Memory complaints, performance and fatigue in patients after subarachnoid hemorrhage

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Abstract

Introduction: Patients who have experienced a subarachnoid hemorrhage (SAH), either aneurysmal (aSAH) or angiographically negative (anSAH), often suffer from memory deficits and frequently report memory complaints and fatigue. However, it remains unclear whether memory complaints relate to memory performance, or if memory complaints (also) relate to fatigue. This current study investigated differences between healthy controls and SAH patients (aSAH and anSAH) on a memory performance task and whether memory complaints relate to memory performance and fatigue in SAH patients. *Methods:* 79 SAH patients and 80 healthy controls were included in this study. Fatigue was measured by means of the Dutch Multifactor Fatigue Scale (DMFS), reported memory complaints patients were measured by two items of the Checklist of Cognition and Emotion (CLCE-24) and memory performance by the 15 Words Test (15WT). *Results:* SAH patients scored significantly lower on a memory performance task and significantly higher on mental and physical fatigue compared to healthy controls. anSAH patients reported a higher degree of physical fatigue compared to aSAH patients but there were no differences between both patient groups in mental fatigue or memory performance. No relation was found between memory complaints and memory performance. However, positive correlations were found between memory complaints and mental and physical fatigue. *Discussion:* The lack of relation between memory complaints and memory performance should be taken into account in clinical practice, even as the finding that anSAH patients do not differ in memory performance and degree of mental fatigue compared to aSAH patients and even report higher levels of physical fatigue. The further investigation of the relation between fatigue and cognitive complaints might offer opportunities for new treatment interventions in SAH patients.

Key words: subarachnoid hemorrhage, memory, memory complaints, mental fatigue, physical fatigue

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A subarachnoid hemorrhage (SAH) is a hemorrhage in the subarachnoid space. When this is caused by the rupture of an aneurysm, it is referred to as aneurysmal SAH (aSAH) and when the cause of the hemorrhage is unknown or different, it is referred to as an angiographically negative SAH (anSAH) (Suarez et al., 2006). Approximately 80% of SAH cases are caused by the rupture of an aneurysm (Lawton & Vates, 2017; Suarez et al., 2006). An aSAH accounts for around 1 in 20 strokes (van Gijn et al., 2007). The incidence is highest in people aged 40 to 60 years old, and estimated at 10.5 cases per 100.000 people per year worldwide (Petridis et al., 2017; Suarez et al., 2006). At the time of the bleeding, most often during daily life activities, symptoms that are often described by survivors of SAH are: an extreme headache with a sudden onset, nausea, vomiting and loss of consciousness (Matsuda et al., 2007; Suarez et al., 2006; Togha et al., 2009). Furthermore, the mortality rate of SAH is high. A significant percentage of 10-25% of the patients die before arriving at the hospital (Petridis et al., 2017). If an aSAH patients arrives at the hospital, there are two common treatment options to prevent the aneurysm from rebleeding. One is a neurosurgical approach called clipping, in which a clip is placed over the opening of the aneurysm to ensure the blood does not flow to the aneurysm but can still reach other arteries. The other method is coiling: through a microcatheter metal coils are placed into the aneurysm to cease blood flow and occlude the aneurysm (Lindgren et al., 2018). For anSAH patients, there is no treatment needed.

After being discharged from the hospital, patients can be severely impacted in their daily life. Cognition is often impaired in SAH patients, deficits are for example found in reaction time, executive functioning, language and memory (Geraghty et al., 2020; Hütter et al., 1995). These cognitive deficits partly explain why patients experience an impaired quality

of life, difficulties in relationships and mood disturbances post SAH (Rinkel & Algra, 2011). According to Al-Khindi et al. (2010), verbal memory is one of the most frequently impaired cognitive domains in aSAH patiens. Research shows impaired performance on a verbal memory task, namely the 15 Words Test (15WT) in 45% of all SAH patients (Buunk, 2016). More specifically, aSAH patients scored significantly lower on the 15WT compared to healthy controls. However, there was no significant difference in memory performance between anSAH patients and healthy controls or both patient groups (aSAH and anSAH). While on the other hand studies in general claim that aSAH patients are more affected compared to anSAH patients by having a poorer functional outcome, one would expect this to be reflected in scores on for example a memory performance task (Nesvick et al., 2019). Furthermore, contrary to the findings of Buunk et al (2016)., Sheldon et al. (2013) did not find a significant difference between SAH patients and healthy controls for the Word Span Test: a test for working memory where participants have to remember word-lists of increasing length. To gain more insight into the memory performance of SAH patients, this study will investigate the difference in scores on a memory performance task between both patient groups and between SAH patients and healthy controls.

In addition to cognitive impairments, reported cognitive complaints are also often examined when looking at the well-being of a patient. While cognitive impairments (concluded from neuropsychological assessment) and cognitive complaints may be about the same cognitive function, several studies indicate that cognitive complaints are not always associated with results of neuropsychological assessment (Caplan et al., 2021). Toomela et al. (2004) found in a small sample study that cognitive complaints were not related to cognitive performance in SAH patients. Furthermore, the prevalence of cognitive complaints is higher than the prevalence of cognitive dysfunction in SAH patients (Rinkel & Algra, 2011). One of the fields where cognitive complaints are reported most by SAH patients is in memory (Al-

Khindi et al., 2010; Passier et al., 2010). Passier et al. (2010) investigated the relation between cognitive impairments and cognitive complaints three months post SAH and found that cognitive impairments were related to cognitive complaints. More specifically, memory impairment turned out as a significant predictor for cognitive complaints in a regression analysis. However, Passier et al. used a general score for cognitive complaints and thus did not differentiate between different cognitive functions while talking about complaints. Therefore, this study will investigate the relation between memory complaints and scores on a memory performance task in SAH patients.

Besides that the ideas vary about whether or not there is a relation between cognitive performance and cognitive complaints, some findings suggest that cognitive complaints might have a relation with fatigue (Stulemeijer et al. 2007). In SAH patients, fatigue is reported by 50-70% of the patients and often not limited to the first year after SAH. Even patients with good neurological outcome over 15 years post SAH, suffer from more mental fatigue compared to healthy controls (25-38% versus 14.7%) (Samuelsson et al., 2021). Mental fatigue is a form of fatigue that obstructs mental functioning and is often experienced after performing mentally demanding activities, while physical fatigue is conceptualized as a form of fatigue associated with a physical feeling of exhaustion and coexisting symptoms as bodily pain (Visser-Keizer et al., 2015). Buunk et al. (2016) focused on long-term (3-10 years post SAH) physical and mental fatigue and found higher levels of mental and physical fatigue in SAH patients compared to healthy controls. Several explanations have been suggested for the high degree of fatigue in patients with brain damage. One of them is that the brain requires more effort to process information compared to a healthy brain, but it could also partly be explained by frequently reported sleep disturbances in patients (Wylie & Flashman, 2017). It is suggested that mental fatigue negatively correlates with specific cognitive dysfunction. A recent study in patient with Traumatic Brain Injury (TBI) found a negative correlation

between fatigue and performances in the field of recognition memory and information processing (Chen et al., 2022). In addition, mental fatigue was a predictor for functional outcome in SAH patients (Buunk et al., 2016). However, about the relation between fatigue and cognitive complaints in SAH patients is not much known, while cognitive complaints are associated with quality of life and can therefore play an important role in rehabilitation for patients (Passier et al., 2012). Stulemeijer et al. (2007) concluded that cognitive complaints had a stronger relation with fatigue than with cognitive deficits in Mild Traumatic Brain Injury (MTBI) patients. In this study we will investigate whether memory complaints are related to mental or physical fatigue in SAH patients. In addition, we will investigate differences in the degree of mental and physical fatigue between both patient groups to find out if aSAH patients score higher on fatigue compared to anSAH patients, based on the idea that aSAH patients generally have worse functional outcome (Nesvick et al., 2019; Khan et al., 2013).

In summary, this study investigates whether there are differences between SAH patients (aSAH and anSAH) and healthy controls in memory performance and the degree of mental and physical fatigue. Furthermore, the relation between memory complaints and memory performance in SAH patients will be investigated, even as the relation between memory complaints and fatigue. This research will therefore be able to contribute to a better understanding of memory complaints and its relation to memory performance and fatigue in SAH patients.

Methods

Participants and procedure

A total of 79 SAH patients who were admitted to the neurosurgery unit of the University Medical Center Groningen (UMCG) took part in this study. The inclusion criteria were: a SAH diagnosis based on computed tomography (CT) angiography, digital subtraction angiography or both, age older than 18 years and sufficient knowledge of the Dutch language. Exclusion criteria were psychological or neurological problems and a poor physical condition which prevents participants from undergoing the neuropsychological assessment. A total of 80 healthy controls were recruited via social media and from within the researcher's social network. Healthy controls were matched to SAH patients based on age and educational level. Participation was on a voluntary basis and there was no compensation offered. Prior to the start of the assessment, all participants submitted informed consent. The study is part of the 'Imaging, Cognition and Outcome of Neuropsychological Functioning after Subarachnoid Hemorrhage (ICONS) study' (Khosdelazad & Jorna et al., 2022), and was approved by the Medical Ethical Committee of the UMCG.

Patients were subjected to a neuropsychological assessment approximately five months post SAH. The neuropsychological assessment took around two hours and covers the domain of, intelligence, memory, information processing speed, attention, social cognition and executive functioning. Furthermore, patients were asked to fill in multiple questionnaires. The healthy controls underwent the same neuropsychological assessment. Besides age and educational level of the participant, information about the participants' sex was collected .

Measurements

Fatigue

Fatigue was measured by means of the Dutch Multifactor Fatigue Scale (DMFS). The DMFS distinguishes between mental and physical fatigue and ways of coping with fatigue. In this study, we focused on the subscales mental and physical fatigue. The DMFS uses a 5-point

Likert scale in which participants can report their level of conformity with several propositions. For all scales of fatigue, a sub score was calculated in which a higher score is associated with more fatigue. The mental fatigue scale consisted of seven items such as 'Thinking makes me feel tired' and 'When I feel tired, I have more difficulty concentrating'. The physical fatigue scale consists of six items such as 'I feel physically fit' and 'After a good night of sleep, I wake up rested'. The raw sub score (ranging from 0 to 35) for mental and physical fatigue was used for statistical analysis as a continuous variable. The subscale of mental fatigue has good reliability and the reliability for physical fatigue is acceptable (Visser-Keizer et al., 2015).

Memory performance

Memory performance was measured using the 15 Word Test (15WT). The 15WT is a verbal memory test which distinguishes between immediate recall, delayed recall and recognition. A score on immediate recall can range from 0-75, equivalent to the number of recalled words in the five trials. The score on delayed recall and recognition can range from 0-15. Memory performance is considered impaired if a person scored below the tenth percentile, based on norm groups corresponding to their age, sex and level of education. For the statistical analysis, continuous variables have been used: the raw scores on immediate recall, delayed recall and recognition.

Memory complaints

Memory complaints patients reported were measured by two items of the Checklist of Cognition and Emotion (CLCE-24). The items that were used are: 'Difficulty remembering information' and 'Difficulty remembering information from a long time ago, forgetful'. For the statistical analysis, a binary variable has been used for which a patient could score either 0

(patients who report memory complaints: answered ‘yes’ on at least one out of two items) or 1 (patients who do not report memory complaints: answered ‘no’ on both items).

Research Questions and Hypotheses

Based on the literature, six research questions and hypotheses were formulated:

Question 1: Is there a difference between scores on a memory performance task (immediate recall, delayed recall and recognition) for SAH patients and healthy controls?

Hypothesis 1: Healthy controls score significantly higher on a memory performance task compared to SAH patients.

Question 2: Is there a difference between the scores on mental and physical fatigue between SAH patients and healthy controls?

Hypothesis 2: The scores on mental and physical fatigue are higher in SAH patients compared to healthy controls.

Question 3: Is there a difference between scores on a memory performance task (immediate recall, delayed recall and recognition) for aSAH patients and anSAH patients?

Hypothesis 3: aSAH patients score significantly lower on a memory performance task compared to anSAH patients.

Question 4: Is there a difference between the scores on mental and physical fatigue between aSAH patients and anSAH patients?

Hypothesis 4: The scores on mental and physical fatigue are higher in aSAH patients compared to anSAH patients.

Question 5: What is the relation between reported memory complaints and scores on a memory performance task in SAH patients?

Hypothesis 5: Memory complaints have a negative correlation with scores on a memory performance task in SAH patients.

Question 6: What is the relation between reported memory complaints and scores on mental and physical fatigue in SAH patients?

Hypothesis 6: Memory complaints have a positive correlation with the degree of mental and physical fatigue in SAH patients.

Statistical Analyses

Statistical analyses were executed using IBM SPSS Statistics version 28. To test the difference between scores on a memory performance task (immediate recall, delayed recall, and recognition), an independent sample t-test was performed between SAH patients and healthy controls. The same analysis was also performed for aSAH patients and anSAH patients separately. To test whether there is a difference between the degree of mental and physical fatigue between SAH patients and healthy controls, an independent samples t-test was performed on mental and physical fatigue for SAH patients versus healthy controls. The same analysis was also performed for aSAH patients and anSAH patients separately. To test whether there was a correlation between scores on a memory performance task and reported memory complaints in SAH patients, a point-biserial correlation analysis was performed, using the Pearson correlation coefficient. Another point-biserial correlation analysis, the Pearson correlation, was used to test whether there was a correlation between reported memory complaints and mental and physical fatigue in SAH patients. All analyses were tested against a significance level of α=.05 In case of violation of the assumption of normality, the non-parametric Mann Whitney U test was used to compare groups.

Results

A total of 279 SAH patients were admitted to the UMCG between August 2019 and March 2023. Patients were excluded for this study for numerous reasons: 61 patients died, 25 patients suffered from neurological comorbidity, 9 had insufficient knowledge of the Dutch

language and 41 had other reasons that kept them from participating. From the 143 patients eligible for inclusion, a total of 79 patients chose to participate, with a mean age of 56.4 years (SD= 12.1 years, range= 28-82). At the time of the neuropsychological assessment, the average time since SAH was 4.9 months (SD=12.1, range=3-18). A total of 80 healthy controls participated in this study, with a mean age of 54.4 years (SD=8.3 years, range=29-73). The distribution of age ($X^2(47)=53.534$, p=.238) and sex ($X^2(1)=.004$, p=.949) did not significantly differ for SAH patients and healthy controls. However, the distribution of educational level significantly differed between SAH patients and healthy controls ($X^2(4)=19.214$, p=<.001), healthy controls were more highly educated than SAH patients. aSAH and anSAH patients did not significantly differ in the distribution of age ($X^2(42)=35.852$, p=.737) and educational level ($X^2(4)=.651$, p=.613), but did differ in the distribution of sex ($X^2(1)=4.309$, p=.038). Characteristics of the SAH patients and healthy controls are presented in Table 1.

Table 1

Characteristics of SAH patients and healthy controls

	aSAH patients (n=54)	anSAH patients (n=25)	SAH patients (n=79)	Healthy controls (n=80)
Sex, number of women	37 (68.5%)	11 (44.0%)	48 (60.8%)	49 (61.2%)
Mean age (at time of SAH) *(SD)*	58.1 *(13.0)*	52.9 *(9.2)*	56.43 *(8.3)*	54.4 *(8.3)*
Mean time since SAH (in months)	5.0	4.3	5.0	
Educational level				
Low (1-4)	12 (22.2%)	4 (16%)	16 (20.3%)	2 (2.5%)
High (5-7)	42 (77.8%)	21 (84%)	63 (79.7%)	78 (97.5%)
WFNS score				
Low (GCS 13-15)	47 (87%)	25 (100%)	72 (91.1%)	

High (GCS 3-12)	7 (13%)	0	7 (8.9%)
Treatment			
No treatment	1 (1.9%)		26 (32.9%)
Clipping	7 (13.0%)		7 (8.9%)
Coiling	35 (64.8%)		35 (44.3%)
Stenting	4 (7.4%)		4 (5.1%)
WEB device	7 (13.0%)		7 (8.9%)

Note. aSAH = aneurysmal subarachnoid hemorrhage, anSAH= angiographically negative subarachnoid hemorrhage, WFNS = World Federation of Neurosurgical Societies, GCS = Glasgow Coma Scale. Educational level is based on Verhage categories ranging from 1 (= *less than 6 years of primary education*) to 7 (= *university degree*) (Verhage, 1964).

Memory performance and fatigue in SAH patients and healthy controls

SAH patients scored significantly lower on immediate recall, delayed recall and recognition compared to healthy controls (Table 2).

The DMFS was completed by 79 patients and 62 healthy controls due to the later introduction of the DMFS to the test battery for healthy controls. The healthy controls who completed the DMFS did not significantly differ from the healthy controls who did not complete the DMFS with regard to age ($X^2(29)=32.128$, p=.314), scores on immediate recall ($X^2(35)=38.901$, p=.298), delayed recall ($X^2(11)=5.926$, p=.878) or recognition ($X^2(7)=1.755$, p=.972) on the 15WT. Furthermore, the results indicated that SAH patients scored significantly higher on mental and physical fatigue compared to healthy controls (Table 2).

Table 2

Descriptive and test statistics of SAH patients and healthy controls on DMFS and 15WT

Measure	Patients Mean (SD)	HC's Mean (SD)	z / t (df)	p
15WT-IR	40.77 (9.92)	44.79 (10.67)	-2.508	**.012***
15WT-DR	8.05 (3.23)	9.46 (2.76)	-2.963	**.003***
15WT-REC	27.97 (2.42)	28.76 (1.59)	-2.071	**.038***
N	79	80		

DMFS-M	22.87 (6.71)	16.55 (4.33)	-6.774[a] (139)	**<.001***
DMFS-P	16.73 (5.33)	13.03 (4.10)	-4.662[a] (139)	**<.001***
N	79	62		

Note. HC = Healthy Control, 15WT-IR = Immediate Recall, 15WT-DR = Delayed Recall, 15WT-REC = Recognition, raw scores on subtests of 15 Word Test, DMFS-M = raw score mental fatigue subscale of DMFS, DMFS-P= raw score physical fatigue subscale of DMFS, [a]=t-score *p<.05.

Memory performance and fatigue in aSAH and anSAH patients

When comparing the performance on the 15WT of aSAH patients to the performance of anSAH patients, results show there are no significant differences between the groups for immediate recall, delayed recall or recognition (Table 3).

anSAH patients scored significantly higher on physical fatigue compared to aSAH patients. However, no significant difference was found on the degree of mental fatigue between aSAH and anSAH patients (Table 3).

Table 3

Descriptive and test statistics of aSAH and anSAH patients on DMFS and 15WT

Measure	aSAH patients M (SD)	anSAH patients M (SD)	z / t (df)	p
15WT-IR	40.09 (10.42)	42.64 (8.71)	-1.356	.175
15WT-DR	8.00 (3.47)	8.36 (2.78)	-.228	.820
15WT-REC	28.15 (2.33)	27.60 (2.60)	-.996	.319
N	37	11		
DMFS-M	22.59 (5.85)	23.48 (8.37)	-.479[a] (77)	.635
DMFS-P	15.83 (5.11)	18.68 (5.38)	-2.224[a] (77)	**.026***
N	37	11		

Note. aSAH = aneurysmal subarachnoid hemorrhage, anSAH = angiographically negative subarachnoid hemorrhage, 15WT-IR = Immediate Recall, 15WT-DR = Delayed Recall, 15WT-REC = Recognition, raw scores on subtests of 15 Word Test, DMFS-M = raw score mental fatigue subscale of DMFS, DMFS-P= raw score physical fatigue subscale, of DMFS, [a]=t-score *p<.05

Memory performance and memory complaints in SAH patients

There was no significant correlation found between immediate recall, delayed recall or recognition and reported memory complaints in SAH patients (Table 4).

Memory complaints and fatigue in SAH patients

From the total of 79 SAH patients, 42 patients reported memory complaints and 37 did not report memory complaints. Memory complaints were significantly related to mental fatigue and to physical fatigue (Table 4). A positive moderate to strong correlation was found between mental fatigue and memory complaints and a positive weak to moderate correlation was found between physical fatigue and memory complaints.

Table 4

Spearman correlations of memory complaints and 15WT and DMFS in SAH patients

	15WT-IR	15WT-DR	15WT-REC	DMFS-M	DMFS-P
Memory complaints					
r	-.021	-.088	-.054	**.543**	**.387**
p	.853	.441	.639	**<.001***	**<.001***

Note. 15WT-IR = Immediate Recall, 15WT-DR = Delayed Recall, 15WT-REC = Recognition, raw scores on subtests of 15 Word Test, DMFS-M = raw score mental fatigue subscale of DMFS, DMFS-P= raw score physical fatigue subscale of DMFS, r=Pearson correlation, *p<.05.

Discussion

In short, this study found that SAH patients scored significantly worse on a memory performance task and reported significantly more mental and physical fatigue compared to healthy controls. anSAH patients reported significantly more physical fatigue compared to healthy controls, but did not differ in mental fatigue or memory performance. Furthermore, reported memory complaints were not related to memory performance in SAH patients. Memory complaints had a positive correlation with mental and physical fatigue in SAH patients.

First of all, the finding that SAH patients scored significantly lower on a memory performance task compared to healthy controls is in accordance with the literature, which also described verbal memory impairments in SAH patients (Al-Khindi et al., 2010; Buunk, 2016). Furthermore, we found a significant difference between the degree of mental fatigue in SAH patients versus in health controls. This finding is in line with previous studies who claimed that fatigue has a high prevalence in SAH patients (Samuelson et al., 2021; Western et al., 2021; Visser-Meily., 2009). Although most of these studies focused on fatigue on the long-term (3-15 years post SAH), this study provides insight into fatigue at five months post SAH. When comparing the mean scores of both groups to a norm group of healthy people, the amount of mental fatigue of the SAH patients would be labeled as 'high (23-24)' and that of the healthy controls as 'average (16-18)', which is as expected. Wylie and Flashman (2017) gave two possible explanations for these findings. First stating that there is more effort required from a damaged brain to process information compared to a healthy brain and secondly that it could be explained partly by frequently reported sleep disturbances in SAH patients. Furthermore, there was also a significant difference between the degree of physical fatigue in SAH patients versus in healthy controls, in accordance with the study of Buunk et al. (2018). When comparing the mean scores of both groups to a norm group of healthy people, the amount of physical fatigue of the patients would be labeled as 'above average (15-18)' and that of the healthy controls as 'average (13-14)'.

When comparing aSAH patients with anSAH patients, no significant differences were found on a memory performance task. This is contrary to our expectations and those that exist in clinical practice. Except for a study by Buunk et al. (2016), who also did not find a difference between anSAH and aSAH patients' scores on immediate or delayed recall on the 15WT. The picture that generally exists among patients and doctors is that the consequences of anSAH are less prominent compared to the consequences of aSAH (Nesvick et al., 2019;

Khan et al., 2013). anSAH patients do not receive treatment, return home earlier and have a lower in-hospital morality rate, which might result in the impression that the consequences are less severe. What also does not correspond to that picture, is that we found no differences in mental fatigue for aSAH and anSAH patients and the degree of physical fatigue was even higher in anSAH patients compared to aSAH patients. From this study it seems that the differential outcome for aSAH and anSAH patients does not apply to memory performance and mental fatigue and that it should be taken into account that physical fatigue may be even higher for anSAH patients.

Contrary to our expectations, we did not find a significant relation between memory complaints and memory performance in SAH patients. Passier et al. (2010) found a relation between cognitive complaints and memory impairment in SAH patients. However, Passier et al. (2010) used a general score for cognitive complaints (CLCE-24 cognition score), while this current study specifically focused on memory complaints. Thereby, some studies also did not find a relation between cognitive complaints and cognitive performance on neuropsychological tests (Caplan et al., 2021; Toomela et al., 2004). An explanation for these results in our study could be that the questions of the CLCE-24 that measured cognitive complaints (‘Difficulty remembering information’ and ‘Difficulty remembering information from a long time ago, forgetful’) are most likely answered by patients with in their mind their daily life. While in daily life with distracting stimuli it might be extra difficult to pay attention to information and remembering it, in a controlled testing environment there are little to no distractions. The presence or absence of distracting stimuli could make a great difference in memory performance and the difficulty patients experience with it, especially because the domain of attention is often impaired in SAH patients (Passier et al., 2010; Hütter et al., 1995). The discrepancy between daily life (CLCE-24 reported complaints) and neuropsychological testing could offer an explanation why there was no relation found

between memory complaints and memory performance in SAH patients. Furthermore, we cannot make any conclusions about the reliability of the self-reported answers of patients. Patients can have several reasons why they do not report truthfully. Ljunggren et al., (1985) described this phenomenon from a psychological point of view. They explain patients are often relieved they survived the SAH, but want to see complete recovery afterwards. When they experience certain symptoms like memory complaints, it could remind them of not being completely recovered which might fuel fear for another SAH. To avoid coping with these feelings and to protect their self-esteem, patients possibly suppress cognitive problems and might not want to report them. In short, this could mean there are also patients who in reality experience memory complaints but do not report them.

At last, in accordance with our expectations we found a positive correlation between memory complaints and mental and physical fatigue. Stulemeijer et al., (2007) concluded that cognitive complaints had a stronger relation with fatigue than with cognitive deficits in MTBI patients. Our findings could possibly be explained by the coping hypothesis (Belmont et al., 2006; van Zomeren et al., 1984). This hypothesis explains that in patients with brain damage, performances are not necessarily lower compared to healthy controls. However, it takes patients more mental effort to compensate for attentional and processing deficits which results in higher levels of experienced fatigue. Patients might experience more difficulty reaching the same level as performance as before which makes them, in addition to fatigue, report cognitive complaints, resulting in a relation between complaints and fatigue. However, scores on a memory performance task do not necessarily decrease when patients are experiencing memory complaints due to the increased effort they perform, resulting in no relation between memory complains and memory performance.

When interpreting the results of the current study, it is important to keep in mind some limitations. First of all, the external validity of the study might be limited. Patients and

healthy controls underwent the memory performance task in a test environment, where distraction was limited. While in real life, patients are often sensitive to stimuli which might influence their performance. Furthermore, it is possible that patients who experience severe mental or physical fatigue chose not to participate in the study as this might be too large of a burden. This could imply the results cannot be generalized to all SAH patients. Thereby, it cannot be ruled out that the differences in the distribution of educational level between healthy controls and SAH patients might have influenced the results. Finally, no statements can be made about the causality between memory complaints and fatigue, only about the relation between both factors, because of the cross sectional design of the study.

For future research, it is important to further investigate the relation between reported cognitive complaints and cognitive performance to test whether this lack of relation does extent to more cognitive domains besides memory. It is important in clinical practice to keep in mind that although memory complaints do not necessarily relate to memory performance in this study, both should be taken seriously as a patient can still suffer from a decline in memory performance without reporting memory complaints. Or when neuropsychological assessment indicates that a patient does not perform worse on a memory performance task compared to a healthy control, a patient can still experience memory problems and be bothered by them in daily life. It is important to not rely on one source of information, neuropsychological assessment or reported complaints, but to use both sources for a valuable overall picture. In addition, for future research it can be helpful to investigate causality between mental and physical fatigue and memory complains, or other cognitive complaints. When there appears to be a causal relation, fatigue could be a spearhead for intervention in reducing cognitive complaints for SAH patients.

Finally, the lack of relation between memory complaints and memory performance should be taken into account in clinical practice, even as the finding that anSAH patients do

not differ in memory performance and in the degree of mental fatigue from aSAH patients and even report higher levels of physical fatigue. The further investigation of the relation between fatigue and cognitive complaints might offer opportunities for new treatment interventions in SAH patients.

References

Al-Khindi, T., Macdonald, R. L., & Schweizer, T. A. (2010). Cognitive and functional outcome after aneurysmal subarachnoid hemorrhage. *Stroke*, *41*(8), e519-e536.

Belmont, A., Agar, N., Hugeron, C., Gallais, B., & Azouvi, P. (2006, July). Fatigue and traumatic brain injury. In *Annales de réadaptation et de médecine physique* (Vol. 49, No. 6, pp. 370-374). Elsevier Masson.

Buunk, A. M., Groen, R. J. M., Veenstra, W. S., Metzemaekers, J. D. M., van der Hoeven, J. H., van Dijk, J. M. C., & Spikman, J. M. (2016). Cognitive deficits after aneurysmal and angiographically negative subarachnoid hemorrhage: Memory, attention, executive functioning, and emotion recognition. Neuropsychology, 30(8), 961–969. https://doi.org/10.1037/neu0000296

Buunk, A. M., Groen, R. J., Wijbenga, R. A., Ziengs, A. L., Metzemaekers, J. D., van Dijk, J. M.C., & Spikman, J. M. (2018). Mental versus physical fatigue after subarachnoid hemorrhage: differential associations with outcome. *European Journal of Neurology*, *25*(11), 1313-e113.

Buunk, A. M., Spikman, J. M., Metzemaekers, J. D., van Dijk, J. M. C., & Groen, R. J. (2019). Return to work after subarachnoid hemorrhage: the influence of cognitive deficits. *PloS One*, *14*(8), e0220972.

Caplan, B., Bogner, J., Brenner, L., Malec, J., Hromas, G. A., Houck, Z. M., ... & Bauer, R. M. (2021). Making a difference: affective distress explains discrepancy between objective and subjective cognitive functioning after mild traumatic brain injury *Journal of Head Trauma Rehabilitation*, *36*(3), 186-195.

Chen, P.-Y., Hsieh, S.-H., Lin, C.-K., Wei, L., Su, Y.-K., Tsai, P.-S., & Chiu, H.-Y (2022). Mental fatigue mediates the relationship between cognitive functions and return to

productive activity following traumatic brain injury: A mediation analysis. *Brain Injury*, *36*(1), 32–38. https://doi.org/10.1080/02699052.2022.2034044

Geraghty, J. R., Lara-Angulo, M. N., Spegar, M., Reeh, J., & Testai, F. D. (2020). Severe cognitive impairment in aneurysmal subarachnoid hemorrhage: predictors and relationship to functional outcome. *Journal of stroke and cerebrovascular diseases*, *29*(9), 105027.

Hütter, B. O., Gilsbach, J. M., & Kreitschmann, I. (1995). Quality of life and cognitive deficits after subarachnoid haemorrhage. *British Journal of Neurosurgery*, *9*(4), 465-476.

Khan, A. A., Smith, J. S., Kirkman, M. A., Robertson, F. J., Wong, K., Dott, C., ... & Kitchen, N. D. (2013). Angiogram negative subarachnoid haemorrhage: outcomes and the role of repeat angiography. *Clinical neurology and neurosurgery*, *115*(8), 1470-1475.

Khosdelazad, S., Jorna, L. S., Groen, R. J. M., Rakers, S. E., Timmerman, M. E., Borra, R. J. H., van der Hoorn, A., Spikman, J. M., & Buunk, A. M. (2022). Investigating Recovery After Subarachnoid Hemorrhage With the Imaging, Cognition and Outcome of Neuropsychological Functioning After Subarachnoid Hemorrhage (ICONS) Study: Protocol for a Longitudinal, Prospective Cohort Study. *JMIR research protocols*, *11*(9), e38190. https://doi.org/10.2196/38190

Lawton, M. T., & Vates, G. E. (2017). Subarachnoid hemorrhage. *New England Journal of Medicine*, *377*(3), 257-266.

Lindgren, A., Vergouwen, M. D., van der Schaaf, I., Algra, A., Wermer, M., Clarke, M. J., & Rinkel, G. J. (2018). Endovascular coiling versus neurosurgical clipping for people with aneurysmal subarachnoid haemorrhage. *Cochrane Database of Systematic Reviews*, (8).

Ljunggren, B., Sonesson, B., Säveland, H., & Brandt, L. (1985). Cognitive impairment and adjustment in patients without neurological deficits after aneurysmal SAH and early operation. *Journal of neurosurgery*, *62*(5), 673-679.

Matsuda, M., Watanabe, K., Saito, A., Matsumura, K. I., & Ichikawa, M. (2007). Circumstances, activities, and events precipitating aneurysmal subarachnoid hemorrhage. *Journal of Stroke and Cerebrovascular Diseases*, *16*(1), 25-29.

Nesvick, C. L., Oushy, S., Rinaldo, L., Wijdicks, E. F., Lanzino, G., & Rabinstein, A. A. (2019). Clinical complications and outcomes of angiographically negative subarachnoid hemorrhage. Neurology, 92(20), e2385-e2394.

Passier, P. E. C. A., Visser-Meily, J. M. A., Van Zandvoort, M. J. E., Post, M. W. M., Rinkel, G. J. E., & Van Heugten, C. (2010). Prevalence and determinants of cognitive complaints after aneurysmal subarachnoid hemorrhage. *Cerebrovascular diseases* *29*(6), 557-563.

Passier, P. E. C. A., Visser-Meily, J. M. A., Van Zandvoort, M. J. E., Rinkel, G. J. E., Lindeman, E., & Post, M. W. M. (2012). Predictors of long-term health-related quality of life in patients with aneurysmal subarachnoid hemrrhage. *NeuroRehabilitation,* 30(2), 137-145. hemorrhage.

Persson, H. C., Törnbom, K., Sunnerhagen, K. S., & Törnbom, M. (2017). Consequences and coping strategies six years after a subarachnoid hemorrhage–A qualitative study. *PloS One*, *12*(8), e0181006.

Petridis, A. K., Kamp, M. A., Cornelius, J. F., Beez, T., Beseoglu, K., Turowski, B., & Steiger, H. J. (2017). Aneurysmal subarachnoid hemorrhage: diagnosis and treatment. *Deutsches Ärzteblatt International*, *114*(13), 226.

Rinkel, G. J. E., & Algra, A. (2011). Long-term outcomes of patients with aneurysmal subarachnoid haemorrhage. *The Lancet Neurology*, *10*(4), 349–356. https://doi.org/10.1016/S1474-4422(11)70017-5

Samuelsson, J., Jakobsson, H., Rentzos, A., Jakola, A. S., & Nilsson, D. (2021). Neurological outcome, mental fatigue, and occurrence of aneurysms> 15 years after aneurysmal subarachnoid hemorrhage. *World Neurosurgery*, *151*, e122-e127.

Sheldon, S., Macdonald, R. L., Cusimano, M., Spears, J., & Schweizer, T. A. (2013). Long-term consequences of subarachnoid hemorrhage: examining working memory. *Journal of the neurological sciences*, *332*(1-2), 145-147.

Stulemeijer, M., Vos, P. E., Bleijenberg, G., & Van der Werf, S. P. (2007). Cognitive complaints after mild traumatic brain injury: things are not always what they seem. *Journal of psychosomatic research*, *63*(6), 637-645.

Suarez, J. I., Tarr, R. W., & Selman, W. R. (2006). Aneurysmal subarachnoid hemorrhage. New England Journal of Medicine, 354(4), 387-396.

Togha, M., Sahraian, M., Khorram, M., & Khashayar, P. (2009). Warning signs and symptoms of subarachnoid hemorrhage. Southern medical journal, 102(1), 21.

Toomela A, Pulver A, Tomberg T, et al. Possible interpretation of subjective complaints in patients with spontaneous subarachnoid haemorrhage. Journal of Rehabilitation Medicine. 2004 Mar;36(2):63-69. DOI: 10.1080/16501970310017414. PMID: 15180220.

Van Gijn, Jan, Richard S. Kerr, and Gabriel JE Rinkel. "Subarachnoid haemorrhage." *The Lancet* 369.9558 (2007): 306-318.

Van Zomeren AH, Brouwer WH, Deelman BG. Attentional deficits: the riddles of selectivity, speed, and alertness. In: Brooks D, editor. Closed head injury: psychological, social and family consequences. Oxford: Oxford University Press; 1984. p. 74–107.

Verhage, F. (1964). *Intelligentie en leeftijd: Onderzoek bij Nederlanders van twaalf tot zevenenzeventig jaar* [Intelligence and Age: Study with Dutch People from Age 12 to 77], Van Gorcum, Assen.

Visser-Keizer, A. C., Hogenkamp, A., Westerhof-Evers, H. J., Egberink, I. J., & Spikman, J. M. (2015). Dutch multifactor fatigue scale: a new scale to measure the different aspects of fatigue after acquired brain injury. *Archives of physical medicine and rehabilitation*, *96*(6), 1056-1063.

Visser-Meily, J. A., Rhebergen, M. L., Rinkel, G. J., van Zandvoort, M. J., & Post, M. W. (2009). Long-term health-related quality of life after aneurysmal subarachnoid hemorrhage: relationship with psychological symptoms and personality characteristics. Stroke, 40(4), 1526-1529.

Western, E., Nordenmark, T. H., Sorteberg, W., Karic, T., & Sorteberg, A. (2021). Fatigue after aneurysmal subarachnoid hemorrhage: Clinical characteristics and associated factors in patients with good outcome. *Frontiers in Behavioral Neuroscience*, *15*. https://doi.org/10.3389/fnbeh.2021.633616

Wylie, G. R., & Flashman, L. A. (2017). Understanding the interplay between mild traumatic brain injury and cognitive fatigue: models and treatments. *Concussion*, *2*(4), CNC50.