Cognitive and Functional Outcome After Aneurysmal Subarachnoid Hemorrhage

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Background and Purpose—Aneurysmal subarachnoid hemorrhage (aSAH) is a medical emergency characterized by the accumulation of blood in the subarachnoid space surrounding the brain. The acute treatment of aSAH is well documented but less is known about the long-term effects of aSAH on cognition and day-to-day functioning.

Methods—We reviewed all studies in the past 10 years that have focused on the effects of aSAH on cognition and day-to-day functioning.

Results—Sixty-one empirical studies examining cognitive and functional outcome in patients with aSAH met inclusion criteria. Survivors of aSAH commonly experience deficits in memory, executive function, and language. These cognitive impairments interact to affect patients’ day-to-day functioning, including activities of daily living, instrumental activities of daily living, return to work, and quality of life. Deficits in cognition and day-to-day functioning are further compounded by depression, anxiety, fatigue, and sleep disturbances.

Conclusions—Much remains to be learned about the brain changes underlying cognitive and functional deficits, including the role of diffuse brain damage and secondary complications like vasospasm and elevated intracranial pressure. A consideration of these issues is necessary to obtain a better understanding of how aSAH affects cognition and day-to-day functioning in the long-term. (Stroke. 2010;41:e519-e536.)

Key Words: subarachnoid hemorrhage □ cerebral aneurysm □ outcome □ outcome assessment

Aneurysmal subarachnoid hemorrhage (aSAH), characterized by the rupture of an intracranial aneurysm and the subsequent accumulation of blood in the subarachnoid space, is a medical emergency associated with substantial morbidity and mortality. Only 50% of those who experience aSAH survive.1 Although SAH may occur as a result of trauma,2 85% of SAH cases are caused by the rupture of a cerebral aneurysm.3 In North America, the incidence of aneurysm rupture is approximately 8 to 11 per 100,000 persons per year.5,6 Although only 7% of all strokes are attributed to aSAH,4 aSAH accounts for 27% of all stroke-related years of life lost before age 65.7 A distinct feature of aSAH is the relatively young age at which it occurs. The peak age of incidence is between 40 and 60 years.8 Many survivors are in their most productive years and have major responsibilities with respect to work and family. The acute treatment of aSAH is well documented,1,9 but many questions remain about the chronic effects of aSAH on cognitive and functional outcome. The present review aims to characterize the long-term effects of aSAH on cognition, day-to-day functioning, mood, anxiety, sleep, and fatigue by considering data from clinical and neuroimaging studies. We have identified issues concerning the interpretation of data from the aSAH outcome literature and can now make informed recommendations for future research.

Methods

The review was restricted to peer-reviewed research articles reporting cognitive and functional outcome in aSAH survivors. Empirical studies examining depression, anxiety, fatigue, and sleep disturbances in aSAH survivors were also included. Studies for the review were identified by searching through Medline and PsychINFO using the search terms “subarachnoid hemorrhage” in combination with “cognit*,” “neuropsychol*,” “quality of life,” “activities of daily living,” “instrumental activities of daily living,” “work,” “return to work,” “depression,” “anxiety,” “fatigue,” and “sleep.” Studies were included if they were published within the past 10 years (from January 1999 until December 2009). Reference lists of suitable studies were scrutinized for additional articles. Only articles in English were reviewed. Case studies were excluded.

Results

Sixty-one research articles were included in the final review. Findings from studies investigating cognitive outcome and functional outcome are presented in Tables 1 and 2, respectively.
Cognitive Outcome

Although cognitive impairments are most frequent within the first 3 months after aSAH, recent studies have demonstrated that residual cognitive impairments persist as long as 75 months after aSAH and perhaps longer. Cognitive domains in which patients with aSAH show frequent impairment include memory, executive function, and language.

Memory

Verbal, visual, short-term and long-term memory have all been investigated after aSAH. Verbal memory is 1 of the most frequently impaired cognitive domains in patients with aSAH with the prevalence of impairment ranging from 14% to 61%. Deficits in visual memory are also frequent with impairment prevalence ranging from 14% to 49%. Older age, fewer years of education, poorer neurological grade on admission, ruptured aneurysms in the anterior circulation, and thick subarachnoid blood in the anterior interhemispheric fissure and sylvian fissures have been shown to be associated with poorer performance on tests of verbal and visual memory. Some investigators have demonstrated a relationship between memory deficits and cerebral edema, but others have observed no correlation.

The wide range in the prevalence of memory impairment can be attributed in part to the use of different standardized tests. Frequently used memory tests include the California Verbal Learning Test, the Visual Reproduction subtest of the Wechsler Memory Scale, and the Rey-Osterrieth Complex Figure–Recall subtest. Memory tests vary in terms of difficulty and sensitivity to impairment. These differences may contribute to variable rates of memory impairment. For instance, Mayer and colleagues found that 31% of aSAH survivors showed impaired visual memory on the Rey-Osterrieth Complex Figure–Recall subtest, whereas only 22% showed impaired visual memory on the Visual Reproduction subtest. The data suggest that the prevalence of cognitive impairment in aSAH survivors is determined in part by the particular test used to measure cognitive performance.

Time of testing in relation to the initial insult also plays a critical role in determining the prevalence of memory dysfunction after aSAH. In a longitudinal study by Powell and colleagues, investigators followed 42 aSAH survivors and assessed cognitive function at 3, 9, and 18 months after aSAH. Verbal memory was measured using the Prose Recall subtest of the Wechsler Memory Scale. Alternate forms of the Prose Recall subtest were used to control for practice effects. Delayed verbal memory significantly improved from 3 to 9 months and from 9 to 18 months postictus, whereas immediate verbal memory showed no significant improvement in the same time period. Despite improvement in delayed verbal memory over 18 months, 14% of patients with aSAH still had significant delayed verbal memory impairment at 18-month follow-up. Improvement in verbal memory over time has been demonstrated by other groups. Studies have also suggested that visual memory improves over time, but results have been inconsistent. Why verbal and visual memory improves over time remains unknown, although attenuation of aSAH-linked intracranial pressure and chronic inflammation may play a role. Nevertheless, the prevalence of memory impairment in aSAH survivors depends on the type of memory in question and on the length of the follow-up interval.

Visual and verbal memory is predominantly mediated by the medial temporal lobes, a network of structures that includes the hippocampus together with the entorhinal, perirhinal, and parahippocampal cortices. A correlation between left hemisphere infarctions and verbal memory impairment has previously been demonstrated, but few studies have investigated the specific brain regions mediating verbal memory impairment in patients with aSAH. Bendel and colleagues performed MRI on 77 patients with aSAH and found significantly reduced bilateral hippocampal volumes among patients with aSAH relative to healthy control subjects at 1-year follow-up. Hippocampal volumes correlated with performance on 1 visual memory test (the Visual Reproduction subtest of the Wechsler Memory Scale) but not with another visual memory test (the Rey-Osterrieth Complex Figure) or with a verbal memory test (the Logical Memory subset of the Wechsler Memory Scale). The investigators did not correlate memory impairment with changes in other brain regions such as the frontal lobes. This may be important given the role of the frontal lobes in memory function and that damage to the frontal lobes often follows aSAH. Reduced frontal lobe integrity could account for the unexpected findings reported by Bendel and colleagues.

Executive Function

Executive function is predominantly mediated by the frontal lobes and encompasses higher-level cognitive abilities like planning, inhibition, problem-solving, attention, and decision-making. Rather than differentiating between different aspects of executive function, the majority of studies treat executive function as a unitary construct. Consequently, the prevalence of executive dysfunction in aSAH survivors is very wide with estimates ranging from 3% to 76%. Interestingly, self-reported deficits in executive function do not appear to correlate with results from objective cognitive tests; Ravnik and colleagues found that patients with aSAH reported attentional deficits most frequently, yet patients performed better on tests of attention than on tests of other cognitive domains. Discordance between self-reported cognitive deficits and results from objective cognitive tests has also been reported in other domains, like memory. This discrepancy may be attributed to patients misinterpreting their cognitive deficits as impairments of attention and memory. Executive dysfunction after aSAH is more pronounced in older patients, those with fewer years of education, and those with poorer neurological grade on admission. Similar to memory, a correlation between executive dysfunction and cerebral edema has been documented by some investigators but not by others. Kreiter and colleagues found that executive dysfunction was less severe among patients with posterior aneurysms compared to those with nonposterior aneurysms. Findings from most other studies, however, suggest no relationship between ruptured aneurysm location and the profile of cognitive impairment. Interestingly, Manning and colleagues found that patients with aSAH who had ruptured...
Aneurysmal SAH results in diffuse, global damage to brain tissue, perhaps through a mechanism involving elevated intracranial pressure, reduction of cerebral blood flow and brain oxygenation, blood–brain barrier breakdown, and global cerebral edema (together these factors contribute to early brain injury; see Cahill and Zhang for a review). Findings from an MRI study by Bendel and colleagues support the “diffuse damage” hypothesis. The authors found that at 1-year follow-up, patients with aSAH showed significantly reduced total gray matter and white matter volume relative to control subjects. Furthermore, the extent of gray matter volume loss was associated with poorer cognitive test performance, including poorer performance on tests of executive function.

Not all neuroimaging studies, however, support the “diffuse damage” hypothesis. An MRI study by Martinaud and colleagues for instance, suggested that executive dysfunction results from focal lesions rather than diffuse damage. Martinaud and colleagues showed that executive dysfunction in patients with aSAH was exclusively correlated with lesions to the left hemisphere. Deficits in executive function (eg, inhibition, planning) correlated with lesions to the left lateral prefrontal lobe, including the left superior frontal gyrus, the left middle frontal gyrus, and the left anterior centrum semiovale. Deficits in behavioral aspects of executive function (eg, reduction of daily activities, irritability, hyperactivity), meanwhile, correlated with lesions to the left ventral striatum. Further research is required to clarify the relative contribution of diffuse and focal brain damage to executive dysfunction after aSAH.

The use of different neuropsychological tests, each of which probes different aspects of executive function, may be a contributing factor to the high variability in executive impairment in patients with aSAH. Proust and colleagues reported that among aSAH survivors treated with endovascular coiling, 29% showed impairment on the Wisconsin Card Sorting Task (a measure of cognitive flexibility), whereas only 7% showed impairment on the Stroop task (a measure of inhibition). Different aspects of executive function thus appear to have different rates of impairment. Among studies conducted in the past 10 years, deficits in cognitive flexibility, as measured by the Wisconsin Card Sorting Task, were found in 8% to 44% of patients with aSAH, whereas deficits in inhibition, as measured by the Stroop task, were found in 17% to 56% of patients with aSAH.

A study by Manning and colleagues highlights the need to address different aspects of executive function. Manning and colleagues evaluated executive function in 35 aSAH survivors who had made a “good recovery” according to the Glasgow Outcome Scale (GOS). Cognitive assessment was conducted a mean of 26 weeks after aSAH. Aneurysmal SAH survivors performed significantly worse than healthy control subjects on the Wisconsin Card Sorting Task, the Tower of London task, and the Stroop task, whereas performance on the Cognitive Estimates task was within normal limits. Each of the tests used by Manning and colleagues captures a slightly different “frontal lobe” function: the Tower of London task assesses planning and problem-solving, the Stroop task assesses ability to inhibit impulsive responding, whereas the Cognitive Estimates task measures ability to make judgments and estimations. The findings by Manning and colleagues suggest that some “frontal lobe” functions are impaired in aSAH survivors (eg, cognitive flexibility, planning, problem-solving, inhibition), whereas others are intact (eg, judgment, estimation). Furthermore, the data suggest that patients who have made a “good recovery” (ie, GOS 5) may still experience profound cognitive deficits over 6 months after aSAH.

Similar to memory impairment, the prevalence of executive dysfunction appears to be influenced by the length of the follow-up period. Several longitudinal studies have found that response inhibition and cognitive flexibility significantly improve within the first 12 months after hospital discharge, but results have been inconsistent. A study by Haug and colleagues suggests that different aspects of executive function have different rates of recovery. Although inhibition improved within 1 year after aSAH, cognitive flexibility and attention showed no improvement over the same time period. Results from longitudinal studies, however, must be interpreted with caution, because tests of executive function may be subject to practice effects (eg, Stroop test, Trail Making Test, Wisconsin Card Sorting Test). Studies that found improvement in response inhibition and cognitive flexibility over time used the Stroop test and Trail Making Test, both of which may have practice effects. An accurate assessment of executive function in aSAH survivors thus requires a careful consideration of specific aspects of executive function as well as follow-up interval and practice effects.

Language function is a broad category that involves comprehension and expression of meaningful written and oral information. Most studies assess language function using the verbal and semantic fluency task, the Token Test, and the Boston Naming Test. In the verbal and semantic fluency task, patients are required to generate words beginning with different letters (eg, F, A, and S) and words belonging to a certain category (eg, animals). The Token Test probes verbal comprehension of increasingly complex commands involving tokens of different colors, shapes, and sizes. In the Boston Naming Test, patients are asked to identify line drawings ranging in complexity (eg, rhinoceros, abacus). The prevalence of language impairment in aSAH survivors is highly variable, ranging from 0% to 76%. Older age, fewer years of education, and aneurysms in the anterior circulation are significant predictors of poorer language function after aSAH. Language function improves significantly within the first 3 months after aSAH and continues to improve until 18
months after aSAH. Longitudinal studies have typically used the verbal and semantic fluency task, which is not subject to practice effects. Consequently, improvement in language function over time cannot be attributed solely to repeated test presentation. Mavaddat and colleagues followed 47 patients with a favorable neurological outcome (ie, GOS scores of 4 or 5 corresponding to “moderate disability” and “good recovery,” respectively) between 6 and 24 months after aSAH. Despite patients having a favorable neurological outcome according to the GOS, 76% of aSAH survivors were significantly impaired on the verbal and semantic fluency task. The data suggest that overall patient status, as measured by the GOS, may not be an accurate indicator of language dysfunction after aSAH.

Functional Outcome
Neuropsychological assessments attempt to characterize performance in individual cognitive domains. In the real world, cognitive domains do not work in isolation, but rather interact with each other to influence behavior. The components of functional outcome include activities of daily living, instrumental activities of daily living, and the ability to return to one’s previous occupation. Each of these domains is addressed in turn.

Activities of Daily Living
Activities of daily living (ADLs) are those one performs for self-care. Examples of ADLs include feeding, grooming, dressing, bathing, personal hygiene, and toileting. ADL impairments are not as prevalent in comparison to some cognitive impairments; studies indicate that deficits in ADLs are present in 4% to 12% of patients who have experienced aSAH. The prevalence of ADL deficits may be affected by the admission neurological grades of patients who are studied, because studies investigating ADL performance after aSAH use patients with a variety of neurological outcomes. Specific ADL deficits at hospital discharge include incontinence and maintaining personal hygiene. At the present time, it is unknown if this constellation of ADL deficits extends to longer follow-up periods. Deficits of visual memory, visuospatial function, and psychomotor functioning are significant predictors of ADL impairment at 3 months after aSAH, thereby highlighting the link between cognition and functional outcome.

The instruments used to measure ADLs are known to have ceiling effects. For instance, in studies that measure ADLs using the Barthel Index, 95% of assessed patients achieve the highest possible score. Furthermore, many ADL measures (eg, the Barthel Index, the Katz Index of Independence in ADLs) rely heavily on patient self-report. Although self-report provides a rich source of information about cognitive and day-to-day functioning, the accuracy of self-reported measures is uncertain. For instance, patients may be uncomfortable or embarrassed at disclosing difficulties with toileting or bathing. Thus, the specific functional profile with respect to ADL impairments at different follow-up periods after aSAH remains unclear.

Instrumental Activities of Daily Living
Instrumental activities of daily living (IADLs) are more complex than ADLs and include tasks like managing finances, shopping, and housekeeping. IADLs are more frequently impaired than ADLs with an estimated prevalence of 44% to 93%. Deficits of visual memory and psychomotor functioning are significant predictors of IADL impairment. Similar to ADLs, the instruments used to measure IADLs may not be sensitive to the subtle cognitive difficulties aSAH survivors may experience when performing tasks like driving and managing finances. When driving on a busy city street, for instance, aSAH survivors might experience transient lapses of concentration or feelings of being overwhelmed; despite these subtle difficulties, aSAH survivors would obtain the maximum favorable score on the Mode of Transportation subscale of the Lawton IADL scale, because their performance fulfills the criteria of traveling independently. Furthermore, commonly used measures of IADL performance, like the Lawton IADL scale, often use a binary scoring system that does not allow for different gradients of IADL performance. IADL measures also rely heavily on self-report, which may not accurately reflect patients’ true performance capabilities. Patients may be reluctant to disclose difficulties with driving, for instance, for fear of having their driver’s license suspended. Additional research is needed to characterize the specific IADL profile in aSAH survivors.

Return to Work
One of the most important components of real-world functioning is the ability to return to one’s previous occupation. Many aSAH survivors are young and have financial responsibilities and families to support. Most studies estimate that among patients who were employed before aSAH, up to 40% are unable to return to their previous occupation. Among patients who were employed before aSAH, up to 40% are unable to return to their previous occupation. Some patients return to jobs with less responsibility, and oftentimes patients must work fewer hours as a result of fatigue and cognitive difficulties. Return to work and working ability are also influenced by the location of brain lesions. Vilki and colleagues found that left hemisphere lesions from aSAH were associated with failure to return to work and significantly reduced working ability. Self-reported planning and reasoning impairments and poorer performance on tests of executive function were also associated with failure to return to work. Despite demonstrating a correlation between left hemisphere lesions and failure to return to work, the investigators did not examine language function in their sample, a cognitive domain predominantly mediated by the left hemisphere. Further research is necessary to determine how different cognitive domains affect one’s ability to return to work after aSAH.

Quality of Life
Quality of life (QoL) is intimately intertwined with life satisfaction and is often subdivided into several dimensions, like social, physical, and mental QoL. To measure QoL, investigators often use the Sickness Impact Profile or the Short Form-36, both of which rely on patient self-report. The most frequently impaired QoL domains in aSAH survivors are emotional functioning, social functioning, and phys-
ical functioning. Deficits in QoL domains, however, are highly variable and depend on the follow-up interval. Many studies have documented improvement in QoL over the 18-month period after aSAH, most notably in the domain of physical functioning, but also in social and emotional functioning. Despite improvement in QoL in the 18 months after aSAH, Scharbrodt and colleagues suggest that deficits in QoL can persist up to 5 years after aSAH, even in patients who have made a “good recovery” according to the GOS. Interestingly, some QoL domains worsen over time; household management, eating habits, and recreational activities, for instance, have been shown to worsen over the first 18 months after aSAH. Similar to ADLs and IADLs, visual memory, visuospatial function, and psychomotor function are significant predictors of poorer QoL after aSAH. Verbal memory, language, and executive function have no relationship to QoL indices, suggesting that impairment in these cognitive domains has little impact on functional outcome. Anxiety, depression, fatigue, neuroticism, and a passive coping style are also associated with reduced QoL after aSAH. Severity of aSAH on hospital admission, as measured by Hunt and Hess grade, can also predict QoL after aSAH; Hütter and colleagues found that patients with a more severe aSAH experienced reduced QoL 4 to 5 years later. The GOS has also shown to be a significant predictor of physical QoL after aSAH, but the correlation is weak to moderate. Patients with ruptured middle cerebral artery aneurysms had poorer QoL in 1 study, especially if the aneurysms were located in the left hemisphere. Little is known about the neuroanatomical correlates of poorer QoL in patients with aSAH.

**Additional Factors Affecting Outcome**

Cognitive and functional outcome are also influenced by mood, anxiety, sleep, fatigue, and method of neurosurgical treatment (e.g., clipping or coiling). The effects of each of these factors is discussed in turn.

**Mood and Anxiety**

One of the most investigated areas of patient outcome after aSAH is depression. The frequency of depression is variable among aSAH survivors with estimates ranging from 5% to 50%. Unlike many cognitive domains that improve over time (e.g., verbal memory and aspects of executive function), depression is unique in that it remains stable over the 18-month period after aSAH. The constant prevalence of depression over time may be attributed to the life-threatening experience of aSAH or to the fear of recurrent hemorrhage. Some studies have found that depression is unrelated to the severity or the specific profile of cognitive impairment, but other investigators have found a correlation. Mavaddat and colleagues showed that depression was associated with poorer performance on tests of language and spatial working memory but not on tests of visual memory. Additional studies should be conducted to gain a better understanding of how depression affects cognition in patients with aSAH.

Anxiety is another common consequence after aSAH, affecting between 27% and 54% of patients. Similar to depression, anxiety does not decrease in prevalence over the 18-month period after aSAH. One potential explanation for the stable prevalence of anxiety relates to patients’ beliefs in the chronic nature of their condition and in treatment control and personal control over their medical condition. Sheldrick and colleagues found that patients’ beliefs in the chronic nature of their medical condition increased over time. Additionally, patients’ beliefs in treatment control and personal control over their medical condition decreased over time. These factors may contribute to mood disturbances, including elevated anxiety and depression. Two of the most frequent symptoms of anxiety are intrusive thoughts related to aSAH and avoidance of reminders about aSAH; at 3 months postictus, 60% of patients reported either intrusive thoughts or avoidance of reminders, whereas 30% reported both symptoms. Patients report these symptoms significantly less often over an 18-month period after aSAH, although some have reported that the prevalence of these reported symptoms remains stable over time. Nevertheless, the prevalence of anxiety among patients with aSAH remains approximately 3 times higher than in the general population.

The high rate of intrusive thoughts and avoidance of reminders reported by patients with aSAH suggests that posttraumatic stress disorder (PTSD) may be a concern. Indeed, 1 of the most striking findings in recent years relates to the high prevalence of PTSD among patients with aSAH with estimates ranging between 18% and 37%. Sheldrick and colleagues demonstrated that the prevalence of PTSD significantly decrease from 5 to 14 weeks after hospital admission. Other investigators, however, found that the prevalence of PTSD remained stable between 3 months and 13 months after aSAH. Additional longitudinal studies are needed to determine the true stability of PTSD in aSAH survivors. PTSD has a detrimental effect on QoL and functional outcome. Investigators have demonstrated that PTSD is a significant predictor of poorer physical and mental QoL, poorer quality of sleep, and increased fatigue. The occurrence of PTSD in patients with aSAH is also mediated by age and one’s coping strategies; younger patients and those with maladaptive coping strategies are most at risk for developing PTSD after aSAH.

**Sleep and Fatigue**

Fatigue is a common self-reported concern expressed by patients with aSAH. Over 31% of patients report feeling tired on a daily basis and patients with aSAH experience significantly more fatigue than age-matched healthy control subjects. Many patients with aSAH also experience profound sleep disturbances, with sleep being characterized as pathological in 37% to 45% of patients. In terms of sleep quality, sleep efficiency and daytime function are significantly below normal levels, and 1 in 3 patients has either insomnia or excessive daytime sleepiness. Other common sleep disturbances include repeated awakenings throughout the night, difficulty falling asleep, and difficulty returning to sleep after awakening. Sleep disturbances and fatigue have a considerable impact on QoL. Although QoL does not differ between control subjects and patients with no sleep dysfunction, patients...
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<th>Authors</th>
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| Benke et al\(^{11}\) | 11 patients, 8 control subjects | Not stated            | Executive function: WCST, TAP  
Verbal memory: CVLT  
Psychomotor function: GP, TMT-A  
Processing speed: CalCAP simple and choice RT  
Visuospatial function: ROCF-Copy, Block design (WAIS-R)  
Visual memory: Visual Reproduction II (WMS-R), ROCF-Recall  
Verbal memory: CVLT  
Language: TT, BNT | Mean 75 months | Executive function: not stated  
Verbal memory: ↓  
Psychomotor function: ↓  
Processing speed: ↓  
Visual spatial function: ↓  
Visual memory: ↓  
Naming: ↓  
Language: ↓ for BNT; NS for TT |
| Mayer et al\(^{12}\); Kreiter et al\(^{21}\) | 113 HH 1–5, mRS 0–5 | Executive function: TMT-B, WCST  
Psychomotor function: GP, TMT-A  
Processing speed: CalCAP simple and choice RT  
Visuospatial function: ROCF-Copy, Block design (WAIS-R)  
Visual memory: Visual Reproduction II (WMS-R), ROCF-Recall  
Verbal memory: CVLT  
Language: TT, BNT | 3 months | Executive function: ↓  
Psychomotor function: ↓  
Processing speed: ↓  
Visual spatial function: ↓  
Visual memory: ↓  
Naming: ↓  
Language: ↓ |
| Mavaddat et al\(^{18}\) | 47 GOS 4–5 | Working memory: Spatial Working Memory (CANTAB)  
Executive function: Stockings of Cambridge (CANTAB), IED (CANTAB)  
Spatial memory: Spatial Span (CANTAB), Spatial Recognition Memory (CANTAB)  
Visual memory: Pattern Recognition Memory (CANTAB)  
Language: verbal and semantic fluency | 6–24 months | Working memory: ↓  
Executive function: NS  
Spatial memory: NS  
Visual memory: ↓  
Language: ↓ |
| Hillis et al\(^{20}\) | 27 HH 1–4 | Attention: digit span  
Executive function: Stroop task  
Visuospatial function: Block Design (WAIS-R)  
Psychomotor function: GP, Digit Symbol  
Verbal memory: RAVLT  
Visual memory: RMT-Faces  
Language: Verbal and semantic fluency | 3 months | Attention: ↓  
Executive function: ↓  
Psychomotor function: ↓  
Visual memory: ↓  
Language: ↓ |
| Manning et al\(^{43}\) | 35 patients, 35 control subjects | GOS 5 | Executive function: WCST, TOL, Stroop test, Cognitive Estimates task, Luria’s Motor and Graphic Sequences  
Short-term memory: Digit span forwards  
Working memory: Digit span backwards  
Visual memory: RMT-Faces, Figure-Form 2 (Adult Memory and Information Processing Battery), Famous Faces Test  
Language: Verbal and semantic fluency | Mean 26 weeks | Executive function: ↓ for all tests except Cognitive Estimates task; NS for Cognitive Estimates task  
Short-term memory: NS  
Working memory: ↓  
Verbal memory: ↓ for all tests except RMT-Words and GBVLT-DR; NS for RMT-Words and GBVLT-DR  
Visual memory: NS for all tests except Famous Faces Test; ↓ for Famous Faces Test  
Language: ↓ |
| Bellebaum et al\(^{45}\) | 16 clipped, 16 coiled, 16 control subjects | HH 1–4 | Attention: Alertness subtest (TAP), Divided Attention subtest (TAP), Go/No-go (TAP)  
Executive function: Cognitive Estimates task, Temporal Judgment (BADS), Key Search (BADS), Dysexecutive Questionnaire (BADS)  
Short-term memory: Digit span forwards  
Working memory: Digit span backwards  
Verbal memory: Logical memory (WMS-R)  
Visual memory: BVRT  
Language: Verbal and semantic fluency | Mean 28 months (clipped), mean 23 months (coiled) | Clipped:  
Attention: NS  
Executive function: NS  
Short-term memory: NS  
Working memory: NS  
Verbal memory: ↓  
Visual memory: ↓  
Language: NS  
Coiled:  
Attention: NS  
Executive function: NS  
Short-term memory: NS  
Working memory: NS  
Verbal memory: ↓  
Visual memory: ↓  
Language: NS |

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<tr>
<td>Salmond et al47</td>
<td>20 patients, 20 control subjects</td>
<td>WFNS 1–5</td>
<td>Decision-making: Cambridge Gambling Task (CANTAB), Information Sampling Task (CANTAB), BlindWheel Task, UpDown Task</td>
<td>Mean 68 months</td>
<td>Speed of decision-making: NS</td>
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<td>Quality of decision-making: NS</td>
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<td>Predecisional processing: NS</td>
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<td>Sensitivity to probability: ↓</td>
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<td>Impulsivity: ↑</td>
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<td>Hadjivassiliou et al95</td>
<td>80 patients (40 coiled, 40 clipped), 31 control subjects</td>
<td>GOS 3–5, WFNS 1–4</td>
<td>IQ: Vocabulary (WAIS-R), Digit Span (WAIS-R), Similarities (WAIS-R), Arithmetic (WAIS-R), Picture Arrangement (WAIS-R), Block Design (WAIS-R) Attention: TMT Executive function: Digit ordering, IED (CANTAB), Stockings of Cambridge (CANTAB) Visuospatial function: Form discrimination test (specially constructed) Working memory: Spatial Working Memory (CANTAB) Memory: Word and face recognition test (specially constructed), short story recall (specially constructed), complex figure recall (specially constructed), Spatial Span (CANTAB) Language: BNT, verbal and semantic fluency</td>
<td>1 year</td>
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<td>Fontanella et al96</td>
<td>20 clipped, 17 coiled, 18 control subjects</td>
<td>GOS 5</td>
<td>Intelligence: Verbal judgment test, Raven Coloured Matrices test Attention: Visual search test Executive function: Picture Arrangement (WAIS-R), Elithorn’s test Short-term memory: bisyllabic words repetition test, Corsi’s block task Verbal memory: Verbal learning test, Logical Memory test Spatial learning: Corsi’s block task Language: verbal, semantic and associative fluency, sentence construction test</td>
<td>6 months</td>
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<td>Clipped:</td>
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<td>Intelligence: NS</td>
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<td>Executive function:↓</td>
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<td>Short-term memory: NS</td>
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<td>for Logical Memory test: NS</td>
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<td>for verbal learning test: NS</td>
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<td>Language: ↓ for sentence construction test, verbal fluency and category fluency; NS for associative fluency</td>
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<td>Colled:</td>
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<td>Intelligence: NS</td>
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<td>Attention: NS</td>
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<td>Executive function: NS</td>
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<td>Short-term memory: NS</td>
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<td>Verbal memory: NS</td>
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<td>for sentence construction test, verbal fluency and category fluency: NS</td>
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<td></td>
<td>NS for associative fluency</td>
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<tr>
<td>Mavaddat et al107</td>
<td>31 patients, 29 control subjects</td>
<td>GOS 4–5</td>
<td>Decision making: Cambridge Gambling Task (CANTAB)</td>
<td>6–24 months</td>
<td>Speed of decision-making: NS</td>
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<td>Quality of decision-making: NS</td>
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<td>Impulsivity: NS</td>
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<td>Risk-taking behavior: ↑</td>
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(Continued)
with sleep dysfunction have significantly lower QoL compared with the former 2 groups.77 Likewise, greater fatigue is associated with poorer QoL.85 Sleep disturbances and fatigue tend to be persistent, showing no significant improvement over a 24-month period after aSAH.14,62,91

### Clipping Versus Coiling

In recent years, there has been debate over the effects of endovascular embolization (“coiling”) and microsurgical clipping of ruptured aneurysms on patient outcome. Findings from the International Subarachnoid Aneurysm Trial, a randomized clinical trial, suggest that clinical outcome, as measured by the modified Rankin Scale,92 is better among clipped patients than among coiled patients.93 The majority of studies indicate that clipped and coiled patients do not differ with respect to verbal memory, visual memory, visuospatial function, attention, executive function, information processing speed, psychomotor function, language, return to work, QoL, depression, anxiety, and sleep disturbances.16,27,28,45,77,94 A few studies, however, indicate that clipped patients are more depressed and perform poorer on tests of executive function, visual memory, and verbal memory relative to their coiled counterparts.16,45,95,96 Why clipping is associated with greater cognitive impairment in these studies is unclear. Patients were not randomly assigned to clipping or coiling treatment, so differences in baseline risk for cognitive impairment cannot be excluded. Another possibility is that clipped patients may have more brain injury; Hadjivassiliou and colleagues95 found that 48% of clipped patients had focal encephalomalacia compared with 0% of coiled patients. Moreover, a significantly greater proportion of clipped patients had infarcts (87%) relative to coiled patients (57%).

Some studies have challenged the notion that clipped patients have greater cognitive deficits than coiled patients. Santiago-Ramajo and colleagues94 observed poorer verbal memory among coiled patients versus clipped patients 4 months after aSAH. Likewise, Frazer and colleagues28 found that coiled patients performed significantly poorer on tests of visuospatial function, executive function, and information processing speed 6 months after aSAH compared to clipped patients. Studies that observed poorer prognosis among coiled patients examined cognitive performance within 6 months of aSAH. Interestingly, of the 4 studies that observed poorer prognosis among clipped patients,16,45,95,96 3 examined cognitive function at least 1 year after aSAH.16,45,95 Clipping and coiling may thus have different effects on cognitive outcome depending on time since treatment with clipped patients having superior cognitive outcome in the short-term and coiled patients having superior cognitive outcome in the long-term. Future studies should investigate the relative efficacy of clipping and coiling on cognitive and functional outcome over longer durations.

<table>
<thead>
<tr>
<th>Authors</th>
<th>Patient Sample Size</th>
<th>HH/WFNS/mRS/GOS Scores</th>
<th>Tests Used</th>
<th>Follow-Up Period</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Akyuz et al108</td>
<td>40 patients (22 had temporary clipping during surgery, 18 did not), 20 control subjects</td>
<td>HH 1–2, GOS 4–5</td>
<td>Executive function: WCST</td>
<td>3 months and 2 years</td>
<td>Patients who received temporary clipping during surgery:</td>
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<td></td>
<td>Executive function: ↓ Patients who did not receive temporary clipping during surgery: ↓ 2 years:</td>
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<td></td>
<td>Executive function: ↓ Patients who received temporary clipping during surgery: ↓</td>
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<td>Executive function: NS</td>
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</tbody>
</table>

↓ indicates that performance of patients with aSAH is significantly lower than that of healthy control subjects, P<0.05; ↑, performance of patients with aSAH is significantly higher than that of healthy control subjects, P<0.05; NS, performance of patients with aSAH is no different from that of healthy control subjects, P>0.05; BADS, Behavioural Assessment of the Dysexecutive Syndrome; BNT, Boston Naming Test; BVRT, Benton Visual Retention Test; CalCAP, California Computerized Assessment Package; CANTAB, Cambridge Neuropsychological Test Automated Battery; CVLT, California Verbal Learning Test; GBVLT, Grober and Buschke Verbal Learning Test; GBVLT-FR, Grober and Buschke Verbal Learning Test–Free Recall; GBVLT-DR, Grober and Buschke Verbal Learning Test–Delayed Recall; GBVLT-TR, Grober and Buschke Verbal Learning Test–Total Recall; GP, Grooved Pegboard; HH, Hunt and Hess Grade; IED, Intradimensional/Extradimensional Set Shift; IQ, intelligence quotient; mRS, modified Rankin Scale; RAVLT, Rey Auditory Verbal Learning Test; RMT, Recognition Memory Test; ROCF, Rey-Osterrieth Complex Figure; ROCF-IR, Rey-Osterrieth Complex Figure–Immediate Recall; ROCF-DR, Rey-Osterrieth Complex Figure–Delayed Recall; TAP, Test of Attentional Performance; TAVEC, Test de Aprendizaje Verbal España–Complutense (Complutense-Spain Verbal Learning Test); TAVEC-LTFR, Test de Aprendizaje Verbal España–Complutense (Complutense-Spain Verbal Learning Test)–Long Term Free Recall; TAVEC-STFR, Test de Aprendizaje Verbal España–Complutense (Complutense-Spain Verbal Learning Test)–Short Term Free Recall; TMT-A, Trail Making Test–Part A; TMT-B, Trail Making Test–Part B; TOL, Tower of London; TT, Token Test; VOSP, Visual Object and Space Perception Battery; WAIS-R, Wechsler Adult Intelligence Scale–Revised; WAIS-III, Wechsler Adult Intelligence Scale–III; WCST, Wisconsin Card Sorting Task; WFNS, World Federation of Neurological Surgeons Grade; WMS, Wechsler Memory Scale; WMS-R, Wechsler Memory Scale–Revised.
### Table 2. Functional Outcome After aSAH

<table>
<thead>
<tr>
<th>Authors</th>
<th>Patient Sample</th>
<th>HH/WFNS/ mRS/ GOS/GCS Scores</th>
<th>Tests Used</th>
<th>Follow-Up Period</th>
<th>Findings</th>
<th>Prevalence of Impairment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mayer et al&lt;sup&gt;12&lt;/sup&gt;</td>
<td>113</td>
<td>HH 1–5, mRS 0–5</td>
<td>QoL: SIP</td>
<td>3 months</td>
<td>QoL: Ambulation: NS Mobility: NS Body care and movement: NS Emotional behavior: ↓ Social interaction: NS Communication: ↓ Alertness behavior: ↓ Eating: NS Sleep and rest: NS Work: NS Home maintenance: NS Recreation and pastimes: NS</td>
<td>N/A</td>
</tr>
<tr>
<td>Ørbo et al&lt;sup&gt;13&lt;/sup&gt;</td>
<td>42</td>
<td>HH 1–4, GOS 3–5</td>
<td>Depression: BDI</td>
<td>1 year</td>
<td>N/A</td>
<td>Depression: 5%</td>
</tr>
<tr>
<td>Powell et al&lt;sup&gt;14&lt;/sup&gt;</td>
<td>49</td>
<td>WFNS 1–2, GOS 4–5</td>
<td>ADLs, IADLs, and QoL: BICRO-39 Anxiety: HADS Depression: HADS, BDI</td>
<td>18 months</td>
<td>Mobility: ↓ Self-organization: ↓ Productive employment: ↓ Personal care: NS Socializing: NS Psychological well-being: NS Anxiety: NS Depression (HADS): NS</td>
<td>Mobility: 43% Self-organization: 47% Productive employment: 49% Personal care: 4% Socializing: 16% Psychological well-being: 12% Anxiety: 18% Depression: 10% (HADS), 16% (BDI)</td>
</tr>
<tr>
<td>Martinaud et al&lt;sup&gt;15&lt;/sup&gt;</td>
<td>74</td>
<td>GOS 3–5</td>
<td>Depression: MADRS Anxiety: Goldberg Scale</td>
<td>20–21 months</td>
<td>N/A</td>
<td>Depression: 12% Anxiety: 27%</td>
</tr>
</tbody>
</table>

(Continued)
Table 2. Continued

<table>
<thead>
<tr>
<th>Authors</th>
<th>Patient Sample Size</th>
<th>HH/WFNS/ mRS/ GOS/GCS Scores</th>
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<th>Prevalence of Impairment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proust et al(^{16})</td>
<td>36 clipped, 14 coiled</td>
<td>GOS 4–5, mRS 0–3</td>
<td>QoL: RNLI Depression: MADRS Anxiety: Goldberg Scale</td>
<td>Median 14 months</td>
<td>N/A</td>
<td>Clipped: Anxiety: 33%ulings of interest: 4%</td>
</tr>
<tr>
<td>Mavaddat et al(^{18})</td>
<td>29 early surgery patients, 18 late surgery patients</td>
<td>GOS 4–5</td>
<td>Depression: BDI</td>
<td>6–24 months</td>
<td>N/A</td>
<td>Depression: 26% (early surgery patients), 22% (late surgery patients)</td>
</tr>
<tr>
<td>Vilkki et al(^{32})</td>
<td>134</td>
<td>WFNS 1–5, mRS 0–4</td>
<td>N/A</td>
<td>Mean 12.5 months</td>
<td>N/A</td>
<td>Return to work: 68% returned to work at same level, 24% reported decreased working ability</td>
</tr>
<tr>
<td>Noble and Schenk(^{37})</td>
<td>83</td>
<td>WFNS 1–4</td>
<td>ADLs: FIM-MS Anxiety and depression: HADS</td>
<td>Mean 114 days</td>
<td>N/A</td>
<td>ADLs: 6% Anxiety and depression: 26%</td>
</tr>
<tr>
<td>Egge et al(^{40})</td>
<td>32</td>
<td>HH 1–3</td>
<td>Depression: BDI</td>
<td>1 year</td>
<td>N/A</td>
<td>Mild/moderate depression: 29–36%</td>
</tr>
<tr>
<td>Bellebaum et al(^{45})</td>
<td>16 clipped, 16 coiled, 16 control subjects</td>
<td>HH 1–4</td>
<td>Depression: BDI Subjective executive dysfunction: DEX</td>
<td>28 months</td>
<td>Clipped: Depression: ↑ Subjective executive dysfunction: ↑ Coiled: Depression: NS Subjective executive dysfunction: NS</td>
<td></td>
</tr>
<tr>
<td>Salmond et al(^{47})</td>
<td>20 patients, 20 control subjects</td>
<td>WFNS 1–5</td>
<td>Depression: BDI</td>
<td>Mean 68 months</td>
<td>Depression: NS</td>
<td>N/A</td>
</tr>
<tr>
<td>Pasternak et al(^{60})</td>
<td>878</td>
<td>WFNS 1–3, GOS 3–5</td>
<td>ADLs: BI</td>
<td>3 months</td>
<td>N/A</td>
<td>ADLs: 88% had BI score ≥95</td>
</tr>
<tr>
<td>Hackett and Anderson(^{61})</td>
<td>230</td>
<td>HH 1–5</td>
<td>QoL: SF-36</td>
<td>Mean 1.2 years</td>
<td>QoL:</td>
<td>Return to work: 66% returned to work</td>
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<table>
<thead>
<tr>
<th>Authors</th>
<th>Patient Sample Size</th>
<th>HH/WFNS/ mRS/ GOS/GCS Scores</th>
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<th>Findings</th>
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<tbody>
<tr>
<td>Kim et al65</td>
<td>385</td>
<td>HH 0–5, mRS 0–4, GOS 3–5</td>
<td>ADLs: BI</td>
<td>Mean 4.7 months</td>
<td>N/A</td>
<td>ADLs: 96% had BI score of 100</td>
</tr>
<tr>
<td>Fernandez et al68</td>
<td>257</td>
<td>N/A</td>
<td>IADLs: Lawton IADL Scale</td>
<td>3 months</td>
<td>N/A</td>
<td>IADL deficits: 54%</td>
</tr>
<tr>
<td>Kirkness et al69</td>
<td>42</td>
<td>HH 1–5, GCS 5–15</td>
<td>ADLs and IADLs: FSE</td>
<td>3 months</td>
<td>N/A</td>
<td>ADLs and IADLs (completely dependent, somewhat dependent or independent with difficulty): Personal care: 55% Ambulation: 81% Travel: 93% Work: 93% Home management: 90% Leisure and recreation: 88% Social integration: 86% Standard of living: 86% Cognition and behavior: 83% Financial independence: 62% Return to work: 18% returned to work</td>
</tr>
<tr>
<td>Carter et al70</td>
<td>182</td>
<td>HH 1–3, GOS 2–5</td>
<td>ADLs: BI OoL: RNLI Depression: ZSRDS</td>
<td>Mean 2.75 years</td>
<td>Return to work: ↓</td>
<td>ADLs: 76% had BI score of 100</td>
</tr>
<tr>
<td>Haug et al71</td>
<td>22</td>
<td>GOS 45, mRS 0–3, HH 1–3</td>
<td>OoL: SF-36, GHQ-30</td>
<td>3 and 12 months</td>
<td>3 months: SF-36: Social functioning: ↓</td>
<td>Return to work: 60% returned to work full-time at 12 months post-SAH, 27% returned to work part-time at 12 months post-SAH</td>
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</tbody>
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Table 2. Continued

<table>
<thead>
<tr>
<th>Authors</th>
<th>Patient Sample Size</th>
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<tbody>
<tr>
<td>Tomberg et al72</td>
<td>51</td>
<td>HH 1–4, GOS 3–5</td>
<td>N/A</td>
<td>Mean 15.7 months</td>
<td>N/A</td>
<td>Return to work: 61% returned to work full-time, 7% were employed part-time</td>
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<tr>
<td>Wermer et al73</td>
<td>610</td>
<td>mRS 0–3</td>
<td>Depression: HADS Anxiety: HADS</td>
<td>Mean 8.9 years</td>
<td>N/A</td>
<td>Return to work: 26% unable to return to work, 24% worked shorter hours/had less responsibility Depression: 9% Anxiety: 11%</td>
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<th>Authors</th>
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<th>Findings</th>
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</tr>
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<tbody>
<tr>
<td>Buchanan et al76</td>
<td>28</td>
<td>GOS 4–5</td>
<td>Personality: Adjective Checklist Psychological distress: BSI</td>
<td>Mean 19 months</td>
<td>N/A</td>
<td>Psychological distress: 58%</td>
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<td>Suicide ideation in past week: 13%</td>
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<td>Return to work: 15% returned to work at same level, 35% worked fewer hours/had less responsibility, 50% received disability benefits</td>
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<td>Increased physical fatigue: 54%</td>
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<td>Increased mental fatigue: 71%</td>
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<td>Decreased social contacts: 57%</td>
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<td>Decreased tolerance for being rushed: 61%</td>
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<td>Decreased tolerance for children and other people: 57%</td>
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<td>Decreased tolerance for lack of order: 54%</td>
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<td>Decreased tolerance for normal sound levels: 46%</td>
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<td>Moderate/severe decrease in libido: 55%</td>
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<tr>
<td>Schuiling et al77</td>
<td>83</td>
<td>WFNS 1–5, mRS 0–5</td>
<td>Sleep: SDL, ESS QoL, SF-36 Depression: BDI</td>
<td>Mean 1.7 years</td>
<td>N/A</td>
<td>SF-36: 53% reported tiredness</td>
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<td>SDL:</td>
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<td>Severe sleep problems: 34%</td>
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<td>Difficulty falling asleep: 25%</td>
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<td>Difficulty returning to sleep: 28%</td>
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<td>Repeated awakenings: 31%</td>
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<td>Snoring: 35%</td>
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<td>Poor concentration: 18%</td>
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<td>Memory deficits: 23%</td>
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<td>Feelings of tiredness: 31%</td>
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<td>Frequent daytime periods of dozing: 6%</td>
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<td>Loss of libido: 27%</td>
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<td>Insomnia: 28%</td>
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<td>Excessive daytime sleepiness: 9%</td>
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<td></td>
<td>Return to work: 22% returned to work full-time, 19% returned to work part-time</td>
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<td></td>
<td></td>
<td></td>
<td>Depression: 28%</td>
</tr>
<tr>
<td>Barth et al82</td>
<td>7</td>
<td>HH 3–4</td>
<td>QoL: SF-36 Depression: HDRS</td>
<td>10–20 months</td>
<td></td>
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<tr>
<td>Visser-Meily et al85</td>
<td>141</td>
<td>GOS 3–5</td>
<td>Anxiety: HADS Depression: HADS Fatigue: FSS</td>
<td>Mean 36.1 months</td>
<td>N/A</td>
<td>Anxiety: 32%</td>
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<td>Depression: 23%</td>
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<td></td>
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<td>Fatigue: 67%</td>
</tr>
</tbody>
</table>

(Continued)
To what extent do aneurysm-securing procedures per se affect cognitive and functional outcome? Insight into this question could be provided by examining patients with perimesencephalic subarachnoid hemorrhage (pSAH), a nonaneurysmal form of SAH characterized by accumulation of blood in the midbrain cisterns.97 Perimesencephalic SAH is typically treated conservatively without surgical intervention. Although early studies investigating outcome after pSAH reported a favorable prognosis, with no change in QoL or return to work,98,99 more recent reports suggest that pSAH may not be as benign as previously believed. Marquardt and colleagues 100 found that 62% of pSAH survivors continued to experience headaches, depression, and forgetfulness on average 23 months after pSAH. Additionally, only 41% of survivors were able to return to their previous occupations. Madureira and colleagues101 observed minor cognitive impairments in 72% of pSAH survivors and depression in 33% on average 39 months after pSAH. Schweizer and colleagues recently reported the case of a high-functioning pSAH survivor with persistent cognitive and functional decline 7 months postictus (T.A.S., T.A.-K., R.L.M., unpublished data, 2010). These findings suggest that reduced cognitive and functional outcome cannot be explained by surgical or endovascular procedures per se.
Deficits in memory, executive function, and language are common cognitive sequelae of aSAH. Performance in these cognitive domains improves with time, but many "recovered" aSAH survivors continue to experience cognitive deficits 2 to 3 years later. Although several studies have documented impairments in ADLs and IADLs among "recovered" aSAH survivors, these findings may underestimate the true prevalence of impairment in day-to-day functioning. Commonly used measures of ADLs and IADLs, in addition to relying heavily on self-report, may be insensitive to the difficulties experienced by aSAH survivors when performing day-to-day tasks like preparing meals and driving. Deficits in cognitive and functional performance are further complicated by depression, anxiety, fatigue, and sleep disturbances.

Results from neuroimaging studies suggest that the cognitive deficits after aSAH can be attributed to macroscopic changes in brain structure. Recent research suggests that aSAH also affects brain function at a microscopic, synaptic level. Tariq and colleagues used a rat model of SAH and found that SAH disrupts long-term potentiation in the hippocampus, a process thought to underlie learning and memory. Interestingly, the investigators observed little neuronal damage after SAH, suggesting that disruption of long-term potentiation is not due to cell death. Disruption of long-term potentiation may explain the memory deficits commonly experienced by aSAH survivors.

Neuropsychological assessment, through providing valuable information about cognitive function, may not be suitable for all patients after aSAH. Many patients with aSAH are not capable of completing neuropsychological tests as a result of test difficulty, poor clinical condition, or severe headache from mental exercise. In a study by Cheng and colleagues, 24% of the original patient sample could not complete neuropsychological assessment due to poor clinical condition, whereas 28% could not complete neuropsychological assessment due to test difficulty or severe headache caused by mental exercise. Consequently, the findings obtained by Cheng and colleagues only pertain to aSAH survivors in relatively good condition. Results from outcome studies may thus underestimate the true prevalence of cognitive impairment after aSAH, because data from poor-grade patients with aSAH are often omitted.

Some investigators have raised concern about the statistical methods used to determine cognitive impairment. Significant differences in cognitive test performance between patients with aSAH and control subjects are often accounted for by severely impaired performance in a minority of patients with aSAH rather than mild or moderately impaired performance in a majority of patients. In support of this hypothesis, investigators have observed a bimodal distribution of cognitive impairment with most patients falling within normal limits and a select few falling within the highly impaired range. Hillis and colleagues, for instance, found that on a test of visual memory, 44% of patients with aSAH performed at or below the 10th percentile, whereas 44% performed at or above the 60th percentile. As a result of this bimodal distribution, studies that compare cognitive performance of aSAH survivors with that of healthy control subjects may overestimate the detrimental effects of aSAH. In addition to reporting group comparisons, studies should report prevalence rates of cognitive impairment. Prevalence rates may provide a more representative indication of cognitive deficits after aSAH.

An unsolved debate in the aSAH outcome literature concerns the degree to which the acute characteristics of aSAH contribute to cognitive outcome. Haug and colleagues showed that greater aSAH severity on admission, as measured by Hunt and Hess grade, was associated with poorer performance on tests of visual memory, verbal memory, and language. Similarly, Kreiter and colleagues found that greater aSAH severity on admission was associated with poorer performance on tests of executive function after controlling for demographic factors. These results are in contrast to findings from other studies suggesting a minimal role of acute clinical factors in determining cognitive outcome in patients with aSAH. Ørbo and colleagues showed that Fisher grade (a measure of the thickness of subarachnoid blood) was the only clinical variable associated with cognitive impairment in patients with aSAH. However, Fisher grade accounted for only 12% of the variability in cognitive impairment. This finding suggests that acute clinical factors such as aSAH severity and the thickness of subarachnoid blood are not the primary determinants of cognitive outcome in patients with aSAH. Rather, investigators have hypothesized that secondary complications (e.g., vasospasm, chronic increases in intracranial pressure) may play a larger role in determining cognitive outcome. Little is known about the secondary complications potentially contributing to cognitive impairment; Haug and colleagues found that cognitive outcome was not associated with postoperative vasospasm or postoperative neurological deficits. Future research should characterize the relative contribution of acute clinical factors and secondary complications in determining cognitive outcome.

The large variability in the prevalence of cognitive deficits can be partially attributed to the heterogeneous nature of aSAH. Patients differ with respect to aneurysm location, infarct location, severity of hemorrhage, and incidence of delayed hydrocephalus and angiographic vasospasm. Different studies have patient samples with unique combinations of these factors; consequently, discerning common patterns across different studies is problematic. The heterogeneity is complicated by different follow-up periods across different studies. Despite previous research illustrating an effect of hemorrhage severity and aneurysm location on neuropsychological performance, most studies do not statistically control for these factors. By controlling for aneurysm location, hemorrhage severity, and other aSAH variables as covariates, future studies could obtain a more consistent picture of patient outcome.

The variable results across studies may also be attributed in part to the definition of impairment. Because most cognitive tests do not have a validated threshold for impairment, the
The majority of studies must define impaired performance using
arbitrary cutoffs. Usually, impaired performance is defined as
performance <2 SDs relative to population norms. However,
not all studies adopt this cutoff. Dr. Orbo and colleagues,
for instance, defined impairment as performance <1 SD relative
to population norms. Dr. Orbo and colleagues
found that 40% of aSAH survivors were impaired on the
Wisconsin Card Sorting Task, 22% were impaired on the
Digit Span test, and 56% were impaired on the Stroop
task—Interference measure. In contrast, other studies adopting
a 2-SD impairment cutoff reported that 11% to 29%
of patients with aSAH were impaired on the Wisconsin Card
Sorting Task, 5% to 11% were impaired on the Digit
Span test, and 7% to 22% were impaired on the Stroop
task—Interference measure. Not surprisingly, the data
indicate that a more liberal impairment cutoff coincides with
a greater prevalence of cognitive impairment. Because studies
differ with respect to impairment cutoffs, it becomes difficult
to compare findings across different studies. Variable cutoffs
of impairment may partially account for the wide range of
dysfunction in different cognitive domains.

Implicit within the notion of impaired day-to-day functioning
is the assumption that using adaptive equipment (eg,
walkers, canes) or relying on help from others to perform
daily tasks equates to having a disability in that particular
domain. Patients with aSAH may choose to use adaptive
equipment or to rely on help from others not out of necessity,
but rather as a prophylactic, precautionary measure. A survivor
of aSAH may use a cane, for instance, to feel more
confident in his or her walking ability; it is not necessarily the
case that the patient is incapable of walking independently.
Future research should test this hypothesis by exploring the
prevalence of patients with aSAH who use functional aids by
choice rather than out of necessity.

Subtle cognitive and real-world deficits that accompany
aSAH often go undetected by gross neurological measures
like the GOS. Consequently, patients who have made a “good
recovery” continue to experience deficits in memory, executive
function, and language many years after aSAH. Oftentimes these patients cannot go back to work, and their QoL is
reduced. By raising clinical awareness about residual impair-
ments in cognition and day-to-day functioning, it is our hope that clinicians and researchers will move toward developing
comprehensive rehabilitation strategies that target these sub-
tle yet debilitating symptoms.

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Disclosures
None.

References


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