning from 3 to 12 months after SAH was examined in 82 patients who returned for reevaluation, results indicated that higher educational attainment was strongly associated with better recovery rates for all cognitive domains, except for executive functioning. These findings suggest that higher educational attainment mitigates the severity of cognitive decrements associated with SAH and are consistent with the cognitive reserve theory.

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INTRODUCTION

I. Research Question

Subarachnoid hemorrhage (SAH) is a sudden event that can be catastrophic with a high initial mortality rate and lasting cognitive deficits in many patients. Previous studies have investigated numerous disease-related factors and demographic variables in an attempt to identify predictors of cognitive and functional outcome after SAH. However, the effect of educational attainment on cognitive outcome in SAH patients has been largely unexplored. Educational attainment as a predictor of cognitive outcome has been previously investigated in many studies of normal aging and with a variety of patient populations, including those with Alzheimer's Disease (e.g., Bennet et al., 2003), Parkinson's Disease (e.g., Glatt et al., 1996), HIV (e.g., Stern, Silva, Chaisson, & Evans, 1996), and traumatic brain injury (e.g., Kesler, Adams, Blasey, & Bigler, 2003). The results of these studies suggest that educational attainment may be related to better cognitive outcome, and that individuals with higher levels of education may preserve functional capacity regardless of injury or disease severity. The cognitive reserve hypothesis has been proposed to explain these findings and what appears to be a "protective" role of education and related variables. In this study, data collected from SAH patients with a wide range of education levels afforded us an opportunity to examine both the independent and interactive effects of education and disease on neuropsychological outcome. Furthermore, a comprehensive evaluation of multiple cognitive functions will yield information with regards to the specific abilities that formal education may promote. Finally, the influence of education on patterns of recovery of cognitive functions after SAH will be examined.

II. Background

1. Description of the Disease

Subarachnoid hemorrhage is defined as bleeding from a cerebral blood vessel into subarachnoid space. The incidence of aneurysmal SAH varies but overall is 10.5 cases per 100,000 persons per year at a mean age approximately 50 years. Cerebral aneurysm formation and rupture is associated with a variety of factors, including increasing age, female gender, hypertension, alcohol, smoking, cocaine use, and genetic factors (Nanda, Vannemreddy, Polin, & Willis, 2000; Vega, Kwoon, & Lavine, 2002; Weibers International Study of Unruptured Intracranial Aneurysms Investigators, 1996). Thirty-day mortality rate from SAH is 30 % to 40% (Longstreth, Nelson, Koepsell & van Belle, 1993). Mortality and morbidity rates increase with age and poor overall health of the patient. The progress made in the neurosurgical management of aneurysmal SAH has lead to a significant increase in the survival rate (Hutter et al., 1999). However, approximately 50% remain disabled due to cognitive dysfunction (Longstreth et al., 1993).

2. The Profile of Neuropsychological Deficits after SAH

In spite of progress that is being made in medical management of SAH, many patients exhibit substantial cognitive deficits, which are observed even in patients whose neurological outcome was rated as good (Glasgow Outcome Scale = 1) (Hutter et al., 1999). Considering the fact that most patients are struck by aneurysm rupture in the middle of their lives, questions about cognitive functioning in surviving patients are highly relevant to their subsequent occupational role and quality of life and deserve particular attention. SAH affects many domains of cognitive functioning and is likely to reflect diffuse injury (Ogden, Mee, & Henning, 1993). Neuropsychological impairment in SAH patients have been documented in areas that include verbal memory, visual memory, psychomotor speed, visuospatial functioning, and executive functioning (for review see Hutter et al., 1999). In addition, impairments in domains of attention, memory, cognitive speed, and flexibility have consistently been shown by studies of neuropsychological outcome after SAH regardless of differences in research methodologies (Bornstein, Weir, Petruk, & Disney, 1987; Laiacona et al., 1989). However, so far no clear pattern of neuropsychological changes after SAH has emerged and there is considerable variation in the nature and severity of deficits. Study of factors that may determine cognitive outcome and patterns of impairment has been and continues to be an important focus in research.

3. Factors that Affect Cognitive Functioning after SAH

Currently, it is not clear which factors best predict cognitive outcome after SAH, although a number of candidates have been proposed. Among candidate factors are exposure of the brain to subarachnoid blood, intracerebral and intraventricular hemorrhage, hydrocephalus, delayed cerebral ischemia or infarction, and aneurysm location (Hutter et al., 1999; Ogden et al., 1993; Stabell & Magnaes, 1997). Lasting adverse neurocognitive effects appear to be caused by the initial bleeding, rather than surgical interventions (Hutter et al., 1999). However, controversy still exists as to which specific factors may have the greatest impact on cognitive functioning after SAH.

In a recent study that used the same patient cohort as is used in the current study, Kreiter et al. (2002) identified several independent predictors of cognitive outcome 3 months after SAH. Consecutively admitted nontraumatic SAH patients alive at 3 months were evaluated with a comprehensive neuropsychological test battery assessing multiple cognitive domains. Review of the entire hospital course was conducted at the time of discharge by a study neurologist to document important events, procedures, and complications. Basic demographic data were obtained by interview of the patient and family. Clinical and radiographic variables, including Hunt Hess grade, focal SAH clot, hydrocephalus, and cerebral edema, were examined for their association with performance on cognitive measures. Results showed that independent predictors of cognitive dysfunction in two or more domains include cerebral edema (i.e., visual memory, verbal memory, motor functioning, and visuospatial functioning), left-sided infarction (i.e., global mental status, visual memory, and verbal memory), and non-posterior circulation aneurysm (i.e., visual and verbal memory).

In addition, it has been suggested that patient-specific characteristics, such as education level, can have a profound effect on cognitive test performance and the course of recovery after SAH. In fact, Kreiter et al. (2002) observed a strong positive association between education and test performance in many cognitive domains, including, reaction time, visuospatial functioning, and language. Other patient-specific characteristics, including age and ethnicity, were also found to play an important role in predicting cognitive outcome. Furthermore, the strength of associations between demographic variables and cognitive performance was observed to generally exceed those of the disease-related variables analyzed in the study (Kreiter et al., 2002).

There is abundant evidence for the effects of education on neuropsychological test performance (Lezak, 1995; Spreen & Strauss, 1991), and many studies have shown that educational attainment is an important factor in determining cognitive functioning in a variety of neuropathological conditions and in normal aging. However, to our knowledge, none of the studies of cognitive functioning after SAH have investigated education as an independent factor that may influence cognitive abilities, or as a modifying factor that may influence the relationship between SAH severity and cognition. Furthermore, only one study included education as a factor that may affect patterns of recovery (Ogden et al., 1993). Education has traditionally been treated as a confounding rather than a modifying factor in investigating cognitive impairment. However, the effects of education on behavioral outcome are more clearly seen when this variable is treated as risk factor rather than as confounding variable (Satz, 1993). As quoted by Satz (1993), Berkman (1986) argued that the effects of IQ and education on disease or behavioral outcome "are not only worthy of scientific exploration in their own right…but ought to be investigated rather than obscured by essentially overadjusting."

4. The Effect of Educational Attainment on Cognition: Review of Literature

A. Overview

While the influence on cognitive competence is likely to be multifactorial, the importance of environmental stimulation in preservation of cognitive capacities has been recognized. In fact, several studies demonstrate that the level of educational and occupational attainment, as well as leisure activities promote learning, and thus, appear to serve a protective role in buffering the effects of brain pathology on cognition. The evidence from these studies and the repeated observations of the disjunction between the extent of brain pathology and the extent of clinical change has led to the formulation of the cognitive reserve hypothesis, which suggests that reserve results from learning (Stern, 2003). This concept accounts for the results obtained by many studies that have demonstrated that higher levels of intelligence, educational or occupational attainment are good predictors of which individuals can sustain greater brain damage before demonstrating functional deficit (Stern, 2002). Educational attainment deserves particular attention, since formal education plays an important role in early learning, as well as in the formation of lifelong patterns, and many studies show that education is the most important non-biological predictor of change in cognitive performance (Albert et al., 1995).

The effect of educational attainment on cognitive outcome in SAH patients has been largely unexplored. The interest in education as a protective factor has mostly been the focus of research in aging and dementia, however supporting evidence has also been obtained in research with other patient populations, including those with HIV (e.g., Stern, Silva, Chaisson, & Evans, 1996), TBI (e.g., Kesler, Adams, Blasey, & Bigler, 2003), and epilepsy (Jokeit & Ebner, 1999; Pai & Tsai, 2005). The concept of cognitive reserve has also attracted research with patients who have psychiatric conditions, such as depression (e.g., Bhalla et al., 2005). In these studies, the evidence for the protective role of education has been demonstrated by showing that education can promote cognitive abilities and moderate the relationship between the severity of neuropathology and cognition by slowing or delaying the onset of cognitive deficits and by promoting recovery. Below we review evidence from studies focusing on the effects that education may have on cognitive functioning in normal aging and in various neuropathological conditions. Also, the potential role of other variables that may correlate with education, such as occupational attainment, income, risk for toxic exposure, and medical treatment choices, will be considered. Furthermore, studies are beginning to suggest that education is important for some facets of cognitive functioning more than others. Research that helps to identify specific cognitive processes that are promoted as a result of education may shed light on the constitution of cognitive reserve. Thus, recent data demonstrating the selective effect of education on cognitive performance will be discussed.

B. Relationship of Education and Cognition in Aging

There is substantial evidence to suggest that cognitive decline in normal aging can be reduced by increased levels of education. Age-related changes in at least some cognitive abilities have consistently been shown in a number of cognitive domains, including perceptual speed (Schaie, 1989), abstraction ability (Albert, Wolfe, & Lafleche, 1990), verbal and visual memory (e.g., Shichita, Hatano, Ohashi, Shibata, & Mutazaki, 1986) and naming (e.g., Albert, Heller, & Milberg, 1988; Ramsey, Nicholas, Au, Obler, & Albert, 1998). In general, evidence gathered from the cognitive aging literature suggests that older adults have limited cognitive resources (i.e., processing speed and working memory) and that age-related decline is more pronounced on tasks that rely heavily on these abilities, or involve novel and complex stimuli (Craik & Byrd, 1982; Kail & Salthouse, 1994; Salthouse & Skovronek, 1992). Biological changes that accompany aging appear to account for decline observed in various domains of cognition. Specifically, neuron loss, decreases in the weight and volume of the brain, myelin degeneration, slowdown in metabolism, dopaminergic and cholinergic neurotransmitter depletions, and changes in cerebral blood flow, all are capable of mediating age-related cognitive decline. Although changes in the cognitive performance of the elderly as a group have been observed, these changes do not occur uniformly in all individuals. In fact, there is great variability in individual responses to aging. Literature on the subject points to educational attainment as an important predictor in determining whether one will begin to demonstrate cognitive decline early or retain cognitive abilities well into advanced age. It appears that environmental stimulation from education contributes to formation of cognitive reserve that, until depleted, provides cognitive resources and enables one to maintain intact abilities.

A number of studies examined the relationship between level of education and cognitive functioning in normal elderly, using longitudinal and cross-sectional designs. The present review will focus on the longitudinal studies, since this design offers distinct advantages in that it allows to focus on identifying predictors of cognitive change over time and to control for variables that may have affected performance at baseline. Of note, the evidence from studies using longitudinal design is generally consistent with the evidence from cross-sectional studies investigating interrelationships between education and cognitive performance in old age (Anstey & Christensen, 2000).

Evidence accrued from studies of normal aging focusing on education and cognitive functioning demonstrates that a higher level of education plays a role in slowing the rate of cognitive decline. In what is now considered a classic study, Blum and Jarvik (1974) examined intelligence levels in 54 elderly (mean age 84.4) who participated in a study on aging twenty years earlier. The investigators found that the scores had declined more in participants with elementary education than in those with high school education.

More recently, Albert et al. (1995) conducted a longitudinal assessment of elderly individuals ages 70 to 79, following participants over a 2.0- to 2.5-year period. Years of education received by subjects ranged from 0 years to 17 years. The investigators used structural equation modeling to examine predictors of maintenance of cognitive function over time. In this study, multiple cognitive domains, including language, memory, conceptualization, and visuospatial ability were evaluated. Education was found to be the best predictor of cognitive function change apart from baseline cognitive performance. Many studies used the scores from Mini Mental Status Exam (MMSE; Folstein M., Folstein, S., & McHugh P., 1975), a brief measure of global cognitive functioning, as an outcome measure in investigating the association of education and cognitive decline. Points on the MMSE range from 0 to 30, with a score of 23 or less generally accepted as indicating the possible presence of cognitive impairment. Lyketsos, Chen, and Anthony (1999) used the MMSE to investigate the relationship between education and cognitive decline over 11.5 years in an epidemiological study of a large community-residing population. Study participants included 18 to 71 years and older individuals, who had education levels ranging from 0 to over 16 years. The MMSE was administered on three occasions and the difference in scores was calculated. The results of the study showed that cognitive decline was found in all age groups, however having more than eight years of formal education was associated with less decline. Furthermore, this association remained significant after adjusting for age, sex, race, and baseline cognitive functioning. These results lend support to the notion about the value of education in relation to cognitive decline. However, it is important to note that education beyond the nine-year level was not associated with additional reductions in decline. This suggests a threshold for a benefit of education, whereby a minimal duration of education is required for it to serve as a protective factor (Lyketsos et al., 1999).

Other studies have also lent support to the role of education in slowing the rate of cognitive decline. In a large epidemiological study of a catchment area, 14,883 participants ages 18 and older, were administered the MMSE on two occasions, with an interval of one year (Farmer, Kittner, Rae, Bartko, & Regier, 1995). The results indicated that education was a significant predictor of cognitive decline in both young and elderly participants with a baseline MMSE score greater than 23. Education did not appear to be protective against cognitive decline for those with poor initial cognitive performance (i.e., the baseline MMSE less than 23). One possible explanation for this finding may be that poor baseline cognitive performance could indicate cognitive impairment due to processes other than normal aging, such as a disease at a stage where education is no longer protective. Of additional interest, both Lyketsos et al. (1999) and Farmer et al. (1995) found that young individuals showed some degree of cognitive decline. This demonstrates that not only elderly, but also young individuals, may be the victims of possible decline in cognitive functions.

White et al. (1994) analyzed the association of education, occupation, and sex with the incidence of cognitive impairment in adults 65 years and older, using a short mental state questionnaire. In this study, the data from three cooperative longitudinal studies of aging were used. The findings revealed that incident cognitive impairment was inversely related to years of schooling and occupational attainment across all three sites. Education and occupation remained significant predictors after controlling for age, gender, history of stroke and baseline score. Moreover, when the influence of education-based occupation and prestige-based occupation was examined separately, the association was stronger for education-based categories. Thus, the occupations characterized by lower educational attainment were consistently predictive of cognitive impairment when other variables were controlled (White et al., 1994).

Support for the role of education in slowing the cognitive decline also comes from studies that have used memory tasks as outcome measures. In the study conducted by Evans et al. (1993), cognitive decline was investigated in participants over the age of 65 with variable levels of formal schooling (i.e., 0-6 years, 7-8 years, 9-11 years, and 12 years and over). Cognitive function was assessed using a test of immediate memory for a brief story and a brief mental status questionnaire, administered on two occasions three years apart. The results showed that those individuals with fewer years of formal schooling consistently had greater declines in scores on both tests regardless of the initial score and independent of age, birthplace, language of interview, occupation, and income. Moreover, the presence of chronic diseases did not predict change in scores on either test of cognitive function or substantially alter the effect of education (Evans et al., 1993). However, in a population-based study of community-dwelling elderly conducted by Colsher and Wallace (1991), an association between more rapid decline and low education level was found in women aged 65 years and older, but not among men.

Shichita et al. (1986) studied the influences of education and activity on visual memory. The Benton Visual Retention Test was administered to 302 Japanese older adults aged 69 to 71 years old. Level of education ranged from having no formal education to completing college or university. In addition, a single activity score was obtained by summing the scores for activities, such as sports, hobbies, reading and social participation. The results of the reevaluation five years later indicated that the level of education and activity contributed to memory. Education was the strongest contributor after controlling for the initial level of performance. Thus, there was less memory decline evident in those with higher levels of education. Shichita et al. (1986) suggested that differences in intellectual lifestyle may explain the findings.

Recently, research by Lee, Kawachi, Berkman, & Grodstein (2003) showed the inverse relationship between educational attainment and cognitive decline. The investigators examined the relation of educational attainment, husband's education, household income, and childhood socioeconomic status to cognitive function and decline in 19,319 community-dwelling women aged 70 to 79 years. All women were nurses, with levels of education ranging from a three-year study for the Registered Nurse diploma to higher levels of education in nursing (i.e., bachelor's degree and master's or doctoral degree). Assessments of cognitive function consisted of the Telephone Interview for Cognitive Status (TICS), immediate and delayed recall tasks, a test of verbal fluency, and the digit span backwards task (WAIS-R; Wechsler, 1981). These tasks were administered on two occasions with the average time interval of two years. The investigators observed strong and consistent relationships between educational attainment and both cognitive function and cognitive decline, whereby women with a graduate degree had significantly decreased odds of a low baseline score and decline in comparison with women with a Registered Nurse diploma. Moreover, other measures of socioeconomic status had little relation to cognition (Lee et al., 2003).

Some investigators pointed out that the protective role of higher education against cognitive impairment may be in reaching higher levels of cognitive performance during life, rather than in slowing the process of decline. This was evident in the results of many longitudinal studies that showed higher baseline levels, or premorbid scores for the more educated subgroup of participants (Albert et al., 1995; Jacqmin-Gadda et al., 1997; Shichita et al., 1986; White et al., 1994). For example, Jacqmin-Gadda et al. (1997) conducted a five-year longitudinal study of the MMSE score in a sample of 2, 357 French community normal elderly aged 65 and older. Over the five years, the decline in the MMSE score was more pronounced for individuals with no education or primary school education, than for those with high school and university level education. However, the results showed that education correlated more with the mean score than with the amount of decline over time.

In addition to the proposed roles of education in enhancing cognitive performance and in slowing the rate of decline, achieving a higher level of education may also cause a delay in the onset of cognitive decline. Butler, Ashford and Snowdon (1996) investigated the relationship of changes in cognitive function, as measured by MMSE scores, with age and education in Catholic sisters ages 75 years and older participating in the Nun Study. The sisters were divided into two levels of education based on whether or not they had earned a bachelor's degree. Longitudinal analyses revealed that in sisters whose initial MMSE scores ranged from 20 to 30, lower education was associated with greater decline in scores over time (i.e., mean time interval 1.6 years) only for those in the age group of 74 to 85 years old. For sisters 85 years and older, greater decline occurred for those with a bachelor's degree. One explanation provided for this observed interaction between age and education was that decline may have occurred earlier in life for those aged 85 or older with lower levels of education (Butler et al., 1996). Thus, although numerous studies showed more rapid cognitive decline in less educated, Butler et al. showed that education (or its correlates) and age may interact in their effects on cognitive decline.

Schmand, Smit, Lindeboom, Smit, Hooijer, Jonker, et al. (1997) found that in less educated people, memory decline is faster and it begins earlier in life. The authors used percent retained on a memory test as a measure of memory decline in community-dwelling elderly 65 to 85 years of age. Learning to criterion method was utilized to ensure equal encoding levels in all subjects. Cross-sectional analysis with these data also revealed faster decline at an earlier age in less educated, however, these finding were restricted to the 76 to 80 years old group. In the oldest cohort, the extent of decline was approximately the same, regardless of the level of education. These results are consistent with those in the Nun Study (Butler et al., 1996).

C. Relationship of Education and Cognitive Decline in Dementia

The results from studies examining the association between education levels and the prevalence or incidence of dementia provide additional support for education as an important factor in moderating the effects of neuropathology on cognition.

Briefly, studies conducted in geographically diverse settings resulted in findings that support the association between education level and the risk of developing dementia. For example, Stern et al. (1994) examined the incidence of dementia in residents of Northern Manhattan in New York City and showed that the risk of Alzheimer Disease (AD) was increased in individuals with either low education levels or low occupational attainment. Higher incidence rates of AD were also shown among the poorly educated in Sweden (Qui, Backman, Winblad, Aguero-Torres, & Fratiglioni, 2001) and higher prevalence rate of this disorder was seen in population studies conducted in China (e.g., Zhang et. al, 1990). A study of the prevalence of dementia in the city of Ashkelon in Israel demonstrated a strong correlation between education and frequency of dementia, which according to the investigators confirmed that schooling is an important protective factor (Kahana, Galper, Zilber, & Korczyn, 2003).

Recently, Bennett et al. (2003) showed that education not only provides a cognitive advantage and raises threshold at which AD pathology begins to manifest in decline in cognitive functioning, but that education also modifies the relation between density of senile plaque and level of cognitive function. This was observed in a cohort of older Catholic clergy which affords a unique opportunity to control for many confounding variables, such as occupation and lifestyle. Bennett et al. also found that the moderating effect of education was not equal across all cognitive abilities, and that perceptual speed was affected the most and episodic memory was affected the least.

Mortimer, Snowdon, and Markesbery (2003) examined both levels of education and head circumference in 294 Catholic sisters that were assessed annually for dementia as part of the Nun Study. It was shown that individuals having both low levels of education and small head circumference were four times more likely to develop dementia than the rest of the sample (Mortimer et al., 2003). Whereas some dementia incidence studies have shown a female preponderance in the incidence (e.g., Ott et al., 1999), other studies have demonstrated male preponderance (e.g., Ganguli, Dodge, Chen, Belle, & DeKosky, 2000). To explain these differences, authors hypothesized that other risk factors (e.g., occupation) may be differentially distributed among men and women (Ganguli et al., 2002).

Furthermore, similar evidence comes from research of other types of dementia. For example, low educational attainment has been associated with vascular dementia (e.g., Gorelick et al., 1993). In addition, lower education (i.e., less than high school graduate) placed individuals with Parkinson's disease (PD) at increased risk for cognitive decline (Glatt et al., 1996). All of these studies point to a relationship between educational attainment and risk of developing dementia and suggest that high education level may serve as a protective factor.

D. Relationship of Education and Cognition: Evidence from Research with Other Patient Populations

While most of the literature relevant to the cognitive reserve hypothesis and to education as a contributor to reserve is reported for aging and dementia, more recently this concept attracted research with other patient populations, such as those with cerebrovascular disease, HIV, epilepsy, and psychiatric disorders. In most studies, the protective role of education is evaluated in the context of a disease that has a progressive course, and no studies in this area have been conducted with patients who sustained an acute brain injury such as SAH, although this concept has recently been applied to traumatic brain injury (TBI). The interest in investigating cognitive reserve in other patient populations stems from frequent observations by clinicians that a cerebral insult of a given magnitude can lead to significant cognitive impairments in one individual while having minimal effect on another. The results of these studies indicate that education is an important factor in predicting cognitive outcome and that difference in educational attainment among patients can explain the disjunction between the extent of pathology and its clinical manifestation.

Briefly, greater educational attainment was shown to be related to better outcome following traumatic brain injury. Kesler, Adams, Blasey, and Bigler (2003) examined whether total intracranial volume (TICV), educational attainment, and premorbid standardized testing data (e.g., Stanford Binet or Differential Aptitude Test) predict cognitive outcome (i.e., post injury IQ) irrespective of injury severity. Their results indicated that education and TICV predicted IQ grouping (≥90 or <90), whereas premorbid standardized testing did not. The authors concluded that higher education and larger premorbid brain volume may decrease vulnerability to cognitive deficits associated with TBI regardless of injury severity, consistent with the notion of cognitive reserve (Kesler et al., 2003).

Stewart, Richards, Brayne, and Mann (2001) investigated the association between vascular risk (hypertention, diabetes, high cholesterol) and cognitive impairment in a community-based Caribbean born population in London. Marked differences were observed between low and high education levels in the strengths of associations between measures of vascular risk and cognitive impairment. For example, hypertention and diabetes were principally associated with impairment in the low education group.

The discrepancy between the behavioral presentation and brain pathology was also noted in patients with cerebral white matter lesions who had high levels of education. White matter lesions are considered to be a marker of cerebrovascular disease. A recent case report described a patient who demonstrated massive cerebral white matter lesions on neuroimaging, but whose cognitive performance on testing was excellent (Duning, Kugel, & Knecht, 2005). The patient had marked changes in all areas of white matter, including regions that have a postulated effect on cognition. The authors suggested that reserve mechanisms shaped as a result of patient's high education and leisure activities played a role in the plasticity of the brain, allowing for some compensation for structural damage (Duninig et al., 2005).

Dufouil, Alperovitch, and Tzourio (2003) examined the influence of education on the relationship between white matter lesions and cognition in a large population-based cohort of elderly individuals. Participants were divided into low and high education groups (<11 years and ≥11 years) and administered tests to assess multiple areas of cognitive functioning. Magnetic resonance imaging scans were rated visually with respect to the presence of hyperintensities in the white matter. Multivariate analyses controlling for risk factors, including age and history of vascular disease, revealed a significant interaction between education and white matter lesions. While there was a clear relationship between severity of white matter lesions and lower cognitive performances in low education participants, none or weaker association was observed between white matter lesions and cognition in those with high education levels. Furthermore, when quartiles of years of education distribution were considered, results suggested a "dose effect," whereby the lower the education level, the stronger the association between severity of white matter hyperintensities and lower cognition. Authors suggested that these results reinforce the view that higher education level might protect against the consequences of brain lesion on cognition (Dufoil et al., 2003).

In HIV research, low education has been identified among risk factors for developing neurocognitive dysfunction. For example, Maj et al. (1994) compared cognitive performance of asymptomatic seropositive patients to that of seronegative patients as part of the World Health Organization Neuropsychiatric AIDS Study. Investigators observed a significant effect of education on neuropsychological performance among asymptomatic seropositive patients, whereby infected individuals with lower levels of education were more impaired than those with higher levels of education. In a similar study, Stern, Silva, Chaisson, and Evans (1996) found that cognitive reserve capacity (estimated based on a combination of years of education, occupation, and scores on Shipley Institute of Living Scale vocabulary subtest) moderated the effect of HIV illness on cognitive functioning. On measures of attention, processing speed, verbal memory, executive functioning, and visuospatial performance, seropositive patients with low cognitive reserve scores displayed more deficits than their high cognitive reserve seropositive counterparts.

The concept of cognitive reserve was also applied in research with epilepsy patients (Jokeit & Ebner, 1999; Pai & Tsai, 2005). Refractory temporal lobe epilepsy (TLE) appears to be associated with a slow cognitive deterioration. It has been suggested that epilepsy-related noxious events exhaust the compensatory capacity of brain functions and that high cognitive reserve capacity might delay the onset of clinical symptoms (Jokeit & Ebner, 1999). Jokeit and Ebner (1999) study supports this theory by demonstrating that in epilepsy patients with high educational attainment, intelligence (as measured by the full scale IQ on WAIS-R) was stable for a longer duration of TLE than in less educated patients. More recently, Pai and Tsai (2005) investigated whether epilepsy patients with high levels of education show less epilepsy-related decline in cognitive abilities over the period of 12 months. In this study, patients with high levels of education ($\geq$ 12 years) performed better in most cognitive domains on Cognitive Ability Screening Instrument at baseline, however no significant difference in cognitive change was observed between high and low education groups at 12 months follow-up.

Among psychiatric conditions, major depression is often associated with cognitive impairments, the magnitude of which varies considerably among depressed individuals.

Bhalla et al. (2005) investigated whether this variability can be explained by educational level in a cohort of elderly patients. Their results indicated that the effect of education was limited to the Boston Naming Test which was used to measure semantic knowledge. There was no evidence that increased education mitigated the severity of cognitive decrements associated with depression. Thus, it appears that the moderating effect of education observed in patients with other pathologies did not generalize to patients with an acute clinical depression. However, authors explained that the lack of finding may be due to the paucity of patients in the lower education range (less than 12 years) in their sample. Furthermore, the lack of significant interaction between education and depression may also be due to the fact that education was dichotomized rather than examined as a continuous variable, which reduces the power of statistical tests.

Finally, in a pseudoexperimental paradigm, Legendre, Stern, Solomon, Furman, and Smith (2003) investigated the influence of cognitive reserve (operationalized as education and occupational attainment) on memory following electroconvulsive therapy (ECT) in patients with depression. ECT treatment is associated with difficulties in the storage and rapid forgetting of verbal information. Results of this study showed that after ECT treatment patients in the low and high cognitive reserve groups encoded similar amounts of information. However, the low cognitive reserve group forgot considerably more verbal information than the high cognitive reserve group after a 30-minute delay.

5. Explanations of Association Between Education and Cognition

A. Brain Reserve Capacity Hypothesis: Passive Model

Education may be neuroprotective by producing direct effects on brain structure (e.g., synapse count), and thus building a “brain reserve.” Cerebral insults produce deleterious effects on the brain reserve capacity, and when a threshold is reached and the reserve is depleted clinical symptoms begin to manifest (Satz, 1993). Proposed biological processes that result from environmental stimulation stem from observations made in animal studies that include an increase in the number of glial cells and in dendritic density in the hippocampus (Rosenzweig & Bennett, 1972), synaptic strengthening due to an increase in synaptic vesicles (e.g., Nakamura, Kobayashi, Ohashi, & Ando, 1999), as well as an increase in vascularization. Furthermore, Winocur (1998) showed that old rats bred in an enriched environment performed better on a memory test than rats bred in a standard environment, demonstrating that environmental changes can affect cognitive abilities. Findings in humans also provide evidence linking environmental enrichment and dendritic systems. For example, Jacobs, Shall, and Scheibel (1993) examined dendritic length and dendritic segment count in supramarginal pyramidal cells of Wernicke's area in twenty neurologically normal right-handed adults. The major finding of this study was that education had a consistent and substantial effect, whereby dendritic measures increased as educational attainment increased.

Some investigators have proposed that education has to be obtained during a critical period in life when it can impact brain development (Lyketsos et al., 1999). However, Katzman (1993) suggested that education may set a stage for lifelong intellectual pursuit that would promote physiologically beneficial neuronal activity. A continuous stimulation of higher cortical functions may thus serve a protective role and ward off or delay disease processes. Brain reserve has been referred to as *passive* model of reserve since it assumes a fixed threshold at which functional impairments will occur to anyone. In contrast, an *active* model of reserve or cognitive reserve, accounts for individual differences in how brain processes cognitive tasks (Stern, 2002).

B. Cognitive Reserve Hypothesis: Active Model

The cognitive reserve hypothesis suggests that greater reserve may exhibit itself in an increased efficiency in task performance or in an ability to utilize alternative strategies by recruiting alternative networks for problem-solving (Stern, 2002). Thus, rather than focusing on quantity of available neural substrate or "hardware," as does the passive model, cognitive reserve focuses on the "software" or qualitative differences in task performance. In this *active* model, individuals actively compensate for damage (Stern, 2002). Higher education or intellectual stimulation causes individuals to have more resilient or efficient cognitive networks, which renders them better able to compensate when damage undermines a network that supported the standard approach for task performance (Stern, 2002).

The support for cognitive reserve comes from numerous research studies that show discontinuity between brain pathology and cognitive functioning (e.g., Stern, Albert, Tang, & Tsai, 1999; Snowdon, 1997). In addition, recent imaging studies show that neural processing may differ across individuals as a function of cognitive reserve (Springer, McIntosh, Winocur, & Grady, 2005; Stern, Scarmeas, & Habeck, 2004). Some studies show that not only formal educational but continuous intellectual stimulation through occupational attainment and various leisure activities appear to contribute to reserve (e.g., Scarmeas, Levy, Tang, Manly, & Stern, 2001; Scarmeas & Stern, 2003). In addition, it has been observed that literacy levels may serve as a protective factor against cognitive decline or against the clinical manifestation of cerebral neuropathology (Ostrosky-Solis, 2004). Literacy levels may be a better measure of the quality of education, or literacy itself may provide reserve (Manly, Touradji, Tang, & Stern, 2003; Stern, 2003). Regardless of its source, cognitive reserve would allow individuals to cope more successfully with age-related or injury related changes. Also, the individual differences in reserve capacity may be responsible for the differential rates of cognitive decline that is observed in the elderly and for the discontinuity between the magnitude of cerebral insult and cognitive functioning observed in various patient populations (Stern, 2002).

C. Alternative Explanations

Although many studies demonstrate that educational attainment can be an important "protective" factor and that it is a powerful predictor of cognitive outcome, many investigators recognize that education may be a surrogate for other factors that could explain the association between education level and cognition. In fact, socioeconomic status, medical care choices, nutritional value in the diet, and risk for toxic exposure are some of the factors that have been shown to correlate with education level and may influence cognitive functioning levels in aging. However, studies of aging that have carefully controlled for such factors found that the association between education and cognitive decline remained strong (e.g., Christensen et al., 1997; Evans et al., 1993). The study of Catholic sisters conducted by Butler et al. (1996) is remarkable for homogeneity of lifestyles in the sample (e.g., communal dining, comparable health care, and teaching occupation). Sisters also enjoy similar social support and intellectual stimulation. This homogeneity in environment minimizes the influence of many variables that typically correlate with education, narrowing the range of explanations for the associations with education observed (Butler et al., 1996). Nonetheless, the extent to which other environmental factors might also influence cognitive decline or cognitive impairment remains unclear and needs to be elucidated in future research. Also, some have suggested that intelligence rather than years of education serves as a protective factor. It is possible that innately higher intellectual ability may lead individuals to receive more education rather than years of education determining cognitive ability. However, the evidence from the studies reviewed above suggests that once having attained higher levels of education, individuals are faced with a much lower risk for cognitive decline, dementia, or cognitive decrements following injury.

6. Exploring Selective Effects of Education

The evidence from studies reviewed above indicates that education may serve as a protective factor against cognitive decline or against the clinical manifestation of cerebral neuropathology. However, it is unclear whether education uniformly promotes all cognitive abilities or acts selectively by enhancing some skills but not others. In fact, the variability in cognitive performance seen in advanced age and as a result of neuropathology may be due to unique combinations of biological and environmental variables that may affect different cognitive abilities to a different extent. For example, Anstey and Christensen (2000) evaluated some of the recent empirical data available on education, blood pressure, cardiovascular and cerebrovascular disease and APOE as predictors of cognitive change in late adulthood. The evidence suggested that all five groups of predictors affect cognitive change, however each predictor’s effect appears to be limited to specific cognitive abilities. Education affected maintenance of mental status, memory and crystallized abilities. Blood pressure most reliably predicts change in speed and mental status, whereas APOE predicts change in speed and memory. Finally, the studies on health and disease were too varied to allow reliable predictions to be made. The results of this evaluation point out that cognitive abilities can be impacted by different factors, and that education may influence some abilities more than others.

We know that cognitive functioning is a confluence of many cognitive domains that include language, attention, memory, abstraction, reasoning, and praxis. Each domain, in turn, is comprised of a multitude of specific abilities. Horn and Cattell (1967) categorized cognitive abilities into crystallized intelligence (e.g., language skills), thought to be acquired through educational opportunities, and fluid intelligence (e.g., processing speed), thought to be influenced by genetic factors. Since then, many more categories of intelligence have been proposed. Although the complexity of human cognition is recognized, many studies that investigate cognitive functioning have used only a limited range of measures to examine cognition, some incorporating only a single measure of cognitive ability (Shichita et al., 1986, Shmand et al., 1997). As a result, such studies provide limited information about the specific role of education. Furthermore, some investigators who have included several measures of cognitive functioning, failed to examine the effect of education separately for each cognitive ability, and rather combined scores to form a single outcome measure. For example, Carmelli, Swan, LaRue, and Eslinger (1997) investigated changes in cognitive performance in 566 elderly men on measures of attention, visual memory, verbal fluency, and psychomotor speed. The test scores were then combined into a composite score that was used to identify “decliners”, “nonchangers” and “improvers” at follow up. The investigators found that education was not a significant predictor of cognitive decline. However, these results may be due to the fact that composite score obscured the effect of education on individual cognitive functions (Anstey & Christensen, 2000). Thus, it is important that individual cognitive abilities or domains be examined with the recognition that the effect of education may be restricted to certain types of cognitive functions.

Much of the evidence that demonstrates that education is not uniformly protective of all cognitive abilities comes from studies of normal aging that have examined multiple aspects of cognition. However, the findings in the literature for the most part have been inconsistent as to which abilities are most influenced by education. Some investigators demonstrated that the effect of education extends primarily to crystallized abilities. Studies show better performance levels among those with higher levels of education on many language measures, such as WAIS Vocabulary, Information, and Similarities subtests (e.g., Christensen et al., 1997), tasks of verbal fluency and verbal comprehension (e.g., Schaie, 1989), as well as on confrontation naming (Inouye et al., 1993). For example, Inouye, Albert, Mohs, Sun, and Berkman (1993) examined the role of education as a predictor of cognitive performance in high-functioning community-dwelling elderly. The investigators observed a "striking effect" of education on many cognitive abilities. Education appeared to have differential effect on test scores, with the strongest relationship pertaining to performance on the verbal abstraction (i.e., Similarities) and naming tests, followed by a less strong relationship to performance on figure copying. Finally, a minimal relationship between education level and memory subtests was observed. Inouye et al. (1993) concluded that education “appears to confer a special advantage on tests that depend upon the use of previously learned material, such as tests of language and conceptualization.”

Christensen and Henderson (1991) compared elderly academics and blue-collar workers with Doctor of Philosophy students and young trade apprentices. The major hypothesis in the study was that the rate of decline with age on various tests of intelligence and memory would be less pronounced for the high-ability group (i.e., participants with high educational attainment). The results revealed that performance on the Similarities task from the Wechsler Adult Intelligence Scale (WAIS) was "protected" in the high ability group. However, the decline in performance on various tasks of logical and visuospatial reasoning, psychomotor speed, and verbal and nonverbal memory was not different for elderly academics and blue-collar workers. Christensen and Henderson (1991) explained that these results could be due to Similarities task being dependent on prior stored information.

Recently, Arbuckle, Maag, Pushkar and Chaikelson (1998) investigated the trajectory of intellectual development in a sample of 132 community-dwelling male army veterans of WWII, whose mean education level of 9.4 years. The M test of intelligence was used and included measures of verbal ability (i.e., verbal analogies, vocabulary and arithmetic), as well as measures of nonverbal skills (i.e., picture completion, picture anomalies and paper formboard). The results showed that education was not predictive of the level of decline in performance on any of the nonverbal measures and the arithmetic test. However, education was related to a greater gain in vocabulary and less decline on verbal analogies.

Numerous studies have shown that the effect of education extends to memory skills (Anstey & Christensen, 2000). However, some demonstrate this only in the verbal domain (e.g., Compton, Bachman, Brand, & Avet, 2000; Schmand et al., 1997).

Compton, Bachman, Brand, & Avet (2000) investigated the effects of education and continued intellectual engagement on cognitive change in highly educated adults (age range: 30 to 60 years and over), who were members of the professional and college communities in the metro Atlanta area. Neuropsychological tasks administered in the study measured verbal and nonverbal abilities and included the various WAIS-R subtests, Wechsler Memory Scale (WMS) Logical Memory, Trail Making Tests (TMT), and Wisconsin Card Sorting Test (WCST). Compton et al. (2000) demonstrated that the effect of education extended to primarily verbal abilities in the domains of abstraction and memory (i.e., WAIS-R Similarities and WMS Logical Memory). The performance on measures of primarily nonverbal abilities was not affected by education levels, and was rather significantly influenced by age.

The results of other studies that attempted to qualify the effects of education showed yet another pattern, demonstrating that the effect of education extends beyond crystallized intelligence and into domains of fluid intelligence. Investigators showed that visuospatial skills (i.e., visual constructional abilities) and visual memory ability (i.e., figure recall) can be promoted by higher educational attainment (e.g., Inouye et al., 1993; Le Carret et al., 2003). Meguro et al. (2001) examined the relationship between cognitive function, age, and education in normal elderly individuals. A thorough examination of cognitive abilities was conducted using a variety of neuropsychological measures, including tests of frontal systems (e.g., attention and working memory), language and non-language functions, visual construction, memory, and global functioning ability (e.g., orientation). Meguro et al. found that the effects of education were distributed among all tests, except Digit Symbol, which was affected by age. In general, studies demonstrate that psychomotor speed is not affected by education level (Anstey & Christensen, 2000).

With regards to the effect of education on various executive functions, the results in the literature have not been consistent. Whereas some investigators reported the effect of education on tasks of working memory, word fluency, conceptualization, and inductive reasoning (e.g., Le Carret et al., 2003; Lee et al., 2003), others found that there was no effect of education on reasoning and set-shifting tasks (e.g., Christensen & Hendersen, 1991; Compton et al., 2000).

A recent epidemiological study by Le Carret et al. (2003) provided many clues about the selective effect of education. This research is unique in its focused attempt to evaluate the impact of education on cognitive functioning and, at the same time, determine the extent to which cognition is affected by other explanatory variables, such as age, gender, occupation, leisure, and depressive symptomatology. The participants (N = 1,022) were French elderly, aged 65 and above, with education levels ranging from no schooling to over 12 years of formal education. A range of neuropsychological measures was administered, including the MMSE, Benton Visual Retention Test (BVRT), category fluency tasks, cancellation tasks, WMS Paired Associates, and WAIS Similarities and Digit Symbol Substitution Test (DSST). The investigators used the Principle Component Model of factor analysis to extract cognitive processes underlying tests. Subsequently, the effect of education and other variables on each component was examined. Le Carret et al. (2003) found a major effect of education on DSST, Similarities, WMS Paired Associates, and verbal fluency. The underlying cognitive components significantly affected by education were determined to be conceptualization abilities and highly controlled processes of attention. High attention demanding occupations also affected these components, whereas leisure activities had a more modest effect on DSST and aspects of cancellation tasks. The cancellation task was also affected by depressive symptoms. Gender was also demonstrated to play a role in affecting cognitive functioning. Specifically, females performed better on verbal tasks (e.g., verbal fluency), and males showed superior performance on nonverbal tasks (e.g., BVRT). Le Carret et al. suggested that these results have an implication for the constitution of cognitive reserve, whereby processes of conceptualization and attention that were promoted in educated subjects may provide a protective role for their cognitive functioning.

In summary, the evidence from studies that have examined the potentially selective effect of education on different aspects of cognition shows that education may not influence all cognitive abilities in a uniform fashion. While studies indicate that many cognitive domains are promoted by educational attainment, this effect does not appear to extend to psychomotor skills. Based on these previous research findings, we expect education level to differentially affect performance on measures of various cognitive domains in our SAH sample. Therefore, in the current study the effect of education on cognitive performance and recovery in SAH patients will be examined across several different domains of cognitive functioning.

7. Education and Recovery of Cognitive Functions

A. Theoretical Perspective

Variability in patient recovery from stroke or acquired brain injury has long been noted by clinicians, and factors that influence recovery have been an important focus in research. Clinicians involved in the rehabilitation of persons with cerebral insult frequently note that pre-injury factors, such as personality or intelligence, interact with brain injury to produce a complex symptom picture and contribute greatly to long-term outcome (Martelli, Bender, Nicholson, & Zasler, 2002). In addition, it has long been surmised that education level is an important "protective" pre-injury factor that affects recovery. For example, Adams and Grant (1986) suggested that the presence of premorbid risk factors, such as low education may slow brain's recovery during early abstinence period in detoxified alcoholics. As sited by Sohlberg and Mateer (2001), preinjury intelligence and education levels were shown to be significant predictors of the degree of function recovery following closed head injury (Brooks and McKinlay, 1987; Grafman, 1986). While the mechanism by which education level may promote recovery is not known, this factor appears important in evaluating long-term outcome and adaptation following brain injury or stroke.

There are compelling theoretical reasons to suggest that having a higher level of education may be beneficial for recovery. Studies of patients recovering from stroke or injury demonstrate that the adult brain is capable of functional reorganization. Neuroimaging studies have demonstrated a complex pattern of brain reorganization subsequent to recovery from stroke that can be viewed as a mechanism enabling recovery (e.g., Chollet et al., 1991; Weiller, 1995). Education and related intellectually stimulating experiences may lead to greater redundancy of neural circuits thereby allowing individuals to take advantage of an alternate neural network. In addition, cognitive requirement associated with educational activities may contribute to increased connectivity of neural networks, reflecting multiple associations among concepts (Solhberg & Mateer, 2001). Preinjury learning and practice of skill during the course of education may result in more automatization of the cognitive skill (Solhberg & Mateer, 2001), which allows for greater efficiency in task performance. The cognitive reserve theory proposed that reserve depends on the efficiency and flexibility of the brain in recruiting alternative systems (Stern, 2002). It may be the case that greater efficiency and flexibility in individuals with high cognitive reserve may render them better able to adopt and develop effective compensatory skills for impaired functions following injury to systems that supported those functions. Thus, individuals with higher levels of education or higher IQ might be able to compensate more effectively (Stern, 2003). High reserve may also provide one with better foundation to build upon during recovery, such that new strategies for problem solving can be adopted more easily in the process of compensation.

While exposure to educational experiences and innate ability appear to contribute to functional capacities and brain physiology, other factors may be considered in the recovery of more educated individuals. Among such factors are having potentially more motivation to participate in rehabilitation, having more access to services, as well as more family support (Solhberg & Mateer, 2001).

B. Education and Recovery of Functions in SAH Patients

Few prospective studies have examined recovery of cognitive functioning in SAH patients using repeated neuropsychological testing (for detailed review see Peery, 2004). These studies investigated numerous clinical and demographic variables in attempts to identify important factors that influence cognitive recovery after SAH. However, the effect of education level has largely been unexplored. A recent study of recovery that was conducted with the same SAH patient cohort as in our study covaried for education levels in order to examine the effect of other demographic and disease related variables on recovery of neuropsychological functioning (Peery et al., 2004). In this study, seven cognitive domains (identical to the ones used in our study) and a measure of overall cognition (Telephone Interview for Cognitive Status; Brandt, Spencer, & Folstein, 1988) were administered 3 and 12 months after SAH. The results revealed that diffusely distributed cognitive functions recovered over time. Factors that contributed to greater cognitive impairment included older age, anterior aneurysm location, amount and location of blood, infarctions, cerebral edema, worse clinical grade, male sex, and not speaking English. Global cerebral edema was found to have particularly negative consequences on cognitive abilities in visuospatial and visual memory domains.

To our knowledge, no studies have been conducted in SAH patients with an emphasis on education or on any other cognitive reserve variable, and only one study has included education among factors of interest (Ogden et al., 1993). Ogden et al. (1993) prospectively examined 89 patients with SAH in New Zealand, most of whom had a “good” neurological outcome on Glasgow Outcome Scale (GOS Grades 1 to 3), administering neuropsychological measures at discharge, and at 10 weeks and 12 months after SAH. They found that verbal memory skills improved and reached normal range for more than 80% of patients in the 10 weeks after SAH. These skills continued to improve throughout the 12-month period. In contrast, nonverbal memory deficits were more frequent, persistent, and severe. Despite showing some improvement, moderate to severe impairment on the Rey Complex Figure Test Recall Trial were observed in 47% percent of the patients at 12 months. In addition, patients demonstrated impairments at both follow-up assessments, and no significant improvement was apparent on tests requiring sustained attention, mental flexibility, psychomotor speed, and complex visuospatial planning and construction. Performance on other neuropsychological measures was not impaired at either follow-up and significantly improved over the recovery period.

Ogden et al. (1993) analyzed disease related factors that may impact recovery of cognitive functions. The grade at discharge was shown to be the best predictor of impairment of cognition at both follow-up assessments, whereas aneurysm site was not shown to be associated with test performance, and complications of SAH (e.g., vasospasm and hydrocephalus) had only minimal predictive value. The authors therefore concluded that the diffuse effects of SAH are more important than focal pathology in influencing cognitive outcome in SAH patients. In addition, older age was associated with slower recovery even after standardized scores were corrected for age.

In addition to analyzing disease related factors, Ogden et al. (1993) also examined the influence of premorbid IQ and education on test scores. None of the test scores were shown to be significantly associated with years of education at either follow-up assessments. The investigators noted that finding no significant association between years of education and some of the test results was surprising. However, in this sample, the number of patients with tertiary education may have been too small to show an association. Of interest, Ogden et al. (1993) did find a significant association between the National Adult Reading Test (NART) verbal IQ and the WAIS-R verbal IQ at 10 weeks and 12 months, and with the WAIS-R Similarities and Comprehension Scores at 12 months. There was also a significant association between the NART performance IQ and the WAIS-R performance IQ and Picture Completion at 10 weeks only, so that poorer scores on these measures were associated with a lower NART performance IQ. It has been argued that literacy may be a better measure of the quality education (Manly, Touradji, Tang, & Stern, 2003). Therefore, the significant associations between the NART and select test scores in this SAH patient cohort may reflect the effect of education on cognitive outcome.

III. The Purpose of the Current Study

In this study, both the independent and interactive effects of education and disease on neuropsychological outcome will be investigated in SAH patients with a wide range of education levels. In addition, the influence of education on first-year recovery will be examined. Seven domains of cognitive functioning will be considered: attention, visuospatial skills, psychomotor speed, verbal memory, language, visual memory, and executive function. The inclusion of data from multiple cognitive domains will allow us to evaluate the potentially selective effects of education on cognitive abilities.

IV. Significance

Investigating the influence of educational attainment on cognitive performance and recovery in patients who have sustained an acute brain injury from SAH is important for a number of reasons. In general, information that identifies factors that impact cognitive performance and influence recovery patterns has prognostic value. Although SAH is a rare disease, most people who suffer SAH are middle-aged and likely had planned to work for 15 or more years before retiring. For these individuals and their families, SAH often has long-term emotional and economic consequences. Therefore, providing SAH patients and their families with information regarding probable prognosis so that they can plan for the future and have realistic rehabilitation goals is very important (Ogden et al., 1993). In addition to providing a prognosis, study of neurobehavioral recovery is important because of the theoretical implications for cerebral reorganization (Kertesz, 1993). This study will also make a contribution to the cognitive reserve literature, as our findings may clarify the impact of educational attainment on cognitive performance and recovery patterns following an acute brain injury, and do so in patients who are younger than those usually assessed in studies of cognitive reserve. Finally, identifying factors associated with the ability to maintain cognitive abilities in face of brain pathology has important implications for prevention of cognitive impairment in many illnesses.

V. Hypotheses

The following hypotheses are tested in this study:

Hypothesis 1: Education level will be a significant predictor of cognitive functioning at 3 months post SAH.

Education is expected to be a significant predictor of cognitive performance in patients at 3 months post SAH in all domains of cognitive functioning that are thought to be promoted by education based on prior research. Specifically, patients with higher levels of education are expected to perform significantly better on measures of language, verbal memory, visual memory, visuospatial skills, attention, and executive functioning relative to patients with lower levels of education. No significant difference in performance on psychomotor measures is expected in patients across education levels, since this ability is believed not to be promoted by education based on prior research. The relationship of education and cognitive performance will be independent of other demographic, clinical, and radiological variables that were previously found to impact cognitive outcome in this patient cohort.

Hypothesis 2: Education level will moderate the relationship between SAH severity and cognitive functioning at 3 months post SAH.

Education will moderate the relationship between SAH severity (as measured by Hunt Hess Worst score) and cognitive performance at 3 months post SAH in all domains that are believed to be promoted by education (i.e., language, verbal memory, visual memory, visuospatial skills, attention and executive functioning, but not psychomotor skills). Thus, for individuals with low levels of education, we predict that there would be a significant relationship between SAH severity and cognitive performance, whereas for individuals with high levels of education, there would be little, if any, relationship between SAH severity and cognitive functioning. This relationship will be independent of other demographic, clinical, and radiological variables that were previously found to impact cognitive performance in this cohort of SAH patients. If this relationship is observed, it will demonstrate evidence for education serving as a buffer against the detrimental effects of injury from SAH on cognition.

Hypothesis 3: Education level will be a significant predictor of recovery of cognitive functioning at 12 months post SAH.

Recovery of cognitive functioning observed at 12 months is predicted to be significantly affected by education level. Patients with higher levels of education are expected to have more cognitive resources to cope with or compensate for processes impaired by brain injury. Thus, we expect that patients with high levels of educational attainment will demonstrate greater recovery on tasks measuring cognitive domains that are believed to be promoted by education (i.e., language, verbal memory, visual memory, visuospatial skills, attention and executive functioning domains), relative to individuals with low educational attainment. No significant difference in recovery of psychomotor skills is expected in patients across education levels. This relationship will be independent of baseline performance and of demographic, clinical, and radiological variables that were previously found to impact cognitive performance and recovery in this cohort of SAH patients.

METHODS

I. Patient Population

Three hundred and twenty-six patients with spontaneous SAH admitted consecutively to the Neurological Intensive Care Unit (NICU) of Columbia-Presbyterian Medical Center between July 1996 and March 2000 were prospectively enrolled in the Columbia University SAH Outcome Project. The diagnosis of SAH was established by computed tomography (CT scan) or by xanthochromia of the cerebrospinal fluid if the CT scan was negative. Exclusion criteria included: (a) SAH from trauma or rupture of an arteriovenous malformation; (b) admission after more than 14 days post SAH onset; and (c) age less than 18 years. The study was approved by the hospital Institutional Review Board. Written informed consent was obtained from each patient or a surrogate if the patient was incapacitated as determined by a study neurologist.

II. Follow-up Assessments

Of the 326 patients, 113 patients (34%) underwent neuropsychological testing at 3 months post SAH. Eighty two patients were neuropsychologically assessed at 3 months, and returned for reevaluation at 12 months post SAH. To examine whether the current cohort is representative of all the participants that were recruited for the study, analyses using T-tests and chi-square tests were conducted to appraise drop out rates and follow-up bias with respect to demographics and disease variables (Kreiter et al., 2002; Peery et al., 2004). The following comparisons among patient groups were made: (a) patients who were alive at 3 months post-SAH and who underwent neuropsychological testing at 3 months (N=113) were compared to patients who were alive, but did not undergo testing (N=135); (b) patients who were alive at 12 months post-SAH and completed both neuropsychological evaluations at 3 and 12 months (N=82) and those who were alive at 12 months, but did not complete both evaluations (N=166); (c) patients who completed neuropsychological testing at 3 months post-SAH (Reference Group) and returned for testing at 12 months (N=82) and those who did not return for reevaluation (N=31). See Figure 1 that depicts the follow-up rates for the 326 patients that were enrolled in the study from July 1996 to March 2000.

III. Demographic Characteristics of the Study Cohort

One hundred and thirteen participants, who comprise the larger sample, ranged in age from 19 to 86 years. Years of education averaged 11.7±4.4, with a range from 0 to 20 years. Seventy seven (68%) of the sample were women, which is consistent with findings in the literature that female gender is a risk factor for the occurrence of aneurysmal SAH (Kongable et al., 1996). One hundred and one (89%) were right-handed. Forty-eight (43%) were white, non-Hispanic; 14 (12%) were African American, non Hispanic; 49 (43%) were Hispanic; and two (2%) were Asian. Demographics of this study group (age, education, sex, handedness, and race/ethnicity) are presented in Tables 1 and 2.

The study group, consisting of those patients who were tested at both time points (3 and 12 months post SAH), totaled 82. For this group, years of education averaged 11.6±4.6, with a range from 0 to 20 years. Fifty seven individuals (70%) of the sample were women and 75 (92%) were right-handed. Thirty-two (39%) were white, non-Hispanic; eleven (14%) were African American, non Hispanic; thirty-seven (45%) were Hispanic; and 2 (2%) were Asian. Demographics of this study group (age, education, sex, handedness, and race/ethnicity) are presented in Tables 3 and 4.

There were 25 Spanish-speakers who were evaluated in their native language at 3 and 12 months post SAH.

IV. Disease Characteristics of the Study Cohort

Disease characteristics (Admission Hunt Hess grade, Worst Hunt Hess grade, aneurysm presence and location, focal SAH clot presence and location, frequency of complications (e.g., infarction, cerebral edema, hydrocephalus, and intracerebral hematoma) are presented in Table 5 for the larger cohort and in Table 6 for the recovery study cohort.

V. Procedure

1. Clinical Management

Ruptured aneurysms were treated with surgical clipping or coil embolization, with the exception of some patients whose extremely poor condition precluded immediate treatment. All patients received oral nimodipine. While patients were in NICU, transcranial Doppler (TCD) sonography was performed daily or every other day. All patients with signs of elevated intracranial pressure or hydrocephalus were treated with external ventricular drainage. More detailed description of treatment can be obtained from Kreiter et al. (2002).

2. Data Collection

A. Demographic, Clinical, and Radiological Assessment

Demographic information, including age, sex, race/ethnicity, primary language, handedness, years of education, and information with regards to past medical history were obtained by interview with the patient and/or family members shortly after admission and by review of the medical record. This information was also verified in each follow-up assessment at 3- and 12-months post SAH.

Medical condition and hospital course, including disease severity and complications, were documented prospectively. Disease severity was measured by Hunt Hess grade (from I to V) and Glasgow Coma Scale (from 3 – 15), which were obtained upon admission by a study neurologist. In addition, worst Hunt Hess grade (from I to V) during hospital stay was recorded and reflected the patient's condition as a result of SAH severity and complications. Each patient's admission, hospitalization, and discharge CT scans were independently evaluated by the study neurologist for the amount and location of SAH, intraventicular hemorrhage, intracerebral hematoma, hydrocephalus, and presence of acute infarction or cerebral edema. Fisher grade (from I to IV), which is a predictor of vasospasm (Fisher, Kistler, & Davis, 1980) and Hijdra score, which measures the amount of subarachnoid blood in 10 cisterns and fissures were documented from the admission CT for all four cerebral ventricles. Aneurysm presence and location were obtained from the medical record of the angiogram. Complications including rebleeding of the aneurysm, delayed cerebral ischemia (infarction) resulting from vasospasm, hydrocephalus, cerebral edema, and increased intracranial pressure were obtained from the medical record of the hospital course and coded dichotomously. Cerebral edema was classified as global or focal, with focal edema classified as being related to infarction, hemorrhage, external ventricular drainage, or other. At 14 days post SAH, or discharge, a brief evaluation of patient cognitive status was conducted using the Telephone Interview of Cognitive Status (TICS). In addition, handicap level was recorded using the modified Rankin scale, a 7-point scale that ranges from 0 to 6, with 6 being "death" and 0 being "no disability."

At 3- and 12-month follow-up assessments, each participant and their nearest relative or spouse were asked to complete basic outcomes assessment in their native language (English or Spanish), which included a structured interview assessing interim medical and social history, medications, rehabilitation, mood, and quality of life.

B. Neuropsychological Assessment Procedures

In addition to the basic outcomes assessment, 3 months and 12 months after the date of the SAH each participant was also asked to complete a comprehensive three-hour battery of neuropsychological tests in the participant's preferred language, either English or Spanish. Tests were administered by a trained psychometrician. See Table 7 for the list of tests by cognitive domain.

Several criteria were used during the development of this battery. First, the tests are commonly used in clinical research and are known to be reliable and valid measures with regard to the cognitive functions they purport to measure. Second, measures were selected to comprehensively assess the functional geography of both cerebral hemispheres. Third, these tests have previously been used in this population and shown to be sensitive to the effects of SAH. Finally, they can be administered to Spanish-speakers or they have equivalent forms available in Spanish. The battery for the Spanish-speakers was the same as that for the English-speakers with the exception of select language based tests (i.e., the Word Accentuation Test was substituted for the National Adult Reading Test and the Auditory Verbal Learning Test was substituted for the

California Verbal Learning Test). The tasks were administered in a fixed order to minimize interference among tests.

The following functions and specific tests were included in the battery:

1. Attention/concentration

a) Digit Span

The Digit Span subtest of the WAIS-R (Wechsler, 1981) assesses basic auditory attention span and mental tracking ability. It consists of two parts, the digits forward and digits backward. Subjects are presented with a series of digit sequences that begin with 3 digits, increase in length by one digit every other trial, up to 9 digits, for a maximum possible score of 16 points per subtest.

b) Digit Symbol

The Digit Symbol subtest of the WAIS-R (Wechsler, 1981) assesses visual scanning and visuo-motor dexterity. Participants are presented with nine pairs of digits and symbols, and they are requested to draw symbols corresponding to 93 digits as quickly as they can in 90 seconds. Their score is the number of symbols they correctly placed within the time limit.

c) Verbal Serial Attention Task (Mahurin & Cook, 1996)

This test is designed to assess mental control for over-learned material and processing speed. It is comprised of nine items. The participant is requested to say a series (e.g., days of the week or months of the year) forward and/or backward. It also includes a verbal analogue of the Trail Making Test part B, which requires one to alternate between saying numbers and letters in sequence. Time and errors are recorded with a maximum possible of 480 seconds, as timing is discontinued after 60 seconds per item.

d) California Computerized Assessment Package (Cal CAP; Miller, 1999)

This test provides assessment of attention, concentration and reaction time. It is comprised of four subtests. In the *Simple* subtest, the subject is presented single digit numbers in the center of a computer screen and asked to press the space bar each time they see a number as quickly as possible. Measures provided by the program include reaction time in milliseconds, hit rate, false positives, and misses. In the *Choice* subtest, similar stimuli are presented, and the subject is asked to press the space bar each time they see the number "7" as quickly as possible. On the *Sequence 1* subtest, the subject is asked to press the space bar each time they see the same digit presented twice in a row. On the *Sequence 2* subtest, the subject is asked to press the space bar each time they see two consecutive numbers that are in numeric order (e.g., a 1 followed by a 2, or a 4 followed by a 5). The ratio of *Sequence 1* subtest divided by *Simple* reaction time subtest was selected as a measure of attention and concentration in this study. This ratio allowed us to isolate the attention component and rule out the psychomotor speed component.

2. Executive function

a) Modified Card Sorting Test (MCST; Nelson, 1976)

This test is designed to assess the ability to form abstract concepts, to shift and maintain set, and utilize feedback. It is a modification of the Wisconsin Card Sorting Test (WCST; Lezak, 1995) in which only unambiguous stimuli are presented and no card shares more than one attribute with the key target cards. The total of 48 cards are used for a maximum possible score of 48. To complete a category, six consecutive correct responses are required, and the subject is explicitly told the rule has changed. As on the WCST, the subject is asked to sort the cards into one of four groups and is provided feedback regarding the correctness of each choice. Perseverative responses are also tabulated as a proportion of total errors for a maximum possible of 100% of errors being perseverative.

b) Trail Making Test (Lezak, 1995)

This test is composed of Part A and B. Part B of this test measures visual search, sequencing, and mental flexibility. It requires the connection, by making pencil lines, between 25 encircled numbers and letters in alternating order. Subjects are asked to work as quickly as they can without making errors. Errors are identified by the examiner during the test and the subject is asked to correct the error before continuing with the remainder of the task. The score is the number of seconds the subject takes to complete the task.

3. Verbal memory

a) California Verbal Learning Test (CVLT; Delis, Kramer, Kaplan, & Ober, 1983).

The CVLT evaluates multiple aspects of verbal memory, including an assessment of the strategies and processes involved in learning and remembering verbal material. It measures both recall and recognition of the word list over a number of trials. The examiner reads the subject a list of 16 items composed of four semantic categories with four exemplars per category in random-blocked order. The list is read five times, and after each time, the examiner asks the subject to recall as many of the items as possible. After the fifth trial, the examiner presents the subject a different list of items to remember (an interference trial). This interference trial is followed by an evaluation of the subject's free recall of the original list without any cueing. Subsequently, the examiner solicits only the words contained within each of the four categories, one by one. After a 20-minute delay, during which time nonverbal tests are administered, free recall is re-evaluated, followed by another evaluation of cued recall. Finally, subjects must identify by recognition the words that were from the original list from the list of foils.

Scores used for the present study are total raw score, long delay free recall raw score, and recognition hits. The total raw score is the sum of the number of words the subject recalled on the first five presentations of the 16-item list. The range of possible scores is 0 to 80. The long delay free recall raw score is the number of words recalled without any cues after the 20-minute delay out of the maximum possible of 16. Recognition hits is the number of words correctly identified as belonging to the original list of 16 words; no adjustment to this score was made for false-positive responses.

b) Spanish Auditory Verbal Learning Test (Artiola, Hemosillo Romo, Heaton, & Pardee, 2000).

This test is similar in construction to the CVLT and was used to test verbal memory in Spanish-speakers.

4. Visual memory

a) WMS-R VRII (Wechsler, 1987).

This subtest provides assessment of visual memory for simple designs. The subject is asked to reproduce drawings of figures 20-minutes after having seen the figures and having to draw them as part of the immediate recall condition.

b) Rey Complex Figure (Lezak, 1995).

This test assesses visual memory for complex material. Subjects are asked to draw a complex figure that they copied earlier. There is a 30-minute delay between the copy and recall conditions. Eighteen elements of the drawing are scored from 0 – 2 points, for a maximum possible score of 36 points.

5. Visuospatial skills

a) Block Design

The Block Design subtest of the WAIS-R (Wechsler, 1981) evaluates visuoconstructional ability and problem-solving. It involves a timed component which minimized ceiling and floor effects. Subjects are presented with blocks and pictured designs and are asked to construct up to nine designs that increase in difficulty, with a possible maximum score of 51 points.

b) Visual Reproduction (VR) Wechsler Memory Scale-Revised (WMS-R; Wechsler, 1987)

The purpose of this test is to provide assessment of visuospatial skill and immediate visual recall. Subjects are asked to draw four images after a 10-second exposure to each. Twenty minutes later, subjects are asked to reproduce the images from memory, assessing delayed visual recall. Finally, they are presented the images again and asked to copy them, measuring visuospatial constructional skill. The copy score, with a maximum possible of 41 points, will be used in this study as a measure of visuospatial skill.

c) Rey Complex Figure (Lezak, 1995)

This test assesses visuospatial perception and construction. Subjects are asked to copy a complex figure as carefully as they can. Eighteen elements of the drawing are scored from 0 to 2 points for a maximum possible of 36 points.

6. Language skills

a) Boston Naming Test (Kaplan, Goodglass, & Weintraub, 1983)

This test assesses confrontation naming ability. Translations into Spanish were used for assessing this ability in Spanish-speakers. Subjects are presented with pictured objects that they are asked to name. The maximum possible score that can be obtained on this measure is 60 points.

b) Token Test (Spreen & Strauss, 1998)

This 36-item version of the Token Test assesses verbal comprehension of commands of increasing complexity. It was translated to Spanish for use with the Spanish-speakers.

7. Psychomotor speed

a) Cal CAP (Miller, 1999)

The *Simple* reaction time measures the psychomotor speed of detecting the stimulus on the screen and responding by pressing a button.

b) Trail Making Test (Lezak, 1995)

Part A assesses complex visual scanning and psychomotor speed. Twenty-five numbers are presented on a page and subjects are asked to connect them in order by drawing a line from one number to the next as quickly as they can without making errors. Errors are identified by the examiner during the test and the subject is asked to correct the error before continuing with the remainder of the task. The number of seconds to complete this task is recorded.

Finally, IQ was estimated with National Adult Reading Test (NART) in English speakers. For this measure, participants are required to read words that are listed in order of decreasing familiarity and increasing phonological complexity. The Word Accentuation Test was substituted for the National Adult Reading Test for Spanish speakers.

STATISTICAL ANALYSIS

I. Data Reduction/Construction of Cognitive Domain Scores

Due to the relatively small sample size and the large number of tests that were administered, the first statistical approach sought to reduce data by combining test scores for tests that tap similar cognitive functions into seven cognitive domain composite scores (Kreiter et al., 2002; Peery et al., 2004). These cognitive domains were identified *a priori* from the literature (Lezak, 1995; Spreen & Strauss, 1998) and were validated by a principal components analysis in a previous study with this patient cohort (Peery et al., 2004). This data reduction procedure serves to reduce the number of dependent measures and to increase the validity of the measures as it permits sampling from a broader array of subtests. Cognitive domain scores served as the dependent variables in subsequent analyses. Tests selected to be included within each domain are listed in Table 7.

All raw scores at 3 and 12 months follow-up were evaluated for non-normal distributions, and scores with significantly skewed distributions were transformed. To accomplish this, we divided the skew statistic by the standard deviation of the skew statistic, and when the result exceeded ±1.96, data were transformed by square root or logarithmic transformation as necessary to satisfy the assumption of normality. Data transformation of this type improves the ability of parametric statistical tests to identify trends, while maintaining relative relationships between scores (Fleiss, 1998).

Following this normalization procedure, we computed standardized scores (z scores) for patients' test performance at 3 and 12 months follow-up. To develop standardized scores, means and SDs for the sample were calculated from the performance of subjects who complete the 3-month follow-up assessment, and by subtracting the sample mean from the raw test scores and then dividing them by the sample standard deviation. This procedure was adopted because published normative data for many tests correct for the effects of education, a variable which was investigated in this study. In addition, normative data for some tests correct for the effects of age, education and/or sex on scores, but this is not consistent across all tests. Finally, normative groups are demographically dissimilar among tests and with respect to the current patient population. Using these data, summary scores were created for the seven cognitive domains for each patient by averaging z-scores from related neuropsychological tests. The Kolmogorov-Smirnov test was used to confirm normality of all domain scores (Fleiss, 1998).

For example, we evaluated the distribution of three raw test scores that comprise the visuospatial domain (Block Design, WMS-R Visual Reproduction Copy, and Rey Complex Figure Test Copy). For each of the three raw test scores, we examined the distribution statistics, and then divided the skew statistic by the standard deviation of the skew statistic for the entire distribution of scores. The result exceeded ±1.96 for WMS-R Visual Reproduction Copy and Rey Complex Figure Test Copy, revealing substantial negative skewness. Therefore, for these tests we replaced each subject's raw score with its logarithmic transformation (Log10 (K-X)) and recalculated the sample distribution statistics (skew, standard deviation of the skew). Following this transformation, the distribution statistics reflected a normal distribution for both WMS-R VR Copy and RCFT Copy tests and the normalization procedure was concluded.

In the next step, the sample mean and standard deviation were calculated for each of the three normalized, raw test scores, and sample z-scores were created by subtracting the sample mean from a subject's test score and dividing it by the sample standard deviation to create a new sample z-score for each subject for each of the three primary test scores and at each follow-up time. This procedure ensured that all individual test scores for visuospatial measures would share the same metric, allowing direct comparisons of performance between tests and between domains. The three sample z-scores were averaged to create a summary score representing the patients' performance on tasks of visuospatial abilities relative to the scores of other subjects in the study. The normality of the final visuospatial domain score was evaluated by calculating the Kolmogorov-Smirnov statistic. This test revealed that the distribution of cognitive domain scores at 3 and 12 months follow-up is not significantly different from normal distribution ($p<0.200$).

II. Data Analysis

The present study was designed to examine the role of education in promoting select cognitive abilities, in serving as a buffer in the face of brain damage, and in affecting recovery patterns in patients 3 and 12 months post SAH.

1. Hypotheses 1 and 2: The Influence of Education on Cognitive Functioning at 3 Months Post SAH

To test the hypothesis that education is a significant predictor of cognitive performance in patients at 3 months post SAH in all domains of cognitive functioning tested except psychomotor, hierarchical multiple regression analysis was used. This procedure allowed us to adjust statistically for the effects of other demographic and disease related variables identified by previous research as independent predictors of cognitive outcome post SAH, and determine what education adds to the prediction over and above these factors. Main effect of education was evaluated after controlling for relevant covariates, including SAH severity. SAH severity was measured by Hunt Hess worst grade, as SAH is most commonly measured by this index (Hunt & Hess, 1968). Separate analyses were conducted for each cognitive domain. The cognitive domain score were entered as a dependent variable.

Our second hypothesis posited that education buffers the effect of injury from SAH on cognitive functioning. This hypothesis implies that there should be an interaction of education and SAH severity in predicting cognitive functioning. Therefore, hierarchical multiple regression analysis was used to evaluate interaction of education and SAH severity, after controlling for relevant covariates. Interaction was made available for analysis by creating a new independent variable that is a cross-product of two original independent variables (education and severity), and including it with the originals in the analysis. Education and SAH severity variables were centered (converted to deviation scores so that each variable has a mean of zero) to avoid problems with multicollinearity (Aiken & West, 1991). A significant interaction would be interpreted to signify that the relationship between SAH severity and cognitive performance varies as a function of education level. For individuals with high levels of education, we predicted that there would be little, if any, relationship between SAH severity and cognitive functioning. In contrast, for individuals with low levels of education, SAH severity will have a significant negative impact on their cognitive functioning.

In all regression models, education level and SAH severity were examined as continuous variables. This approach is thought to be more sensitive in its ability to detect significant effects when they do exist, particularly when examining the interaction effects with a relatively small sample size (Cohen, 1983). While splitting of a continuous variable is common practice in research, this approach results in loss of information and reduces the power of the statistical test. Examining education as a continuous predictor variable is also more informative, since it uses all of the information available in the predictor variable to provide direct estimates of the percentage of variance accounted for by education and effect size of this predictor variable (Aiken & West, 1991).

Post-hoc probing procedures were conducted to follow-up significant interactions in order to compare the difference in relationship between severity and cognitive domain scores at different levels of education. The procedure for post hoc tests is outlined in Aiken and West (1991). This procedure involves the computation of two conditional group variables for education level, one in which the low education group was coded by subtracting 1 SD from education level and one in which the high education group was coded by adding 1 SD to education level. One regression generated the slope for the lower education group and a second regression generated a slope for the higher education group. These slopes will then be used to plot regression lines on the basis of two equations, substituting high (1 SD above the mean) and low (1 SD below the mean) values for severity of SAH (centered) in each equation.

2. Hypothesis 3: The Influence of Education on Recovery of Cognitive Functioning at 12 Months Post SAH

To test the hypothesis that education level is a significant predictor of recovery of cognitive functioning in all domains except psychomotor, hierarchical multiple regression analysis was conducted for each domain with the inclusion of 3 months cognitive domain score in the model and the change score as the outcome variable. This allowed us to examine change in cognitive functioning over time, while holding constant the initial difference in performance. To obtain change scores, cognitive domain scores at 3 months were subtracted from the cognitive domain scores at 12 months. This method of assessing the importance of education as a predictor of cognitive change has been selected to address the fact that the range of possible change in test scores may depend on the initial score. For example, patients who demonstrated good performance on cognitive measures at the initial testing have less room to improve. Similarly, patients who demonstrated severely impaired performance at the initial testing may have sustained too much brain damage for improvement to take place. Therefore, change in test scores requires adjustment for baseline score before examining change as a function of education level. The change score method has been selected also because it has frequently been used in the literature on this topic (Albert et al., 1995, Evans et al., 1993, Shichita, Hatano, Ohashi, Shibata, & Mutazaki, 1986). Patients' performance at initial testing was entered into the model first, followed by covariates that included SAH severity, and then education. The selection of covariates was conducted as described below.

3. Covariates

Selection of covariates and their specified order of entry was based on the results of the previous study that has examined the same patient cohort and identified independent predictors of cognitive dysfunction and recovery after SAH in two or more domains (Kreiter et al., 2002; Peery et al., 2004). Based on the results of this research, the following clinical variables were considered for inclusion as covariates in multivariate analyses: global edema, left-sided infarction, and non-posterior circulation aneurysm. These and other relevant clinical and radiographic variables (e.g., focal SAH clot), as well as demographic variables (e.g., age and gender), were examined for univariate associations with cognitive domains used in this study. Domain scores that exhibit unequal variance between risk factor levels were tested with a t-test, without assuming equal variance. In order to be included in the regression model variables had to have significant relationship with a given cognitive domain.

In addition, univariate analyses of other medical risk factors that are associated with poor cognitive functioning were conducted. These included past history of cerebral infarct, head injury with loss of consciousness, seizures, SAH, and myocardial infarction. Covariates that had a significant univariate relationship with a dependent measure were entered into regression on the first step. Significance was judged at a value of $p<0.05$ for all analyses.

III. Exploratory Analyses

Since the majority of Spanish speakers (84%) were in the low education range, we were unable to control for primary language and ethnicity confounds. To address this confound and in order to ensure that excluding Spanish speakers does not alter the overall pattern of results, regression models were repeated with a subgroup of patients who are English speakers. In this analysis, hierarchical multiple regression was conducted with the neuropsychological data at 3 months post SAH.

RESULTS

I. Generalizability of Results

To appraise drop out rates and follow-up bias with respect to participants' demographic and disease variables, analyses were conducted using t-tests to examine continuous variables and chi-square tests to examine discrete variables (Kreiter et al., 2002; Peery et al., 2004).

First, patients who were alive at 3 months post-SAH and who underwent neuropsychological testing at 3 months (N=113) were compared to patients who were alive but did not undergo testing (N=135). Demographic and disease variables were compared between groups. Results are represented in Table 8. Patients who underwent neuropsychological testing at 3 months were significantly younger and less often of White ethnicity than those who did not undergo neuropsychological testing. It is likely that patients who have a high level of education will be more likely to participate in a follow-up study that entails a time-consuming neuropsychological evaluation. However, no significant difference in education was found in patients who underwent neuropsychological evaluation at follow-up and those who did not ($p>0.05$). The two groups also did not differ significantly in terms of gender and with regard to clinical disease characteristics and severity, complications, and independent functioning two weeks after SAH as determined by the modified Rankin scale ($p>0.05$). Therefore, this suggests that the performance of those patients who completed neuropsychological testing at 3 months is a reasonable estimate of the neuropsychological status of the larger group as a whole.

The second analysis of follow-up bias included a comparison between all patients who were alive at 12 months post-SAH and completed both neuropsychological evaluations at 3 and 12 months (N=82) and those who were alive at 12 months, but did not complete both evaluations (N=166). This analysis was performed to evaluate generalizability of the results of the recovery study to the remainder of the sample as well as to other SAH survivors. Results are represented in Table 9. Those who were in the study group were significantly more likely to be Hispanic and significantly less likely to be White. However, the two groups did not differ significantly in terms of age, years of education, or with regard to clinical disease characteristics and severity, complications, and independent functioning two weeks after SAH as determined by the modified Rankin scale ($p>0.05$). Since 14 variables were examined, at least one variable would be expected to be found significant at the .05 alpha level, despite no real difference between the groups. Thus, the study group is closely representative of all of the SAH patients.

The final analysis of follow-up bias included a comparison between all patients who completed neuropsychological testing at 3 months post-SAH and returned for testing at 12 months (N=82) and those who did not return for reevaluation (N=31). This was done to evaluate the equivalence of the recovery study group and reference group, which was utilized for baseline analyses so that, if not significantly different, the neuropsychological performance of the entire reference group (N=113) would be justified, thereby, providing more powerful and more reliable data for developing standardized scores. There were no significant differences between the groups at the 0.05 level (See Table 10). Thus, the recovery study group is representative of the reference group.

II. Data Reduction

1. *Raw Data*

Means and standard deviations of the study group's test performance for all patients followed at 3 months post SAH (N=113) are represented in Table 11. Means and standard deviations of the study group's performance on all tests at 3- and 12-month evaluations (N=82) are presented in Table 12. These tables, when compared to the maximal test score values shown in Table 7, shows that a ceiling effect was not operative at either time point.

2. *Cognitive Domains*

To reduce the number of variables to be submitted to a multivariate regression analysis, test scores for tests that tap similar cognitive functions were combined into seven cognitive domain composite scores (Peery et al., 2004). All raw scores at 3 and 12 months follow-up were evaluated for non-normal distributions, and scores with significantly skewed distributions were transformed. To accomplish this, we divided the skew statistic by the standard deviation of the skew statistic, and when the result exceeded ±1.96, data were transformed by square root or logarithmic transformation as necessary to satisfy the assumption of normality. Data transformation of this type improves the ability of parametric statistical tests to identify trends, while maintaining relative relationships between scores (Fleiss, 1998). See Table 13 for the list of tests that required transformations, the types of transformations that were employed.

We then computed z-scores for patients' test performance at 3 and 12 months follow-up based on the mean and standard deviation of the patient performance at 3-month evaluation. Individuals' performance on each test was standardized by subtracting the sample mean and dividing by the sample standard deviation. In cases where raw scores represented time or errors, individual performance was subtracted from the sample mean so that standardized scores were all on the same scale with good performance being higher than poor performance. Means and standard deviations for each test at each testing time are represented in Table 14. Using these data, summary scores were created for the seven cognitive domains for each patient by averaging z-scores across the related neuropsychological tests. The mean of the tests comprising each domain was then calculated for the sample at each testing time to obtain the seven domain scores for performance at 3 and 12 months post SAH. See Table 15 for domain scores' means and standard deviations for patients who underwent repeat testing.

Finally, the assumption of normal distribution of the domain scores was examined using Kolmogorov-Smirnov and skew statistical tests. All domain scores were normally distributed except those for the psychomotor ($p = 0.002$) domain. For this domain, an additional transformation by reflection and square root was conducted, which yielded a distribution that was not significantly different from the normal distribution ($p = 0.119$). For results of the Kolmogorov-Smirnov tests see Table 16. Thus, all of the domain scores were considered useable for the multivariate analysis. Of note, results of regression analyses using transformed psychomotor domain scores were not discrepant from results of analyses using scores that did not undergo an additional transformation. Therefore, psychomotor domain scores with no additional transformation were used in the regression analyses in order to preserve the original scale and ease interpretation.

III. Univariate Predictors of Cognitive Outcome

All demographic, clinical, and radiographic variables that have previously been shown to impact cognitive outcome after SAH in this patient cohort (Kreiter et al., 2002) were examined using t-tests for univariate association with cognitive domains used in the current study (See Tables 17 and 18). Significance was judged at a value of $p<0.05$ for all analyses. All domain scores were significantly worse in patients who were older (>50 years old), were not fluent in English, or were of non-white race/ethnicity. Verbal memory skills were significantly worse in males than in females. Among clinical and radiographic variables, the presence of a non-posterior circulation aneurysm negatively impacted cognitive functioning in all domains. Patients who demonstrated global edema scored lower than patients with no global edema on measures of cognitive functioning in attention, verbal memory, visual memory, and visuospatial domains. Patients with a left-sided infarction scored lower than patients with no infarction in this location in domains of attention, verbal memory, and visual memory. The presence of a focal SAH clot in the right sylvian region was associated with low scores on measures of verbal memory, visual memory, visuospatial and psychomotor skills. Focal SAH clot in the left sylvian region negatively impacted scores only in the visual memory domain, and anterior interhemispheric clot negatively impacted scores only in the verbal memory domain. Finally, the presence of right-sided infarction or of anterior communicating aneurysm was not significantly associated with cognitive performance in any of the domains. Demographic and disease variables that were shown to have significant univariate associations with cognitive performance were included as covariates in the multivariate analyses. See Table 19.

In addition, past medical and neurological histories of patients in the current study cohort were examined, and their history of substance use was recorded. Thirteen patients (12%) reported drinking two or more alcoholic beverages per day. Forty-eight patients (42%) were smokers, and six patients (5%) reported history of cocaine use. None of the patients was previously diagnosed with learning disability or dementia. Univariate analyses of other medical risk factors that are associated with poor cognitive functioning were conducted. These included past history of cerebral infarct, head injury with loss of consciousness, seizures, SAH, and myocardial infarction. None was significantly associated with any of the cognitive domains (See Table 20).

Finally, when correlations between SAH severity index (i.e., Hunt Hess Worst Score) and cognitive domain scores were conducted, there was a significant negative relationship found for all cognitive domains, except language (See Table 21). Thus, patients with more severe SAH consistently performed worse on most cognitive measures. Correlations between years of education and cognitive domain scores resulted in a significant positive relationship that was observed across all cognitive domains.

IV. Educational Attainment as a Predictor of Cognitive Outcome: Multivariate Model

1. The influence of education on cognitive functioning 3 months post SAH

The impact of educational attainment on cognitive performance at 3 months post SAH was assessed using separate hierarchical linear regression analyses for each cognitive domain. We hypothesized that after adjusting for demographic and clinical SAH factors that were previously found to impact cognitive outcome in this patient cohort, education would emerge as a significant predictor of performance in all cognitive domains except for psychomotor. Demographic and clinical SAH variables that were related to cognitive scores at the univariate level were included in the model as covariates. Covariates were entered in the model first, followed by an indicator of SAH severity (i.e., Hunt Hess Worst Score), then education. In all regression models, education level and SAH severity were examined as continuous variables. Cognitive domain score was entered as a dependent variable. In order to test our hypothesis positing that education will be a significant moderator of the relationship between SAH severity and cognitive domain scores, an interaction term was added on the final step. The interaction was made available for analysis by creating a new independent variable that is a cross-product of two original independent variables (education and severity). Education and SAH severity variables were centered (converted to deviation scores so that each variable has a mean of zero) to avoid problems with multicollinearity (Aiken & West, 1991). Finally, post-hoc probing procedures were conducted as outlined by Aiken and West (1991) to follow up significant interactions in order to compare the difference in relationship between severity and cognitive domain scores at different levels of education. Results of the final regression model for each cognitive domain are presented in Table 22. Significance was judged at a value of $p<0.05$ for all analyses.

A. Attention

After controlling for the deleterious effects of age, global edema, left-sided infarction, non-posterior circulation aneurysm, and index of SAH severity, education emerged as the most robust independent predictor of performance on attention measures, accounting for 29% of the variance (ß =0.592, *p*=0.000); (Model $R^2 = .492$). Of the SAH clinical factors, global edema was the only other independent predictor of attention scores (ß = -0.161, *p*=0.044). All of the SAH clinical factors and age accounted for 19.8% of the variance. The interaction between education and SAH severity was not significant (ß = 0.086, *p*=0.233).

B. Executive Functioning

In a regression analysis controlling for age, non-posterior circulation aneurysm, and index of SAH severity, we found that education was the most robust independent predictor of performance on executive functioning measures, accounting for 12% of the variance (ß =0.381, *p*=0.000); (Model R^2 = .352). Age was the only other independent predictor of executive functioning scores (ß =-0.217, *p*=0.012). Age and all of the SAH clinical factors accounted for 23.1% of the variance. The interaction between education and SAH severity was not significant (ß = -0.013, *p*=0.878).

C. Verbal Memory

After controlling for the effects of age, gender, global edema, left-sided infarction, non-posterior circulation aneurysm, focal SAH clots, and index of SAH severity, education emerged as a robust independent predictor of performance on verbal memory measures, accounting for 6% of the variance (ß =0.271, *p*=0.003); (Model R^2 = .479). Other independent predictors of scores in this domain were male sex (ß =-0.389, *p*=0.000), left-sided infarction (ß = -0.192, *p*=0.020), and non-posterior circulation aneurysm (ß = -0.237, *p*=0.009), with all of the covariates accounting for 40% of the variance. The interaction between education and SAH severity did not reach significance (ß =0.114, *p*=0.154).

D. Visual Memory

Education emerged as the most robust independent predictor of performance on visual memory measures after adjusting for the deleterious effects of age, global edema, left-sided infarction, non-posterior circulation aneurysm, focal SAH clots, and index of SAH severity, all of which accounted for 31% of the variance (Model R^2 = .409). Education accounted for 10% of the variance (ß=0.359, *p*=0.000). Age was the only other independent predictor of visual memory scores (ß = -0.255, *p*=0.003). The interaction between education and SAH severity was found not to be significant (ß = 0.045, *p*=0.580).

E. Visuospatial Skills

In a regression analysis controlling for age, non-posterior circulation aneurysm, global edema, anterior interhemispheric focal SAH clot, and index of SAH severity, we found that education was the strongest and the only significant predictor of performance on measures of visuospatial skills, accounting for 31% of the variance (ß =0.630, *p*=0.000); (Model R^2 = .541). None of the other factors was a significant predictor of visuospatial scores in the final model. When the interaction between education and SAH severity was tested, it was found not to be significant (ß = 0.080, *p*=0.252).

F. Language

After controlling for the effects of age, non-posterior circulation aneurysm, and index of SAH severity, education emerged as the most robust independent predictor of performance on language measures, accounting for 34% of the variance (ß =0.662, *p*=0.000); (Model R^2 = .500). Other factors were not significant predictors of language scores in the final model and accounted for 13% of the variance. To determine whether educational attainment moderated the relationship between SAH severity and language scores, the interaction was tested. The education and SAH severity interaction factor was found to be significant (ß = 0.149, *p*=0.043), and it accounted for 2% of the variance in language scores. The presence of the significant interaction informed us that the relationship between the predictor (SAH severity) and the outcome (language domain score) differed depending on the level of the moderator (education). It was then necessary to follow up this interaction with post-hoc probing procedures in order to test our hypothesis positing that SAH severity would be significantly related to language outcome at low levels of education, but not at high levels of education.

Post-hoc probing of significant moderator effect was conducted as outlined in Aiken and West (1991) and is detailed below. This procedure allows to generate two simple slopes, one slope depicting the relationship between the predictor (i.e., SAH severity) and the outcome (i.e., language scores) at a low level of the moderator (i.e., education), and the other slope depicting this relationship at a high level of the moderator. This approach also permits one to test whether either of the simple slopes is significantly different from zero. To accomplish this, two new conditional group variables for education level were computed, one in which the low education group was coded by subtracting 1 SD from the mean education level and one in which the high education group was coded by adding 1 SD to the mean education level. We then ran two regression analyses incorporating each of these new variables. One regression analysis generated the slope for the lower education group (1 SD below the mean; 7 years of education), and a second regression generated a slope for the higher education group (1 SD above the mean; 16 years of education). These slopes were then used to plot regression lines on the basis of two equations, substituting high (1 SD above the mean; Hunt Hess Worst Score = 3.93) and low (1 SD below the mean; Hunt Hess Worst Score = 1.67) values for severity of SAH (centered) in each equation. Post-hoc regression analyses revealed that for patients with lower educational attainment (i.e., 7 years of education), higher grade of SAH severity was significantly associated with lower scores on language measures (ß = -.266, p=0.016). However, for patients with higher levels of education (i.e., 16 years of education), the association between SAH severity and language scores was not significant (ß = 0.050, p=0.626). That is, the relationship between SAH severity and performance on language measures was moderated by the level of educational attainment, such that at lower levels of education, a significant negative relationship was present between SAH severity and language scores, and at higher levels of educational attainment, there was no significant relationship between severity and language scores. Figure 2 depicts the slopes of the regression lines for high and low educational attainment, 1 SD above and below the mean, respectively, and reflects the relationship described above.

The procedure described above was also used to generate slopes for other values of the moderator. Additional post-hoc regression analyses revealed that for patients with 9 years of education, a higher grade of SAH severity was significantly associated with lower scores on language measures (ß = -.187, p=0.029). However, for patients with 10 years of education, the association between SAH severity and language scores did not reach significance (ß = -0.147, p=0.057). Furthermore, there was no significant relationship between severity and language scores for patients who were high school graduates (i.e., 12 years of education; ß = -0.068, p=0.362) or patients who had one additional year of education post high school (i.e., 13 years of education; ß = -0.029, p=0.724). Figure 3 depicts the slopes of the regression lines for the various levels of educational attainment.

<u>*G. Psychomotor Skills*</u>

After controlling for the effects of age, non-posterior circulation aneurysm, focal right sylvian SAH clot, and index of SAH severity, education emerged as a robust independent predictor of performance on psychomotor measures, accounting for 16% of the variance (ß =0.445, *p*=0.000); (Model R^2 = .425). Age was the only other significant independent predictor of scores on psychomotor measures (ß = -0.296, *p*=0.000), accounting for 21.3% of the variance. The interaction between education and SAH severity was not significant (ß = -0.006, *p*=0.941).

2. The influence of education on recovery of cognitive functioning from 3 to 12 months post SAH

To test the hypothesis that education level is a significant predictor of recovery of cognitive functioning from 3 to 12 months post SAH in all domains except psychomotor, separate hierarchical multiple regression analyses were conducted for each domain with the inclusion of the baseline score (i.e., the 3-months cognitive domain score) in the model and the change score as the outcome variable. This allowed us to examine change in cognitive functioning over time, while holding constant the initial difference in performance (Albert et al., 1995; Evans et al., 1993; Shichita, Hatano, Ohashi, Shibata, & Mutazaki, 1986). To obtain change scores, cognitive domain scores at 3 months were subtracted from the cognitive domain scores at 12 months. Patients' performance at initial testing was entered into the model first, followed by covariates (i.e., age, SAH severity, and other factors identified as independent predictors of recovery in this cohort; Peery et al., 2004) and then, education. Education level and SAH severity were examined as continuous variables. Results of the final regression model for each cognitive domain are presented in Table 23. Significance was judged at a value of $p<0.05$ for all analyses.

A. Attention

After adjusting for the baseline score and controlling for the effects of age and SAH severity, education emerged as the most robust independent predictor of improvement in performance on attention measures, accounting for 16.5% of the variance (ß =0.548, *p*=0.000); (Model R^2 = .202). The baseline score was the only other independent and robust predictor of change in attention scores (ß =-0.536, *p*=0.000).

B. Executive Functioning

In a regression analysis controlling for the effects of the baseline score, age, and SAH severity, the main effect of education did not reach significance (ß =0.188, *p*=0.094); (Model R^2 = .372). Education accounted for 2.4% of the variance, while the baseline executive functioning score accounted for 27% of the variance and was shown to be the most robust predictor of change in this domain (ß = -0.653, *p*=0.000). Finally, age (ß = -0.213, *p*=0.037) and SAH severity (ß = 0.195, *p*=0.044) were also shown to be significant predictors of change. Thus, while a higher level of education was associated with higher scores on the executive functioning measures at 3 months post SAH, education level did not significantly impact recovery in this cognitive domain.

C. Verbal Memory

After adjusting for the baseline score and controlling for the effects of age and SAH severity, education emerged as a robust independent predictor of improvement in performance on verbal memory measures, accounting for 5.6% of the variance (ß =0.259, *p*=0.035); (Model R^2 = .146). The baseline score was the only other independent and robust predictor of cognitive change (ß =-0.394, *p*=0.002), accounting for 7% of the variance.

D. Visual Memory

Education emerged as the most robust independent predictor of improvement in performance on visual memory measures after adjusting for the baseline score and controlling for the effects of age, global edema, and SAH severity (ß = 0.396, *p*=0.002). Education accounted for 11% of the variance (Model R^2 = .225). The baseline score (ß =-0.286, *p*=0.036) and global edema (ß = 0.242, *p*=0.042) were also significant predictors of cognitive change, whereas age and the severity index did not significantly impact change in scores over time.

E. Visuospatial Skills

Education emerged as the most robust independent predictor of improvement in performance on visuospatial skills after adjusting for the baseline score and controlling for the effects of age, global edema, and SAH severity (ß = 0.447, *p*=0.002). Education accounted for 9.5% of the variance (Model R^2 = .286). The baseline score (ß =-0.352, *p*=0.018) and global edema (ß = 0.242, *p*=0.033) were also significant predictors of cognitive change, whereas age and SAH severity did not significantly impact change in scores over time.

F. Language

After controlling for the effects of the baseline score, age, and index of SAH severity, education was found to be a significant independent predictor of recovery on language measures, accounting for 8.5% of the variance (ß =0.446, *p*=0.012); (Model R^2 = .165). The baseline score (ß = -0.432, *p*=0.014) and age (ß = 0.293, *p*=0.016) were also significant predictors of cognitive change, accounting for 7% of the variance, whereas SAH severity did not significantly impact change in scores over time.

G. Psychomotor Skills

In a regression analysis controlling for effects of the baseline score, age, and SAH severity, the main effect of education was significant (ß =0.221, *p*=0.034), suggesting that education is the most robust predictor of improvement in scores on psychomotor measures after the baseline score (ß = -0.792, *p*=0.000). Education accounted for 3.5 % of the variance, while the baseline score accounted for 38.8% of the variance (Model R^2 = .438). None of the other factors was significant predictors of change in psychomotor scores in the final model.

3. Supplementary Analysis

Since the majority of Spanish-speakers (84%) were in the low education range (i.e., 0 to 11 years of education), we were unable to control for primary language and ethnicity confounds. However, when regression models were repeated using the neuropsychological data at 3 months post SAH and confining analyses to a subgroup of patients who are English-speakers, the overall pattern of results was not altered, except for the visual memory domain where the main effect of education did not reach significance (ß = 0.161, *p*=0.158) and for language, where the interaction effect was a trend (ß = 0.193, *p*=0.074) (See Table 24).

DISCUSSION

I. Summary of Regression Findings

The current study examined the influence of educational attainment on cognitive functioning at 3 months after SAH and on the rate of recovery of cognitive functioning from 3 to 12 months after SAH. Seven cognitive domains were examined: attention/concentration, language, verbal memory, visuospatial skills, visual memory, psychomotor speed, and executive functions. After controlling for the influence of age, sex, SAH severity, and disease complications, education emerged as a significant predictor of outcome in all domains of cognitive functioning at 3 months post SAH. Education also moderated the relationship between SAH severity and language scores, such that at lower levels of education, a significant negative relationship was present between SAH severity and language scores, and at higher levels of education, there was no significant relationship between severity and language scores. When the impact of educational attainment on recovery of neuropsychological functioning from 3 to 12 months after SAH was examined, results indicated that higher educational attainment was strongly associated with better recovery rates for all cognitive domains, except for executive functioning. These results were obtained after controlling for the initial performance, SAH severity, age, and other SAH-related complications.

II. The Influence of Education on Cognitive Functioning at 3 Months Post SAH

As was hypothesized, education emerged as a significant independent predictor of scores at 3 months post SAH on measures of attention, executive functioning, verbal memory, visual memory, visuospatial skills, and language. Education was also a significant independent predictor of psychomotor scores, which was contrary to our expectations based on the previous findings in the literature (Anstey & Christensen, 2000). This discrepancy appears to be due to the fact that studies have used different measures to evaluate psychomotor speed. In our study, we used the Trail Making Test A (TMT A) and the Cal CAP (Simple Reaction Time) tests to assess abilities in this domain, while other studies have utilized the WAIS-R Digit Symbol (Compton et al., 2000; Meguro et al., 2001) or the Symbol Digit Modalities test (Christensen & Hendersen, 1991). While the results of these studies did not reveal the effect of education on psychomotor abilities, other investigators who have used the TMT A did find the effect of education on performance in this domain (e.g., Le Carret et al., 2003).

In all cognitive domains, a higher education level was strongly associated with better test performance, irrespective of the severity level of SAH. Moreover, the strength of these associations generally exceeded those of the disease-related variables and other demographic variables we analyzed. For example, Kreiter et al. (2002) showed that global edema was a significant predictor of scores in domains of verbal memory, visual memory, and visuospatial skills. Our results showed that global edema was no longer a significant predictor of scores in these domains after other predictors, including education, were entered into the regression model. Global edema remained a significant predictor of performance in the attention domain, however, education was a more robust predictor of attention scores. For verbal memory, left-sided infarction, non-posterior circulation aneurysm, and male gender remained significant predictors of test scores, however, the main effect of education was significant after controlling for these and other important demographic and disease-related variables. As often observed, older age negatively impacted test performance, and this effect reached significance for the executive functioning, visual memory, and psychomotor domains. Finally, a higher level of SAH severity (i.e., Hunt Hess Worst score) had a negative effect on cognitive performance for all domains, however, there was no main effect of SAH severity in any of the regression models after controlling for other SAH-related factors, complications, and education.

Our hypothesis that education would be a significant moderator of the relationship between SAH severity and cognitive performance was supported only for the language domain. For this domain, higher grade of SAH severity was significantly associated with lower scores on language measures for patients with lower educational attainment (i.e., $\leq 9^{th}$ grade), whereas this association was not significant for patients with higher levels of educational attainment (i.e., $\geq 10^{th}$ grade). Thus, our results show that education was significantly associated with cognitive domain scores irrespective of SAH severity, except in the language domain, where severity did impact language scores at low levels of education. This provides evidence for the moderating or buffering effect of education for language abilities in the face of acute brain injury.

The results of our regression analyses for language suggest a “dose effect” of education, whereby the lower the education level, the stronger the association between the severity of SAH and lower test scores. These findings are consistent with the findings in patients with white matter lesions, where it was observed that the lower the education level, the stronger the association between severity of white matter hyperintensities and lower cognition (Dufoil et al., 2003). It is important to note that education beyond the nine-year level was not associated with additional “protection” by buffering cognition against injury. This suggests a threshold for a benefit of education, whereby a minimal duration of education is required for it to serve as a protective factor. This is consistent with some observations made in the aging literature, where education beyond the 9th grade was not associated with additional reductions in cognitive decline (Lyketsos et al., 1999).

In summary, the results of our analyses of the data collected at 3-month follow-up revealed that higher education is a significant predictor of better scores on cognitive measures, irrespective of the level of SAH severity. These findings also provide evidence that higher education mitigates the severity of the cognitive decrements associated with SAH. These results are consistent with the cognitive reserve theory that suggests that individuals with higher levels of education will be better able to maintain higher levels of cognitive functioning in the face of brain injury, possibly through taking advantage of an alternate neural network (Stern, 2002).

III. The Influence of Education on Cognitive Recovery at 12 Months Post SAH

In this study, we also explored whether education level was related to recovery of cognitive functioning from 3 to 12 months post SAH. Our hypothesis, positing that educational attainment will be a significant predictor of recovery, was corroborated for all cognitive domains, except executive functioning. For executive functioning, the regression analysis revealed a statistical trend for education, whereas the initial performance (i.e., score at 3 months post SAH), age, and SAH severity were significant predictors of recovery in this domain.

The finding that education was not a significant predictor of recovery in executive functioning is in contrast to our findings at baseline that pointed to education as the most robust predictor of performance on measures in this domain, age being the only other independent predictor. Our hypothesis that education will significantly affect change in executive functions was based on the results of studies that reported the effect of education on tasks of working memory, word fluency, conceptualization, and inductive reasoning (e.g., Le Carret et al., 2003; Lee et al., 2003). However, the results in the literature have not been consistent. For example, some investigators found that there was no effect of education on reasoning and set-shifting tasks (e.g., Christensen & Hendersen, 1991; Compton et al., 2000). In our study, we used the Modified Wisconsin Card Sorting Test (MWCST; Accuracy and Perseverative Errors) and the Trail Making Test B (TMT B; completion time) to evaluate patients' executive functions. Abilities that these tests target include abstraction, problem-solving, set-shifting, and strategic planning. Our data suggest that a higher level of education may lead individuals to have higher baseline scores on measures of these abilities, however, higher education does not appear to significantly influence the recovery of these functions. Instead, the recovery of these functions was better predicted by factors, such as age, whereby younger patients showed more recovery.

One possible explanation for the lack of significance of the main effect of education for executive functioning is that this domain is different from other cognitive domains in that it is comprised of higher order abilities that depend on many underlying functions. For example, a successful completion of the Modified WCST requires abilities that include intact attention, working memory, and visuospatial functioning, as well as the ability to verbally mediate one's own performance. Thus, the recovery in executive functions appears to depend on the recovery of many underlying cognitive functions. In fact, Ogden et al. (1993) observed that deficits in executive functions (e.g., mental flexibility) were among the most persistent deficits in SAH patients. The improvements enabling the brain to integrate multiple abilities in order to perform more complex tasks may be more dependent on factors, such as age and the extent of injury to the brain, as was observed in our study. Alternatively, it is possible that more time is required to observe recovery in this domain, and that during this time more educated patients will begin to show more improvement as they become better able to utilize alternative methods in solving problems in order to compensate for their deficits.

In terms of other domains, education was the strongest predictor of recovery in visual memory, visuospatial skills, and language. Peery et al. (2004) found that the presence of global cerebral edema had particularly negative consequences for recovery of cognitive abilities in visuospatial and visual memory domains. Specifically, these authors reported that patients with cerebral edema demonstrated worse performance on visual memory tasks at 3 months, but faster recovery by 12 months, resulting in less difference between those with and without cerebral edema by one year. However, our analyses showed that while global edema remained a strong predictor of recovery in these domains, once education was entered into the model, education emerged as a more robust predictor of cognitive recovery. Gender was not found to be a significant predictor of visual and verbal memory. For all domains, performance at 3 months post SAH was a significant predictor of change from 3 months to 12 months post SAH, whereby patients with lower scores at baseline demonstrated the most improvement, as they likely had more room to improve. It should be noted, that, while we observed improvements in cognitive abilities across all domains, particularly among patients with lower scores at baseline, individuals within our sample demonstrated varying slopes of recovery, with some patients showing little or no improvement over time. For example, some patients who demonstrated good performance on cognitive measures at the initial testing may have demonstrated similarly high-level performance at follow-up, having had less room to improve. Similarly, patients who demonstrated severely impaired performance at the initial testing may have sustained too much brain damage for improvement to take place. Adjusting for the baseline score allowed us to control for these differences in the initial level of performance before examining cognitive change over time as a function of education level. However, additional analyses would be required to identify "non-improvers" within our sample and to draw conclusions with regard to factors that influenced their performance on cognitive measures.

Finally, a finding that education was a significant predictor of change in psychomotor scores was contrary to our expectations based on previous findings in the literature (Anstey & Christensen, 2000). This finding was consistent with results of our analyses of the psychomotor data at baseline. As discussed above, the discrepancy between the results obtained for psychomotor domain in this study and the findings for this domain in previous studies is likely due to the fact that different measures were used to evaluate psychomotor speed.

IV. Cognitive Reserve and Recovery of Cognitive Functioning

Our finding demonstrating differential rates of recovery as a function of education is consistent with the repeated observation that education level appears to be a "protective" pre-injury factor that affects recovery (Solhberg & Mateer, 2001). For example, preinjury intelligence and education levels were shown to be significant predictors of the degree of function recovery following closed head injury (Brooks and

McKinlay, 1987; Grafman, 1986). In addition, the presence of premorbid risk factors, such as low education, was shown to slow brain's recovery during early abstinence period in detoxified alcoholics (Adams & Grant, 1986).

There are compelling theoretical reasons to suggest that having a higher level of education may be beneficial for recovery. Education and other intellectually stimulating experiences may lead to greater redundancy of neural circuits. The cognitive requirement associated with learning activities leads to building multiple associations among concepts and, thus, may lead to increased neuronal interconnectivity (Solhberg & Mateer, 2001). In addition, learning and practice of skill during the course of education may result in more automatization of the cognitive skill which allows for greater efficiency in task performance (Solhberg & Mateer, 2001). As a result of these processes that enable greater efficiency and flexibility in utilization of neuronal networks, the brain is optimized against injury, or one can be said to have a greater cognitive reserve capacity. This argument is in line with the cognitive reserve theory that posits that reserve manifests itself in the efficiency of neural networks and in the ability of the brain to recruit alternative neural systems (Stern, 2002). It is likely that factors that promote interconnectivity and redundancy of neural circuits not only help the brain to withstand injury, but also increase the brain's capacity for reorganization once injury occurs. Studies of patients recovering from stroke or injury demonstrate that the adult brain is capable of functional reorganization (Seitz, Kleiser, & Butefisch, 2005). Neuroimaging studies have demonstrated a complex pattern of brain reorganization subsequent to recovery from stroke that can be viewed as a mechanism enabling recovery (e.g., Chollet et al., 1991; Weiller, 1995). As cortical areas undergo synaptic reorganization and novel synaptic connections are established (e.g., through axonal sprouting and formation of long-term potentiation), the presence of greater redundancy and interconnectivity among neural networks may result in better rewiring capacity or plasticity, rendering individuals with higher levels of cognitive reserve better able to adapt and compensate for injured processes. Thus, a higher cognitive reserve capacity may provide one with a better foundation to build upon during recovery.

In SAH patients, Ogden et al. (1993) examined the influence of premorbid IQ and education on test scores, and they found significant associations between the NART and select test scores at 12 months, which may reflect the effect of education or literacy on cognitive outcome. These investigators suggested that many cognitive difficulties observed in SAH patients are likely to be associated with underlying impairments of concentration and the ability to process information more efficiently, possibly as a consequence of acute encephalopathy. Thus, even subtle cognitive impairments would necessitate greater effort to carry out tasks that would have been relatively easy before the SAH. The results of our study showed that SAH patients with higher levels of education demonstrated more improvement, possibly because they were better able to recruit additional neural resources for cognitive control and task performance.

While the mechanism by which education level may promote recovery is not known, the results of our study once again point out that education is an important factor to consider when evaluating outcome and adaptation following brain injury or stroke. However, it should be noted that while exposure to educational experiences appears to contribute to recovery of cognitive capacities, other factors need to be considered. For example, more educated individuals may be more motivated to participate in rehabilitation and may have more family support or more access to care (Solhberg & Mateer, 2001).

V. Education and Cognitive Functioning: Is the association causal?

The association between higher education and better cognitive functioning could be causal. If this is the case, then education truly promotes cognitive abilities and moderates the effect of brain injury on cognition, possibly through the mechanisms of brain reserve (e.g., increased number of synapses) and/or cognitive reserve (e.g., increased efficiency in utilizing brain networks). However, the association between education and cognitive functioning could also be confounded by other factors, such as intellectual ability or IQ, which may be the true causal link. If this is the case, then it could be that individuals with higher IQ or intelligence (genetically based or a function of environmental exposure) tend to pursue higher education. Still, education may impart reserve over and above that obtained from innate intelligence (Stern, 2002). The association between education and cognitive ability can also be mediated by factors, such as occupational attainment or mentally stimulating leisure activities, which can promote cognitive functioning throughout life. However, studies have demonstrated separate or synergistic effects for education, occupational attainment, and leisure activities, suggesting that each of these experiences contributes independently to reserve (Stern et al., 1994; Stern, Alexander, Prohovnik et al., 1995).

It is also possible that higher education is a surrogate for other factors, such as the socioeconomic status and access to care. Individuals with higher educational and occupational attainment also tend to adopt lifestyles (e.g., exercise and diet), which themselves causally reduce the risk of cognitive dysfunction after brain injury.

Interestingly, studies of aging that have carefully controlled for such factors found that the association between education and cognitive decline remained strong (e.g., Bennet et al., 2003; Butler et al., 1996). For example, Butler et al. (1996) found that cognitive decline occurred earlier in life for Catholic sisters aged 85 or older with lower levels of education. The lifestyles in the sample (e.g., communal dining, health care, and teaching occupation) were remarkably homogeneous. These sisters also enjoyed similar social support and intellectual stimulation. This minimized the influence of many variables that typically correlate with education, narrowing the range of explanations for the observed associations with education (Butler et al., 1996). Nonetheless, the extent to which various life-time experiences and innate factors influence reserve is unclear. Cognitive reserve is most likely multifactorial in nature, and a complex interplay of factors may be at work in building reserve.

VI. Education, Ethnicity, and Primary Language

The results of previous research (Kreiter et al., 2002) examining the predictors of cognitive outcome in this patient cohort suggested that nonwhite ethnicity and that the lack of fluency in English were associated with low scores in a number of cognitive domains. In addition, Peery et al. (2004) reported that English speakers significantly outperformed Spanish speakers on measures of visuospatial abilities. These authors noted that primary language, English or Spanish, was not expected to have an impact on cognition, since the tests were all conducted in the patients' preferred language. Our finding that education level is significantly associated with cognitive outcome post SAH in all cognitive domains may help to clarify these previously obtained findings. In this cohort of SAH patients, primary language and ethnicity variables were confounded with education. The majority of patients who were primarily Spanish-speakers (84%) were in the lower education range, as they did not graduate from high school (0 to 11 years of education; mean = 7 years). Similarly, the mean education level for nonwhite patients was 9.68 years (range 0 to 16 years), whereas the mean education level for whites was 14.42 years (range 9 to 20 years). Thus, the associations between nonwhite ethnicity and the lack of English fluency with poor cognitive outcome found in previous studies (Kreiter et al., 2002; Peery et al., 2004) likely represent the effect of low educational attainment on cognition.

Nonetheless, it is possible that cultural experience also affects performance on cognitive tests. For example, it has been shown that cultural experience influences how African Americans approach neuropsychological tasks and that this effect is independent of the quality of education (Manly, Byrd, Touradji, & Stern, 2004). The effects of culture may reflect differences in educational background, cultural value systems, and/or test-wiseness (i.e., familiarity with a test situation and presumed examiner demands). However, in our study, it is unlikely that the observed associations between education and cognitive outcome were due to differences in primary language or in cultural experience that differed for English- and Spanish-speakers. In the current study, when regression models were repeated using the neuropsychological data at 3 months post SAH and confining analyses to a subgroup of patients who are English-speakers, the overall pattern of results was not altered, except for the visual memory domain where the main effect of education did not reach significance, and for language, where the interaction effect was a trend. The difference in findings in the case of visual memory and language domains may be due to the fact that the analyses for these domains were conducted using a smaller sample and a more restricted range of education. For an interaction effect, a larger sample size may be necessary in order to achieve adequate statistical power. However, the discrepancy in findings for visual memory may also suggest that performance on visual memory measures may have been influenced by cultural variables. In fact, studies show that cultural characteristics can account for some differences in scores for nonverbal measures. For example, Jacobs et al. (1997) compared the test performance of English and Spanish speakers matched for age and education. Spanish speakers scored significantly lower on almost all of the nonverbal measures (including the Benton Visual Retention Test), whereas no significant differences in performances between these two groups were observed for language-based measures. Of note, in our study, the test scores comprising the Verbal Memory domain included a test developed for Spanish-speakers, as opposed to a direct translation, which may have removed cultural, linguistic, or educational bias. Additional research is necessary to better understand the effect of specific cultural and educational factors on cognitive test performance in order to develop more culture-fair measures (Manly et al., 2002).

VII. The Effect of Education on Global Cognitive Functioning

While the focus of this study was to examine the potentially selective effects of education on aspects of cognition, and, therefore, the seven different cognitive domains were analyzed separately, an analysis of all of the domains combined may yield a more clinically sensitive indicator of global cognitive functioning and cognitive change over time. Thus, on an exploratory basis, we evaluated the effects of education on overall cognitive functioning at baseline and over the nine-month interval. A global cognitive functioning score was computed by averaging the seven cognitive domain scores and was then used as a dependent variable in the regression analysis of the baseline data. The difference between the global cognitive functioning scores from 3 to 12 months post SAH was used as a dependent variable in regression analysis of recovery. The selection of covariates to be included in these regression models was guided by the results of prior research that identified independent predictors of global mental status post SAH (Kreiter et al., 2002; Peery et al., 2004). In these studies, global mental status was measured with the Telephone Interview for Cognitive Status (TICS; Brandt, Spencer, & Folstein, 1988). This test correlates highly with the Mini-Mental State examination, and it samples multiple domains of cognitive functioning, including orientation, mental tracking, immediate and delayed verbal recall of a 10-word list, information, repetition, and motor inhibition (Lezak, 1995).

The results of our exploratory analyses showed that after controlling for the effects of age, gender, and an index of SAH severity, education emerged as the most robust independent predictor of the overall cognitive performance, accounting for 30% of the variance (ß =0.587, p=0.000); (Model R^2 = .566). Other predictors were also significant and, altogether, accounted for 26% of the variance. The interaction between education and SAH severity was not significant (ß = 0.091, p=0.161). See Table 25. When recovery of overall cognitive functioning was examined, after controlling for the effects of the baseline score, age, and the SAH severity index, education was found to be a significant independent predictor, accounting for 12.3% of the variance (ß =0.485, p=0.001); (Model R^2 = .173). The baseline score (ß = -0.467, p=0.003) was also a significant predictor of the overall change in cognitive functioning, accounting for 3.2%

of the variance, whereas SAH severity did not significantly impact change in scores over time. See Table 26.

It should be noted that whereas a global measure of cognitive functioning must be included in future studies when analyzing the effects of education, it is important that individual cognitive abilities also be examined with the recognition that the effect of education may be restricted to certain types of cognitive functions. For example, Anstey & Christensen (2000) concluded in their recent review of empirical data from studies in normal aging that education affected maintenance of mental status, memory and crystallized abilities, whereas education did not affect abilities on speed tasks.

VIII. Generalizability of the Results

The pool of participants was evaluated for any follow-up bias since any systematic pattern of dropout from the study had the potential to skew the results toward reflecting the characteristics of only the remaining participants. Participants who were tested at 3 and 12 months (N=82) were found to be more often Hispanic than the rest of the study patients who were alive at 12 months post SAH but did not complete both evaluations (N=166). Considering the demographics of the neighborhood immediately surrounding the hospital where these data were collected, it is likely that this finding reflects the composition of the local community. Living nearby, it was more convenient to return to the hospital for follow-up, as well as more likely that soon after the SAH, local Hispanics were taken directly to Columbia, as opposed to another hospital. Regarding disease characteristics, age, and sex, the study group is comprised of a typical sample of the patients who qualified for participation. As such, generalization of the results from the current study to other SAH populations would seem to be valid.

When the 14 disease-related and demographic variables were examined, no differences were found between patients who completed neuropsychological testing at 3 months post SAH and returned for testing at 12 months (N=82) and those who did not return for reevaluation (N=31). Thus, the recovery study group (N=82) was considered representative of the larger reference group (N=113), suggesting that the effect of education on recovery rate found for those who completed both evaluations may be generalized to all those who were tested at the 3-month follow-up.

The comparison between those patients who underwent testing at 3 months (N=113) and patients who did not undergo testing (N=135) revealed that patients who were tested were younger and more likely to be Hispanic than those who were not. The ethnicity factor was likely influenced by the hospital's catchment area, which is located in a Hispanic community. As there were no differences between the reference group (i.e., patients who were examined at 3 months) and the recovery study group (i.e., patients who were examined both at 3 and 12 months), as stated above, the difference in ethnicity is likely to reflect the recovery study group as well. While the results of the current study may be more accurately generalized to a younger contingent of patients, the generalization of results to other SAH populations remains valid to the extent that the differences between the study group and the rest of the sample were due to proximity of the hospital to their homes.

IX. Strengths of the Current Study

The current study has several strengths. First, this study is prospective and patients were followed longitudinally at 3 and 12 months post SAH. This allowed us to examine the effect of education, while controlling for various factors that may have influenced performance at baseline. The absence of longitudinal data in many studies investigating the effect of education or other proxies of cognitive reserve (e.g., occupation) limits clear interpretation and synthesis of study findings. Second, our sample contained patients with a wide range of education levels (0 to 20 years), which was rarely found in studies that have investigated the effects of education. The wide range of education allowed us to examine the possible "dose effect" of education on cognitive outcome. Third, whereas many studies of cognition in patients post SAH and most studies of the effects of education on cognition use only a few neuropsychological measures to evaluate outcome, we used a comprehensive neuropsychological battery, covering a broad range of cognitive abilities. An extensive battery is more likely to detect cognitive deficits and recovery in cognitive functioning, and it also allowed us to investigate the potentially selective effects of education.

In terms of methodology, examining education as a continuous predictor variable in the multiple regression analysis is more informative, since this approach uses all of the information available in the predictor variable to provide direct estimates of the effect size and percent of variance accounted for (Aiken & West, 1991). Researchers have frequently utilized median splits or taken upper and lower quartiles for their continuous variables when using analysis of variance. While splitting a continuous variable is common practice in research, this approach results in the loss of information and reduces the power of the statistical test.

Finally, our study group was quite heterogeneous, including nonaneurysmal patients and patients with ruptured aneurysms in various locations, as well as patients of all clinical grades. Thus, the results of the current study should generalize to most SAH patients. Also, our data have been obtained from a multiethnic sample, and thus, the results can be generalized to patients of varied ethnic and cultural backgrounds.

X. Possible Limitations of the Current Study

1. Practice Effects

In order to examine recovery from 3 to 12 months post SAH, the design of the current study called for repeated administration of a neuropsychological test battery. Patients were evaluated on two separate occasions (mean time interval = 9.5 months). Repeated neuropsychological testing raises the possibility that improvement observed between the two follow-ups may be explained by practice effects, rather than "real" change in cognitive status.

There are, however, a number of reasons practice effects likely do not explain the current findings. First, practice effects vary as a function of test-retest interval, whereby shorter retest intervals tend to enhance practice effects (Dikmen, Heaton, Grant, & Temkin, 1999). Some neuropsychologists argue that practice does not typically have a significant effect beyond two months after the initial testing (Spreen & Strauss, 1991), but clinicians typically wait six months before retesting patients on standardized measures. Dikmen et al. (1999) found that there was a significant drop in the effects of practice when the test-retest interval was greater than three months. In the current study, the mean interval between the two follow-up evaluations was over nine months, and therefore improvements in cognitive functioning that were observed in this cohort are less likely to be due to practice effects.

Second, in a study of test-retest reliability and practice effects in 384 normal and neurologically stable adults who were evaluated on the Expanded Halstead-Reitan

Neuropsychological Test Battery, Dikmen et al. (1999) showed that the amount of test-retest changes due to practice effects is not uniform across participants, and that practice effects vary as a function of participant characteristics. For example, individuals who are younger tend to benefit more from practice than older individuals. However, no significant effect of age on cognitive change was observed in the current study or in the previous study by Peery et al. (2004). Dikmen et al. (1999) also found that more cognitively able individuals (i.e., defined as having better Digit Symbol performance on the initial evaluation) benefit more from practice. In the current study, patients of all clinical grades (i.e., Hunt Hess Worst Grades 1 through 5) were evaluated, and it may be possible that practice effects were only operative among less cognitively impaired patients. However, this was not observed since there was a significant negative association between the baseline score and improvement for all cognitive domains. This finding is more consistent with the interpretation that more cognitively impaired patients are more likely to improve because they have more potential for improvement, rather than their improvement being due to practice. Furthermore, in the SAH literature, Stabell and Magnaes (1997) argue that practice effects are not likely to introduce significant variability in a sample of patients with memory impairments, as was true in the current study.

Importantly, Dikmen et al. (1999) also noted that among participant characteristics, level of education can affect the magnitude of practice effects, whereby better-educated individuals may benefit more from practice. However, in their study, this was observed only for tasks with problem-solving or novelty components (i.e., Category Test and measures that comprise PIQ). In our test battery, the Modified WCST, a measure of executive functioning, also involves these components. However, education was not a significant predictor of change in performance on measures of executive functioning. Instead, the severity of SAH was a more robust and a significant predictor of change in this domain. Thus, the tendency toward improvement in this domain is more likely to be due to recovery.

Finally, other investigators found that practice effects vary with the type of test. In evaluating a variety of neuropsychological tests for practice effects over 20 trials in a month among both brain-injured and non-brain-injured participants, Watson et al. (2000) found that tests of reaction time, Digits Forward, and Digits Backward showed the least effect of practice. Dikmen et al. (1999) also found little effects of practice on measures of attention and motor skill. These findings support the interpretation that the significant improvements observed in the domains of psychomotor speed and attention by Peery et al. (2004) may represent recovery. In general, results of the study by Dikmen et al. (1999) indicate larger practice effects on measures with problem-solving or novelty components. For example, these authors observed practice effects on the WAIS Performance subtests and not on the Verbal subtests. Measures of naming are also thought to be less susceptible to practice effects. For example, Zec, Markwell, Burkett, and Larsen (2005) reported only a small practice effect on the Boston Naming Test (0.21 words; p=0.06) for “normal” older adults when comparing two assessments with a range of 9 to 15 months apart.

Nevertheless, some contribution of practice effects cannot be ruled out in this study or in many of the prospective studies of recovery post SAH. The use of parallel forms of neuropsychological tests is an alternative future studies may adopt to control for possible practice effects. However, whereas the use of alternate forms may mitigate practice effects, it does not totally eliminate these effects (Benedict, 2005). Furthermore, parallel test forms may not be equivalent in their levels of difficulty, sensitivity, and validity (Dikmen et al., 1999).

2. Recording Years of Education as an Index of Educational Attainment

In the current study, we measured education by asking each patient about his or her highest level of education (i.e., number of years completed), and this information was also corroborated in an interview with a family member. However, quantity of education does not speak to quality of education. Years of education may not be commensurate between individuals. Schools in the United States differ in many characteristics, such as pupil expenditures, teacher quality, pupil/teacher ratios, and length of school year (Manly et al., 2002). Several researchers have demonstrated that school characteristics were able to account for much of the difference in academic achievement and other outcomes (e.g., wage earnings) between African Americans and Whites (e.g., Hedges, Laine, & Greenwald, 1994). Thus, many have argued that a qualitative, rather than a quantitative, measure of education be used, especially when evaluating a multi-ethnic sample. For example, literacy levels may be a better measure of education and may better capture the quality of education than years of education (Manly, Touradji, Tang, & Stern, 2003; Stern, 2003). In the current study, the battery included the National Adult Reading Test (NART) for English-speakers, and the Word Accentuation Test (WAT) was substituted for the National Adult Reading Test for Spanish-speakers. However, as many patients did not complete these measures, utilizing only those patients who had completed these tests would have resulted in a much smaller sample size. It is recommended that future studies consider using a measure of literacy to operationalize the quality of education in order to diminish possible bias from cultural or ecomonic influences on availability or utilization of formal education.

3. Measuring Severity of SAH

SAH severity is most commonly measured by the Glasgow Coma Scale (GCS) and the Hunt Hess grade (Hunt & Hess, 1968). However, the extent to which severity of SAH pathology can be appropriately measured is questionable. SAH is a complicated disease because the way in which the brain is injured is very diverse, with different complications in each patient. In the current study, we utilized the Hunt Hess Worst grade as a measure of severity of SAH. This measure grades the overall condition of the patient. See Appendix 1. As patients present with progressively worse states of consciousness as opposed to focal neurological signs, the Hunt Hess clinical grade captures the effect of diffuse cognitive damage caused by SAH. Peery et al. (2004) found that impaired clinical presentation predicted impaired cognition, overall. In our analyses for each cognitive domain, we also controlled for individual SAH-related factors and complications that were previously shown to be predictors of outcome for that domain. However, our measure of SAH severity did not take into account patients' functional status or their level of independence. Future studies can consider utilizing the Modified Rankin scale as a measure of SAH severity since this scale takes into account the bleed severity and secondary complications, as well as perioperative complications, and also reflects the functional disability status of the patient.

4. Other Limitations

There are several important variables that are known to affect cognitive outcome that were not addressed in this study, including depression and whether patients were taking medications. Depression is known to negatively affect cognitive functioning, particularly in attention and processing speed. Medications, such as antiepileptic drugs, also may have slowed their motor or processing speed, thereby affecting their performance on timed tasks. Thus, scores on cognitive measures at each follow up, as well as a cognitive change between follow-up times, may have been lowered by these factors. Future studies should examine whether the effect of education on cognitive outcome is mediated by depression and medication treatment.

In addition, it is possible that individuals with higher levels of education may have had more access to care (e.g., through having a better health insurance policy). These individuals may have been more likely to utilize rehabilitation services. In our study, while information with regard to patient participation in rehabilitation services was recorded, this information was nonspecific with regard to the kinds of services that patients had received and whether cognitive rehabilitation was part of their treatment. Future studies should consider the role of participation in cognitive rehabilitation services when examining the effect of educational attainment on recovery of cognitive functioning.

XI. Future directions

The cognitive reserve hypothesis provides a good framework from which to study the effects of stroke, not only at the initial stages of recovery, but also in terms of recovery over the lifespan. Using the cognitive reserve model, future research should focus on what other variables influence cognitive and functional outcome.

In terms of the unique contribution of educational attainment, few studies have attempted to identify the mechanisms that underlie this effect (Byrd, Jacobs, Hilton, Stern, & Manly, 2005; Le Carret, Rainville, et al., 2003). For example, Le Carret, Rainville, et al. (2003) found that individuals with higher levels of education performed better on the Benton Visual Retention Test (BVRT) and were observed to make a more systematic and exhaustive search when selecting responses in a multiple-choice format. These authors reported that higher scores on the BVRT in more educated individuals were only partially mediated by visuospatial perceptual abilities, but were also mediated by a more efficient executive working memory. Future studies that will help to identify mechanisms underlying the effect of education will provide important information regarding the ways that education can optimize the brain against injury. Such information can also guide potential future interventions.

XII. Clinical Implications

There are several possible clinical implications that emanate from the current study. The relationship among acute brain injury, patient variables (e.g., education), and cognitive recovery may provide rehabilitation professionals with useful information regarding the types and levels of services needed for individuals in the vocational rehabilitation planning process. Individuals with lower levels of education are more likely to be more cognitively impaired. Thus, special attention should be paid to evaluating this group so that safety and responsibility issues, such as managing finances or adherence to a complex schedule for medications, are addressed. In addition, studies examining the extent to which education and other cognitive reserve variables are associated with cognitive outcomes may facilitate the identification of individuals likely to suffer the greatest post-injury and post-treatment cognitive deficits and, therefore, inform decisions about the selection of medical treatments that may minimize cognitive impairment in the most susceptible patients. Finally, these results also raise the possibility that individual cognitive reserve could be increased through some set of interventions that promote learning.

Table 1: Age and Education Of Study Group at 3 Months post SAH

	N	Minimum	Maximum	Mean	Std. Deviation
Age (y)	113	19	86	49.43	12.97
Education (y)	113	0	20	11.69	4.36

Table 2: Sex, Handedness, Language, And Race/Ethnicity Of Study Group at 3 Months post SAH (N=113)

Variable	Levels	N	%
Sex	Male	36	32.0%
	Female	77	68.0%
Handedness	Right	101	89.0%
	Left	9	8.0%
	Ambidextrous	3	3.0%
Primary Language	English	81	72.0%
	Spanish	32	28.0%
Ethnicity	White	48	42.5%
	Black	14	12.0%
	Asian	2	2.0%
	Hispanic	49	43.5%

Table 3: Age and Education Of Study Group at 12 Months post SAH

	N	Minimum	Maximum	Mean	Std. Deviation
Age (y)	82	19	87	51.01	13.29
Education (y)	82	0	20	11.63	4.55

Table 4: Sex, Handedness, Language, And Race/Ethnicity Of Study Group at 12 Months post SAH (N=82)

Variable	Levels	N	%
Sex	Male	25	30.5%
	Female	57	69.5%
Handedness	Right	75	91.5%
	Left	6	7.3%
	Ambidextrous	1	1.2%
Primary Language	English	56	68.0%
	Spanish	26	32.0%
Ethnicity	White	32	39.0%
	Black	11	13.5%
	Asian	2	2.5%
	Hispanic	37	45.0%

Table 5: Disease Characteristics in Study Group (N=113)

	Presence/Location/Severity	N	%
Admission Hunt Hess	I & II	63	56
	III, IV, V	50	44
Worst Hunt Hess	I & II	41	36
	III, IV, V	72	64
Aneurysm	Anterior	82	73
	Posterior	19	27
Focal SAH Clot	Anterior Interhemispheric	11	10
	Right Sylvian	16	14
	Left Sylvian	15	13
Infarction	Yes	34	30
	No	79	70
Cerebal Edema	Yes	27	24
	No	86	76
Hydrocephalus	Yes	26	23
	No	87	77
Intracerebral Hematoma	Yes	19	17
	No	94	83

Table 6: Disease Characteristics in Study Group (N=82)

	Presence/Location/Severity	N	%
Admission Hunt Hess	I & II	45	55
	III, IV, V	37	45
Worst Hunt Hess	I & II	30	37
	III, IV, V	52	63
Aneurysm	Anterior	18	22
	Posterior	14	17
Focal SAH Clot	Anterior Interhemispheric	9	11
	Right Sylvian	13	16
	Left Sylvian	11	13
Infarction	Yes	26	33
	No	54	67
Cerebal Edema	Yes	22	27
	No	60	73
Hydrocephalus	Yes	18	22
	No	64	78
Intracerebral Hematoma	Yes	14	17
	No	68	83

Table 7: Neuropsychological Battery By Cognitive Domains

Cognitive Domain	Neuropsychological Test	Scoring	Authors
Attention / Concentration	Digit Span Forward	Accuracy (0-16)	Wechsler, 1981
	Digit Span Backward‡	Accuracy (0-16)	Wechsler, 1981
	Digit Symbol Total	Accuracy (0-93)	Wechsler, 1981
	Verbal Serial Attention Task time‡	Time (0"- 240")	Mahurin & Cook, 1996
	Cal CAP (Sequence 1 RT ÷ Simple RT)	Time	Miller, 1999
Visuospatial Skills	Block Design raw score	Accuracy (0-51)	Wechsler, 1981
	WMS-R VR Copy‡	Accuracy (0-41)	Wechsler, 1987
	Rey Complex Figure Copy‡	Accuracy (0-36)	Lezak, 1995
Psychomotor Speed	Cal CAP Simple RT ‡	Time	Miller, 1999
	Trails A ‡	Time	Lezak, 1995
Verbal Memory	CVLT/AVLT total raw score (trials1 thru 5)	Accuracy (0-80)	Delis, Kramer, Kaplan, & Ober, 1983 (CVLT) / Artiola et al., 2000 (AVLT)
	CVLT/AVLT long delay free recall raw scores	Accuracy (0-16)	
	CVLT/AVLT recognition hits‡	Accuracy (0-16)	
Language Skills	Boston Naming Test raw score‡	Accuracy (0-60)	Kaplan, Goodglass, & Weintraub, 1983
	Token Test‡	Accuracy (0-163)	Spreen & Strauss, 1998
Visual Memory	WMS-R VRII raw score	Accuracy (0-41)	Wechsler, 1987
	Rey Complex Figure delayed recall raw score	Accuracy (0-36)	Lezak, 1995
Executive Functions	MCST total correct raw score	Accuracy (0-48)	Nelson, 1976
	MCST average percent perseverative errors‡	Accuracy (0-100)	Nelson, 1976
	Trails B time‡	Time	Lezak, 1995

Cal CAP = California Computerized Assessment Package, RT = reaction time, CVLT = California Verbal Learning Test, AVLT = Auditory Verbal Learning Test, WMS-R= Wechsler Memory Scale-revised, VR = Visual Reproduction, MCST = Modified Card Sorting Test.

‡ Tests requiring transformations for significant skewness.

Table 8. Comparison of Patient Characteristics for SAH Patients Who Underwent Neuropsychological Testing at 3 Months and Those Lost to Follow-Up.

Variable	Neuropsychological Testing (n=113)	No Neuropsychological Testing (n=135)	*p*
Demographics			
Age (years)	49.3±13.0	54.6±15.4	0.005
Women	68%	59%	NS
White	42%	60%	0.006
Education (years)	11.8±4.3	12.3±3.6	NS
Clinical			
Admission Hunt-Hess Grade			NS
1, 2	56%	45%	
3-5	44%	55%	
Worst Hunt Hess Grade			NS
1, 2	37%	33%	
3-5	63%	67%	
Hijdra SAH Sum score	12.9±8.6	13.0±7.5	NS
Intracerebral hemorrhage	16%	17%	NS
Aneurysm	91%	84%	NS
Nonaneurysmal SAH	9%	16%	NS
Cerebral edema	25%	30%	NS
Hydrocephalus	22%	29%	NS
Infarction	31%	33%	NS
14-Day Modified Rankin	2.7±1.5	2.9±1.8	NS

Values are mean±SD or (%). *P* values refer to χ_2 test results for discrete variables and t-test results for continuous variables.

Table 9. Comparison of Patient Characteristics for SAH Patients Alive at 12 Months Who Underwent Neuropsychological Testing at 3 and 12 Months and Those Who Did Not Complete Both Evaluations.

Variable	Neuropsychological Testing at 3 and 12 Months (n=82)	No Neuropsychological Testing (n=166) at Both Testing Times	*p*
Demographics			
Age (years)	50.7±13.2	52.2±15.0	NS
Women	70%	59%	NS
White	39%	56%	0.007
Education (years)	11.6±4.6	12.3±3.7	NS
Clinical			
Admission Hunt-Hess Grade			NS
1, 2	55%	49%	
3-5	45%	51%	
Worst Hunt Hess Grade			NS
1, 2	37%	34%	
3-5	63%	66%	
Hijdra SAH Sum score	13.9±8.7	12.8±7.7	NS
Intracerebral hemorrhage	17%	15%	NS
Aneurysm	92%	85%	NS
Nonaneurysmal SAH	8%	15%	NS
Cerebral edema	27%	26%	NS
Hydrocephalus	22%	27%	NS
Infarction	33%	30%	NS
14-Day Modified Rankin	2.9±1.5	2.8±1.8	NS

Values are mean±SD or (%). *P* values refer to χ_2 test results for discrete variables and t-test results for continuous variables.

Table 10. Comparison of Patient Characteristics for SAH Patients Who Underwent Neuropsychological Testing at 3 Months Only Versus Those Who Completed Both Evaluations.

Variable	Neuropsychological Testing at 3 Months Only (n=31)	Neuropsychological Testing at both 3 and 12 Months (n=82)	*p*
Demographics			
Age (years)	46.9±11.7	50.7±13.2	NS
Women	69%	70%	NS
White	46%	39%	NS
Education (years)	11.9±4.0	11.6±4.6	NS
Clinical			
Admission Hunt-Hess Grade			NS
1, 2	60%	55%	
3-5	40%	45%	
Worst Hunt Hess Grade			NS
1, 2	37%	37%	
3-5	63%	63%	
Hijdra SAH Sum score	11.0±7.9	13.9±8.7	NS
Intracerebral hemorrhage	14%	17%	NS
Aneurysm	83%	92%	NS
Nonaneurysmal SAH	17%	8%	NS
Cerebral edema	20%	27%	NS
Hydrocephalus	23%	22%	NS
Infarction	26%	33%	NS
14-Day Modified Rankin	2.4±1.7	2.9±1.5	NS

Values are mean ± SD or (%). *P* values refer to $\chi 2$ test results for discrete variables and t-test results for continuous variables.

Table 11: Neuropsychological Test Performance for Study Participants at 3-Month Follow-up.

Domain	Test	N	Mean	Std. Deviation
Attention	Digits forward	113	5.49	1.53
	Digits reversed	112	4.12	1.38
	Digit symbol raw	111	39.33	19.45
	TSAT time	112	147.46	85.25
	Cal CAP Attention	101	1.7124	.4762
Language	BNT correct	105	42.82	14.59
	Token Test	79	41.0000	33.0974
Visual Skills	WMSR VR Copy	106	34.94	5.32
	RCFT Copy	112	29.9464	6.9982
	Block design raw	110	18.87	11.95
Verbal Memory	CVLT total	107	43.45	13.91
	CVLT long delay free recall	106	8.30	4.33
	CVLT recognition hits	106	13.02	2.97
Visual Memory	WMSR VR II	110	19.71	12.12
	RCFT Delayed recall	112	14.4465	7.3129
Psychomotor Speed	Simple RT mean (sec)	102	410.79	176.16
	Trails A time	112	61.29	47.74
Executive Functions	MCST Total Correct	106	24.51	10.96
	MCST Total % Perseverative errors	106	31.6149	29.0339
	Trails B time	94	119.50	77.12

Table 12: Neuropsychological Test Raw Scores for Study Participants at 3 and 12-Month Follow-up (N=82).

Domain	Test	3-Months		12-Months	
		Mean	Std. Deviation	Mean	Std. Deviation
Attention	Digits forward	5.46	1.38	5.83	1.719
	Digits reversed	3.98	1.39	4.20	1.42
	Digit symbol	37.81	18.94	39.90	18.88
	TSAT time	148.71	85.05	140.63	83.69
	Cal CAP Attention	1.74	0.48	1.75	.43
Language	BNT correct	43.78	14.67	44.45	15.16
	Token Test	42.76	32.71	55.32	34.33
Visual Skills	WMSR VR Copy	34.78	5.77	34.85	6.05
	RCFT Copy	29.46	7.22	29.48	7.50
	Block design raw	17.38	11.82	19.68	11.91
Verbal Memory	CVLT total	43.13	14.57	47.59	15.74
	CVLT long delay free recall	8.11	4.54	9.36	4.26
	CVLT recognition hits	12.78	3.28	13.48	2.92
Visual Memory	WMSR VR II	19.36	12.00	22.03	12.12
	RCFT Delayed recall	14.48	7.32	16.80	8.14
Psychomotor Speed	Simple RT mean (sec)	422.23	194.22	392.79	198.13
	Trails A time	63.95	50.84	51.45	31.10
Executive Functions	MCST Total Correct	24.14	10.75	26.74	10.05
	MCST Total Perseverative errors	7.68	9.55	4.79	5.66
	Trails B time	119.16	72.93	107.25	59.31

Table 13: Results Of Tests For Deviation From Normality in Distribution of Scores.

Domain (P value)	Test	Z score of skewness*	Transformation
Attention (NS)	Digit Span Forward	0.145	NA
	Digit Span Reversed	2.74	Square Root
	Digit Symbol	0.09	NA
	TSAT time	4.09	Log
	Cal CAP Attention	-0.63	NA
Visuospatial (NS)	Block Design	1.44	NA
	WMS-R VR copy	-7.66	Reflect and Log
	RCFT copy	-7.38	Reflect and Log
Psychomotor Speed (.002)	Cal CAP Simple RT	9.53	Log
	Trails A time	9.10	Log
Verbal Memory (NS)	CVLT total	-1.49	NA
	CVLT LDFR	-1.62	NA
	CVLT recognition	-7.48	Reflect and Log
Language (NS)	Boston Naming Test	-2.68	Reflect and Square Root
	Token Test	-16.73	Reflect and Log
Visual Memory (NS)	WMS-R VRII	-0.42	NA
	RCFT delay	0.61	NA
Executive Functions (NS)	MCST total	-1.47	NA
	MCST % PE	3.33	Square Root
	Trails B time	4.30	Log

* Z Score of Skewness = Skewness / Standard Error of Skewness

Table 14: Standardized Scores (Mean ± Standard Deviation) for Study Participants at 3 and 12-Month Follow-up (N=82).

Cognitive Domain	Neuropsychological Test	3 Months	12 Months
Attention / Concentration	Digit Span Forward	-0.0233 ± 0.9393	0.2498 ± 1.0747
	Digit Span Backward	-0.0472 ± 0.9668	0.1102 ± 0.9916
	Digit Symbol Total	-0.0868 ± 0.9701	-0.0087 ± 0.9823
	Verbal Serial Attention Task time	0.0165 ± 1.0031	0.1000 ± 0.9726
	Cal CAP (Sequence 1 RT ÷ Simple RT)	0.0964 ± 1.0088	0.0653 ± 0.9613
Visuospatial Skills	Block Design raw score	-0.0759 ± 0.9823	0.0984 ± 0.9849
	WMS-R VR Copy	-0.0382 ± 1.0682	-0.0268 ± 1.1211
	Rey Complex Figure Copy	-0.0727 ± 1.0250	-0.0576 ± 1.0594
Psychomotor Speed	Cal CAP Simple RT	-0.0305 ± 1.0521	-0.0577 ± 1.4006
	Trails A	-0.0937 ± 1.0668	0.1366 ± 0.8915
Verbal Memory	CVLT/AVLT total raw score (trials1 thru 5)	-0.0227 ± 1.0477	0.2401 ± 1.1488
	CVLT/AVLT long delay free recall raw scores	-0.0447 ± 1.0470	0.2044 ± 0.9961
	CVLT/AVLT recognition hits	-0.0791 ± 1.1027	0.1138 ± 0.9850
Language Skills	Boston Naming Test raw score	0.0346 ± 1.0067	-0.0409 ± 1.1204
	Token Test	0.0164 ± 0.9646	0.3599 ± 0.9884
Visual Memory	WMS-R VRII raw score	-0.0407 ± 0.9890	0.1665 ± 1.0055
	Rey Complex Figure delayed recall raw score	-0.0294 ± 1.0156	0.3329 ± 1.1025
Executive Functions	MCST total correct raw score	-0.0254 ± 0.9827	0.1371 ± 0.9473
	MCST average percent perseverative errors	-0.0031 ± 1.0080	0.1588 ± 0.7450
	Trails B time	-0.1240 ± 1.0538	0.0893 ± 0.8206

Table 15: Domain Scores (Means and Standard Deviations) for Study Participants at 3 and 12-Month Follow-up (N=82).

Cognitive Domain	Neuropsychological Test	3 months	12 months	Change Score (12 mo – 3 mo)
Attention / Concentration	Digit Span Forward	-0.0356±0.7261	0.1122±0.7682	0.1479±0.3975
	Digit Span Backward			
	Digit Symbol Total			
	Verbal Serial Attention Task time			
	Cal CAP (Sequence 1 RT ÷ Simple RT)			
Visuospatial Skills	Block Design raw score	-0.0061±0.8942	0.0736±0.9102	0.0797±0.3960
	WMS-R VR Copy			
	Rey Complex Figure Copy			
Psychomotor Speed	Cal CAP Simple RT	-0.0248±0.9101	0.2384±0.9350	0.2192±0.5431
	Trails A			
Verbal Memory	CVLT/AVLT total raw score (trials1 thru 5)	-0.0123±0.9162	0.2384±0.9350	0.2872±0.5175
	CVLT/AVLT long delay free recall raw scores			
	CVLT/AVLT recognition hits			
Language Skills	Boston Naming Test raw score	-0.0083±0.9737	0.0868±1.0068	0.1346±0.3951
	Token Test			
Visual Memory	WMS-R VRII raw score	-0.0082±0.9419	0.2735±0.9972	0.2717±0.4069
	Rey Complex Figure delayed recall raw score			
Executive Functions	MCST total correct raw score	-0.0455±0.8403	0.0679±0.7429	0.1329±0.5772
	MCST average percent perseverative errors			
	Trails B time			

Table 16: Results Of Kolmogorov-Smirnov Tests.

Domain	*p* values
Attention	0.200 (NS)
Visuospatial	0.200 (NS)
Psychomotor Speed	0.119 (NS)
Verbal Memory	0.200 (NS)
Language	0.060 (NS)
Visual Memory	0.200 (NS)
Executive Functions	0.142 (NS)

Table 17. Univariate Analysis of Demographic, Clinical, and Radiological Variables Associated with Poor Cognitive Domain Scores at 3 Months post SAH (N=113).

Risk Factors		Attention	Executive Functioning	Verbal Memory	Visual Memory	Visuospatial Skills	Language	Psychomotor Speed
	%*	*p*	*p*	*p*	*p*	*p*	*p*	*p*
Demographic								
Higher age	53%	0.001	0.001	0.000	0.000	0.000	0.084	0.000
Nonfluent in English	28%	0.000	0.000	0.036	0.000	0.000	0.000	0.000
Nonwhite ethnicity	58%	0.000	0.000	0.002	0.001	0.000	0.000	0.000
Male sex	32%	0.094	0.058	0.000	0.051	0.685	0.135	0.730
Clinical/Radiographic								
Global Edema	24%	0.012	0.230	0.005	0.011	0.025	0.268	0.064
Any infarction	30%	0.209	0.297	0.120	0.058	0.138	0.405	0.518
Left-sided infarction	18%	0.026	0.211	0.000	0.009	0.348	0.080	0.291
Right-sided infarction	17%	0.632	0.667	0.492	0.151	0.191	0.500	0.347
Non-posterior circulation aneurysm	73%	0.002	0.001	0.001	0.001	0.001	0.003	0.032
Anterior Communicating aneurysm	24%	0.279	0.156	0.061	0.223	0.340	0.578	0.609
Focal SAH clot Anterior Interhemispheric	10%	0.651	0.084	0.035	0.143	0.933	0.940	0.597
Focal SAH clot Right Sylvian	14%	0.069	0.058	0.018	0.002	0.009	0.419	0.009
Focal SAH clot Left Sylvian	13%	0.282	0.128	0.072	0.022	0.516	0.387	0.072

* Percentage of the study population with the give risk factor

Table 18. Pearson Correlations for Age and Cognitive Domain Scores at 3 Months post SAH.

	Attention	Executive Functioning	Verbal Memory	Visual Memory	Visuospatial Skills	Language	Psychomotor Speed
	r	*r*	*r*	*r*	*r*	*r*	*r*
Age	-0.265**	-0.375**	-0.288**	-0.408**	-0.339**	-0.227**	-0.456**

** Correlation is significant at the 0.01 level (2-tailed). * Correlation is significant at the 0.05 level (2-tailed).

Table 19. Demographic, Clinical, and Radiological Covariates Used in the Multivariate Analyses for Each Cognitive Domain (Baseline Data).

Covariates	Attention	Executive Functioning	Verbal Memory	Visual Memory	Visuospatial Skills	Language	Psychomotor Speed
Demographic							
Higher age	√	√	√	√	√	√	√
Male sex			√				
Clinical/Radiographic							
Global Edema	√		√	√	√		
Left-sided infarction	√		√	√			
Non-posterior circulation aneurysm	√	√	√	√	√	√	√
Focal SAH clot Anterior Interhemispheric			√				
Focal SAH clot Right Sylvian			√	√	√		√
Focal SAH clot Left Sylvian				√			

Table 20. Univariate Analysis of Past Medical History Risk Factors Associated with Poor Cognitive Outcome (N=113).

Risk Factors		Attention	Executive Functioning	Verbal Memory	Visual Memory	Visuospatial Skills	Language	Psychomotor Speed
	%*	*p*	*p*	*p*	*p*	*p*	*p*	*p*
Cerebral Infarct	2%	0.581	0.787	0.736	0.783	0.266	0.272	0.804
Head Injury with Loss of Consciousness	4%	0.936	0.603	0.811	0.493	0.222	0.417	0.520
Previous SAH	2%	0.441	0.657	0.588	0.340	0.568	0.291	0.699
Seizures	4%	0.503	0.610	0.141	0.062	0.628	0.641	0.580
Myocardial Infarction	3%	0.273	0.870	0.286	0.434	0.449	0.423	0.399

* Percentage of the study population with the given risk factor

Table 21. Pearson Correlations for Education and SAH Severity with Cognitive Domain Scores at 3 Months post SAH.

	Attention	Executive Functioning	Verbal Memory	Visual Memory	Visuospatial Skills	Language	Psychomotor Speed
Cognitive Reserve Index	*r*	*r*	*r*	*r*	*r*	*r*	*r*
Education (years)	0.646**	0.508**	0.372**	0.503**	0.690**	0.653**	0.562**
SAH Severity Index							
Hunt Hess Worst Score	-0.204*	-0.222*	-0.255**	-0.216*	-0.189*	-0.180	-0.200*

** Correlation is significant at the 0.01 level (2-tailed). * Correlation is significant at the 0.05 level (2-tailed).

Table 22. Results of the Final Model of Regression Analysis of Variables Associated with Cognitive Performance at 3 Months post SAH.

	Executive Functions		*Attention*		*Verbal Memory*		*Visual Memory*		*Visuospatial*		*Language*		*Psychomotor*	
	ß	*p*	*ß*	*p*	*ß*	*p*	*ß*	*p*	*ß*	*p*	*ß*	*p*	*ß*	*p*
Age	-.217	.012	-.060	.421	-.156	.062	-.255	.003	-.127	.084	-.001	.885	-.296	.000
Male Sex	-	-	-	-	-.389	.000	-	-	-	-	-	-	-	-
Global Edema	-	-	-.161	.044	-.115	.200	-.150	.096	-.139	.078	-	-	-	-
Left-sided infarction	-	-	-.132	.076	-.192	.020	-.155	.065	-	-	-	-	-	-
Non-posterior circulation aneurysm	-.151	.077	-.083	.274	-.237	.009	-.146	.087	-.101	.172	-.035	.635	-.026	.751
Focal SAH clot Anterior Interhemispheric	-	-	-	-	-.046	.587	-	-	-	-	-	-	-	-
Focal SAH clot Right Sylvian	-	-	-	-	.057	.519	.018	.851	.037	.639	-	-	-.077	.362
Focal SAH clot Left Sylvian	-	-	-	-	-	-	-.066	.433	-	-	-	-	-	-
Severity	-.134	.106	.005	.954	-.034	.703	.013	.885	-.011	.893	-.108	.143	-.063	.438
Education	.381	.000	.592	.000	.271	.003	.358	.000	.630	.000	.662	.000	.445	.000
Education X Severity	-.013	.878	.086	.233	.114	.154	.045	.580	.080	.252	.149	.043	-.006	.941
R^2 for entire model	.352		.492		.479		.409		.541		.500		.425	

Table 23. Multivariate Analysis of Variables Associated with Cognitive Change from 3 to 12 Months post SAH.

	Attention		*Executive Functions*		*Verbal Memory*		*Visual Memory*		*Visuospatial*		*Language*		*Psychomotor*	
	ß	*p*	*ß*	*p*	*ß*	*p*	*ß*	*p*	*ß*	*p*	*ß*	*p*	*ß*	*p*
Baseline score	-.536	.000	-.653	.000	-.394	.002	-.286	.036	-.352	.018	-.432	.014	-.792	.000
Age	.028	.794	-.213	.037	-.030	.798	-.148	.189	.170	.097	.293	.016	-.122	.205
Global Edema	-	-	-	-	-	-	.242	.042	.242	.033	-	-	-	-
Severity	-.078	.460	.195	.044	-.116	.309	-.064	.574	.147	.178	.084	.469	-.027	.760
Education	.548	.000	.188	.094	.259	.035	.396	.002	.447	.002	.446	.012	.221	.034
R^2 for entire model	.202		.372		.146		.225		.286		.165		.438	

Table 24. Results of the Final Model of Exploratory Regression Analyses of Variables Associated with Cognitive Performance at 3 Months post SAH for English Speakers Only.

	Executive Functions		*Attention*		*Verbal Memory*		*Visual Memory*		*Visuospatial*		*Language*		*Psychomotor*	
	ß	*p*	*ß*	*p*	*ß*	*p*	*ß*	*p*	*ß*	*p*	*ß*	*p*	*ß*	*p*
Age	-.210	.035	-.128	.214	-.186	.063	-.336	.005	-.182	.090	.063	.558	-.263	.027
Male Sex	-	-	-	-	-.450	.000	-	-	-	-	-	-	-	-
Global Edema	-	-	-.146	.196	-.105	.334	-.177	.164	-.166	.160	-	-	-	-
Left-sided infarction	-	-	-.189	.057	-.199	.036	-.181	.102	-	-	-	-	-	-
Non-posterior circulation aneurysm	-.207	.034	-.085	.399	-.290	.006	-.141	.228	-.139	.189	-.014	.894	-.084	.469
Focal SAH clot Anterior Interhemispheric	-	-	-	-	-.050	.609	-	-	-	-	-	-	-	-
Focal SAH clot Right Sylvian	-	-	-	-	.054	.595	.018	.880	.050	.650	-	-	-.071	.557
Focal SAH clot Left Sylvian	-	-	-	-	-	-	-.068	.554	-	-	-	-	-	-
Severity	-.234	.101	-.011	.941	-.022	.845	.129	.329	.067	.584	-.078	.464	-.018	.881
Education	.404	.000	.442	.000	.250	.011	.161	.158	.483	.000	.487	.000	.230	.045
Education X Severity	.079	.576	.065	.621	.074	.474	-.129	.280	-.046	.676	.193	.074	-.113	.345
R^2 for entire model	.366		.350		.481		.253		.335		.306		.173	

Table 25. Multivariate Analysis of Variables Associated with Global Cognitive Functioning 3 Months post SAH.

	*Global Cognitive Functioning**		
	ß	*p*	R^2 Change
Age	-.204	.003	.172
Male sex	-.157	.016	.035
Severity	-.173	.009	.046
Education	.587	.000	.304
Education X Severity	.091	.161	.008
R^2 for entire model	.566		

* Global cognitive functioning score was computed by averaging the domain scores for the seven cognitive domains

Table 26. Multivariate Analysis of Variables Associated with Global Cognitive Change from 3 to 12 Months post SAH.

	*Global Cognitive Functioning**		
	ß	*p*	R^2 Change
Baseline score	-.467	.003	.032
Age	.037	.737	.000
Severity	.098	.383	.018
Education	.485	.001	.123
R^2 for entire model	.173		

* Global cognitive functioning score was computed by averaging the domain scores for the seven cognitive domains

Figure 1. Schematic of follow-up rates.

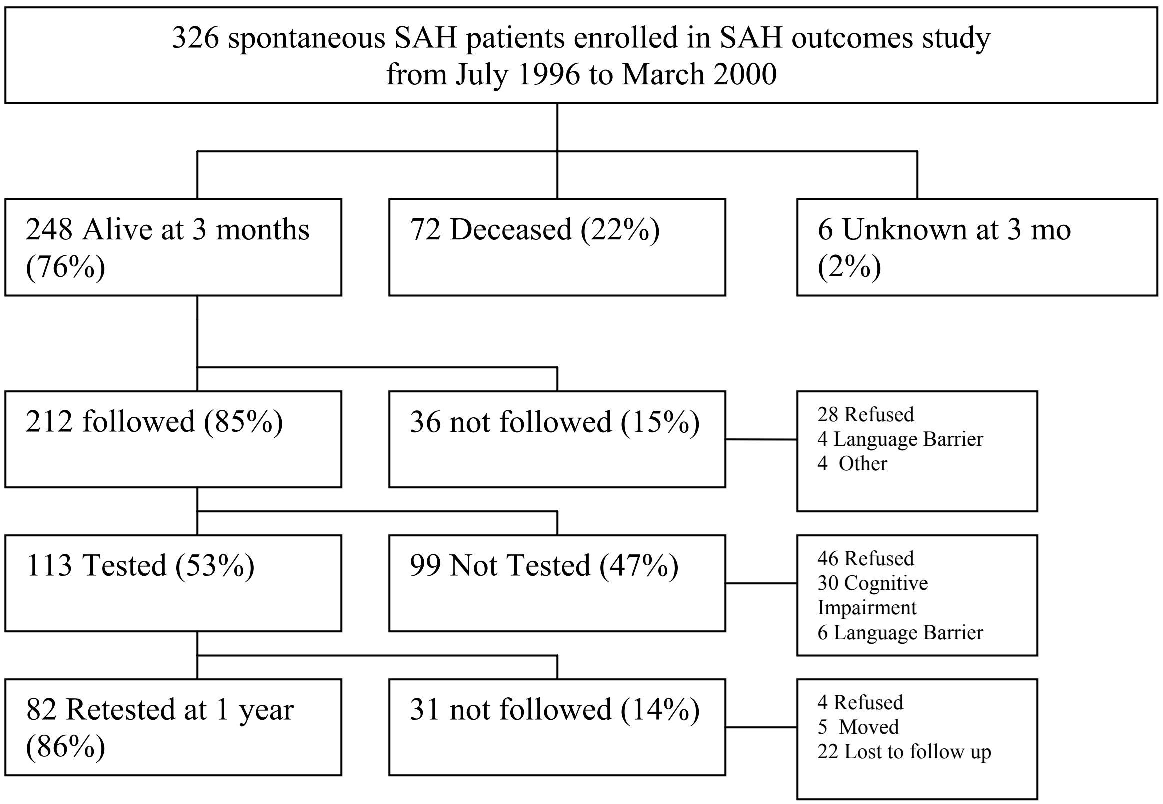

Figure 2. Results of Post-Hoc Analysis: Regression Lines for Relations Between Language Scores and SAH Severity 1SD Above and Below the Mean of Education.

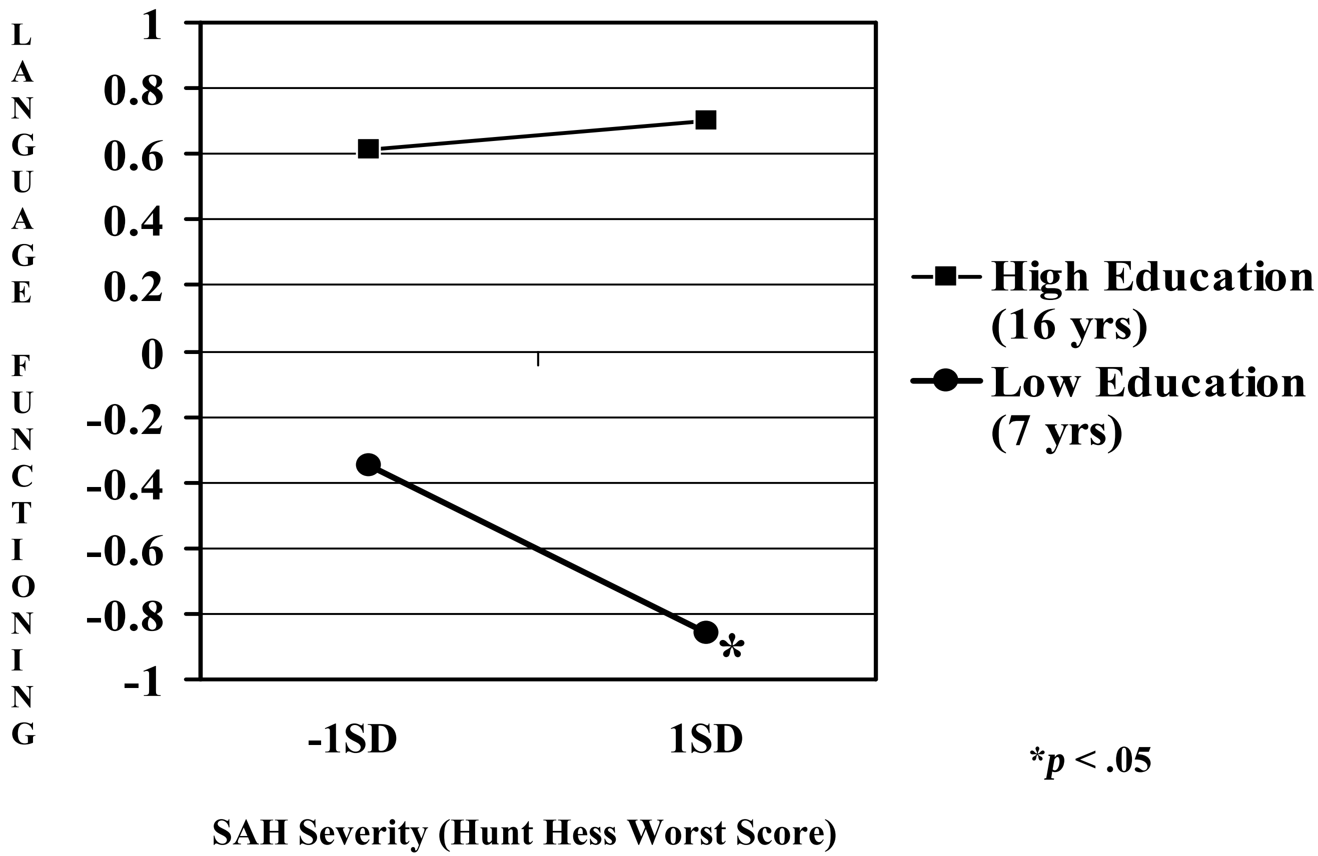

Figure Caption. Slopes were calculated based on the regression equation for the interaction between SAH severity and education for the language domain. Using data from the entire sample, slopes were estimated for 1 SD above and below the mean of education (i.e., at 16 and 7 years of education).

Figure 3. Results of Post-Hoc Analysis: Regression Lines for Relations Between Language Scores and SAH Severity for Other Values of Education.

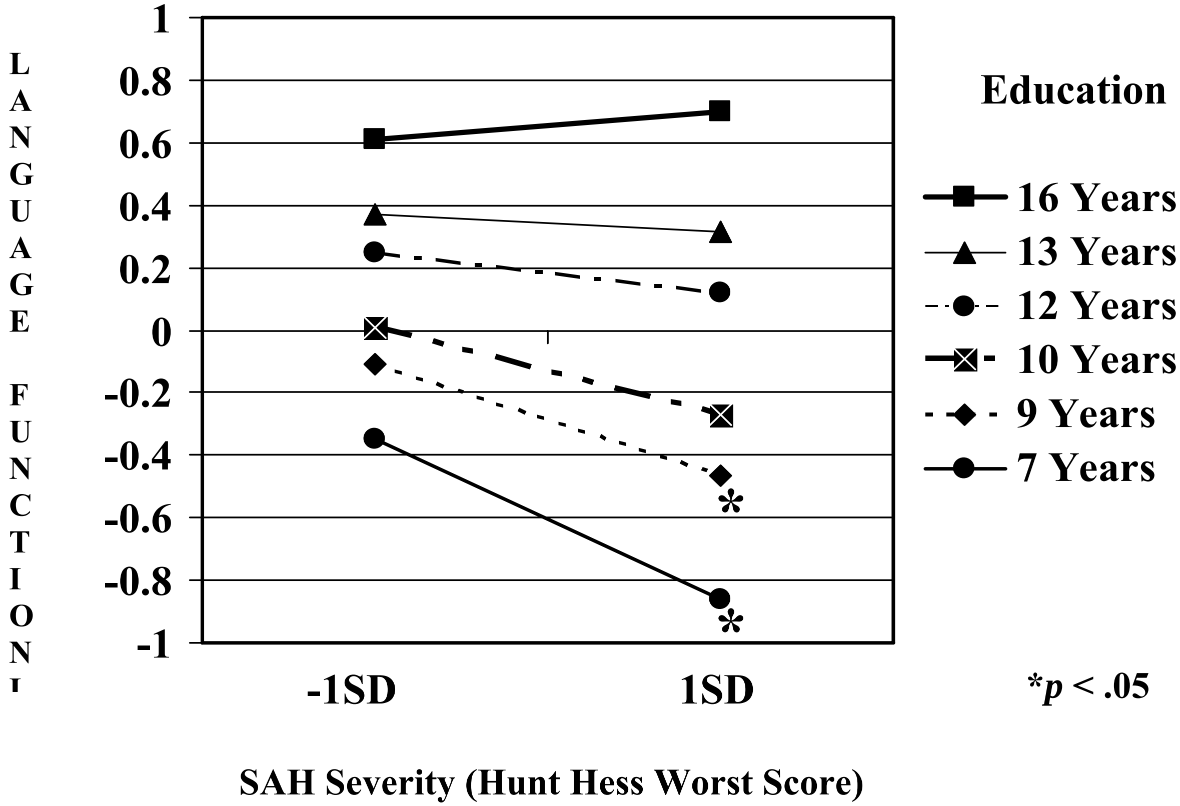

Figure Caption. Slopes were calculated based on the regression equation for the interaction between SAH severity and education for the language domain. Using data from the entire sample, slopes were estimated at various values of the moderator or education (i.e., at 16, 13, 12, 10, 9, and 7 years of education).

Appendix 1. Hunt Hess Scale (Hunt & Hess, 1968)

Grade	Neurologic condition
0	Unruptured
1	Asymptomatic
2	Severe Headache or meningismus; no neurological deficit
3	Drowsy; minimal neurological deficit
4	Stuporous; moderate to severe hemiparesis
5	Deep coma; decerebrate posturing

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