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## Neuropsychological outcome following minimal access subtemporal selective amygdalohippocampectomy

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#### ABSTRACT

*Purpose:* The present study provides a detailed account of neurocognitive outcome following minimal access subtemporal selective amygdalohippocampectomy (SAH) and establishes rates of neurocognitive decline in the largest sample to date. Use of a subtemporal surgical approach to SAH has been proposed to possibly reduce the risk for postoperative neurocognitive decline since lateral neocortical tissues is not resected and the temporal stem is preserved. The current study extends prior research with subtemporal SAH patients to include not only group level analyses but also analyses based on reliable change data. *Methods:* Neurocognitive comparisons are made between 47 patients that underwent subtemporal SAH. Statistical comparisons were made between neurocognitive performance at the group level and with use of reliable change scores.

*Results:* Approximately 75% of patients were seizure free postoperatively. At the group level, there were no significant postoperative changes. For the left SAH patients, reliable change scores demonstrated a decline in approximately one third of patients for memory, verbal intellect, and naming. Right SAH patients showed decline primarily in memory.

*Conclusions:* These results indicated good seizure control following subtemporal SAH with greatest risk for neurocognitive decline following dominant SAH and best cognitive outcome following non-dominant SAH. Findings demonstrated the importance of reliable change analyses that make individual based comparisons and take into account measurement error. Despite preservation of the lateral neocortical tissue and the temporal stem, subtemporal SAH presents a risk for cognitive decline in a notable portion of patients.

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#### 1. Introduction

Resective surgery has been demonstrated to be a successful treatment option for patients with medically intractable epilepsy<sup>1-3</sup> resulting in seizure freedom for more than 70% of patients.<sup>4-9</sup> Unilateral resection of temporal lobe structures has known risks to neurocognitive functions especially memory and language.<sup>10-13</sup> Numerous surgical approaches have been developed in part to reduce neurocognitive sequela associated with resective surgery.<sup>8,14-16</sup> Post-operative neurocognitive change has been evaluated at the group level and by use of reliable change scores which likely provide a more accurate indication of statistically meaningful change.<sup>10,17-19</sup>

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Mesial temporal lobe (MTL) surgery has known neurocognitive risks which include potential decline in verbal memory, language functions, and aspects of intellectual functions following dominant MTL surgery as well as potential decline in non-verbal memory and aspects of intellect following non-dominant MTL surgery.<sup>10,13,20-22</sup> Dominant MTL surgery appears to present the greatest risk for post-operative neurocognitive decline. Post-operative neurocognitive change has often been evaluated at the group level; however, use of reliable change scores may provide a more accurate estimate of risk for post-operative decline by accounting for test measurement error and practice effects.<sup>10,17–19</sup> Without use of reliable changes scores, lack of decline or presence of improved performance may be due to practice effects from repeated testing and/or measurement error. However, reliable change scores have only been reported in a very small sample following subtemporal selective amygdalohippocampectomy.<sup>8</sup> Surgical approach to MTL resective surgery may have differential effects on neurocognitive outcome.



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Selective amygdalohippocampectomy (SAH) for treatment of MTL onset seizures has been used to minimize the amount of tissue resected in a standard or modified anterior temporal lobectomy (ATL) and potentially reduce post-operative neurocognitive sequelae.<sup>8,16</sup> The three approaches to SAH include transcortical, transsylvian, and subtemporal.<sup>23</sup> Subtemporal SAH may present a lower risk for post-operative neurocognitive decline since it. (1) minimizes the amount of neocortical tissue resected (unlike ATL). (2) does not involve resection of potentially functional lateral temporal neocortical tissue (unlike a transcortical approach), and (3) does not involve transection of the temporal stem/uncinate fasciculus which contains fibers connecting frontal and temporal structures (unlike the transsylvian approach).<sup>8,24</sup> Only a few studies have evaluated post-operative neurocognitive outcome following subtemporal SAH and all of those studies have had very small samples sizes.<sup>8,25-29</sup> In general, previous studies have shown favorable neurocognitive outcome following subtemporal SAH although, only Little et al.,<sup>8</sup> attempted to account for statistically reliable change as defined elsewhere.<sup>18,30</sup> Therefore, a detailed account of neurocognitive outcome using reliable change statistics following subtemporal SAH with a sufficiently large sample remains to be done.

The aim of the present study was to compare pre and postoperative neurocognitive performance following subtemporal SAH in the largest sample to date. Neurocognitive performance was compared at the group level and with reliable change scores. Dominant temporal lobe compared to non-dominant temporal lobe SAH patients were expected to experience a higher proportion of decline on measures of neurocognitive function.

#### 2. Methods

#### 2.1. Patients and procedures

The present study was conducted at St. Joseph's Hospital and Medical Center, Phoenix, Arizona with approval of the institutional review board (IRB). Data collection was considered exempt by the institutions IRB since data (pre and post-operative) were obtained as part of each patient's standard clinical care. Obtained data were archival and included consecutive patients seen for both preoperative and postoperative neuropsychological evaluation from 2006 to 2011. At this institution, patients are typically referred for postoperative evaluation 6-9 months following SAH. Patients included in this study had focal onset mesial temporal lobe complex partial seizures as established by video-electroencephalogram (V-EEG) and clinical observation during epilepsy monitoring unit stay. A total of 61 consecutive patients that underwent SAH (right n = 28and left n = 33) were available for statistical comparison. Patients were excluded if they had undergone surgical resection other than subtemporal SAH (n = 4), had lesions other than MTS (n = 0), had more than 50% missing data (n = 2), had right hemisphere or bilateral speech dominance based on Wada testing (n = 2), or had a post-operative neuropsychological evaluation greater than 12 months post SAH (right n = 2 and left n = 4). The final sample included a total of 47 patients (right n = 22 and left n = 25) that underwent subtemporal SAH. Minimal access subtemporal selective amygdalohippocampectomy involves keyhole access through the zygoma to the temporal floor and requires minimal retraction.<sup>8</sup> Cortical incision was through the fusiform gyrus or collateral sulcus with subsequent resection of the majority of the amygdala, head of the hippocampus, and body of the hippocampus. For a thorough review of the minimal access subtemporal SAH surgical technique please refer to Little et al.<sup>8</sup>

Patients included in this study completed preoperative evaluation including inpatient V-EEG, brain MRI (most cases),

neuropsychological evaluation, and Wada test/intracarotid amobarbital test. Language dominance was established by Wada testing. Postoperative neuropsychological evaluation was completed as an outpatient.

#### 2.2. Pathology and seizure freedom

Variables of clinical interest included results from preoperative brain magnetic resonance imaging (MRI), post-operative histopathology if available, and post-operative seizure control. For statistical purposes, evidence of MTS was considered present if noted by MRI and/or histopathology. Results from brain MRI (n = 47) were classified as showing unilateral right or left mesial temporal sclerosis (MTS), bilateral MTS, or no MTS based on the neuroradiologist's clinical report. No patients were included if they had presence of pathology other than MTS (e.g., neoplasm, cortical dysplasia, etc.). Post-operative histopathology was available for 10 right SAH and 9 left SAH patients and presence of MTS was noted based on the pathologist's clinical report. Patients were classified as being either seizure free or having recurrent seizures based on report of the neurosurgeon 3 months post surgery and at the time of the neuropsychological evaluation. Seizure freedom was defined as no recurrent seizures. Recurrent seizures were defined as having 1 or more post-operative seizures. Assignment of Engle classification was not possible due to the archival nature of the data and insufficient information regarding the frequency and diurnal occurrence of postoperative seizures.

#### 2.3. Neuropsychological measures

Neuropsychological evaluation included measures of intellect, processing speed, language, visuospatial functioning, executive functioning, learning, memory, fine motor speed, and mood. Intelligence was measured with the Wechsler Abbreviated Scale of Intelligence (WASI<sup>31</sup>). On this measure, the Verbal Intelligence Quotient (VIQ) is comprised of the Vocabulary and Similarities subtests. The Performance Intelligence Quotient (PIQ) is comprised of the Block Design and Matrix Reasoning subtests. All four subtests are used to calculate the Full Scale Intelligence Quotient (FSIQ). Exclusion of attention and processing speed measures in calculation of intelligence quotients by the WASI is similar to the newest version of the Wechsler Adult Intelligence Scale, or WAIS-IV. Processing speed was assessed with the Wechsler Adult Scale of Intelligence-III (WAIS-III<sup>32</sup>) Coding subtest and the Halstead-Reitan Trail Making Test Part A (Trails A<sup>33</sup>). Attention was measured with the WAIS-III Digit Span subtest.<sup>32</sup> Confrontation naming was assessed by the Boston Naming Test (BNT<sup>34</sup>). Executive functioning was examined with the Halstead-Reitan Trail Making Test Part B (Trails B<sup>33</sup>). The Rey-Auditory Verbal Learning Test (RAVLT<sup>35</sup>) trials 1–5 total score was used to evaluate verbal learning (Learning) and long delay total score was used to measure verbal memory (Delay). The Brief Visuospatial Memory Test-Revised (BVMT-R<sup>36</sup>) trials 1-3 total score was used to evaluate nonverbal learning (Learning) and the delayed recall total score was used to evaluate nonverbal memory (Delay). Fine motor speed was tested with the Halstead-Reitan Finger Tapping Test (FTT<sup>33</sup>) for the right and left hands. The Beck Depression Inventory-II (BDI-II<sup>37</sup>) was used to measure depressive symptoms. All test scores, with the exception of the BDI-II, were converted to standardized scores based on published normative data. Standard scores (SS) were used for the WASI indices, which have a mean of 100 and a standard deviation of 15. Age corrected scaled scores (ACSS) were used for the WAIS-III subtests which have a mean of 10 and a standard deviation of 3. T-scores were used for Trails A and B, BNT, RAVLT, BVMT-R, and FTT which have a mean of 50 and a standard deviation of 10.

#### 2.4. Reliable change scores

Reliable change scores were calculated using the Jacobson and Truax formula<sup>38</sup> with correction for potential practice effect.<sup>10</sup> Reliable change scores are standardized scores obtained by correcting the simple difference between post-operative and preoperative scores for the standard error of the difference and practice effect. For details regarding the RCI equation please refer to Jacobson & Truax 1991.<sup>38</sup> A 90% confidence interval (CI) was used in this study since it has been commonly used in epilepsy research.<sup>10,17,18</sup> The 90% CI allows for 5% chance of error on both ends of the distribution. Similar to the methods of Baxendale and Thompson,<sup>39</sup> reliable change scores were derived from test-retest data reported in the tests statistical manual for the WASI<sup>31</sup> and clinical samples for other tests (BVMT-R, <sup>40</sup> RAVLT & BNT,<sup>17</sup> Digit Span & Coding,<sup>19</sup> and FTT & TMT<sup>41</sup>). Although it is preferable to have test-retest data derived from an epilepsy sample with retest delay at a similar interval to that of short-term outcome evaluations (e.g., 3-12 months post first testing), test-retest data from an epilepsy sample was not available for all measures. However, even with shorter test-retest intervals, practice effects were small and it would be unlikely that larger practice effects would be obtained with longer retest time intervals. Consequently, test-retest data used in the present study likely provided a reasonable estimate of reliable change. Still, the most important aspect of calculating reliable change scores is that it removes the error in an individual's score (performance) that is related to the standard error of measurement unique to that test. Thus, reliable change scores help estimate whether or not an individual's difference in performance between two time points, in this case pre-operative versus post-operative performance, is significantly different by taking into account each test's reliability coefficient and each test's standard deviation.

#### 2.5. Statistical analysis

Statistical analysis was completed by use of PASW 18.0 and SAS software. Chi-square and Analysis of Variance (ANOVAs) were used for comparison of patient's demographics variables. Hotelling T-squared was used to compare pre and post operative neuropsychological performance at the group level with side of SAH (right or left), presence/absence of MTS, and presence/ absence of post-operative seizures as between group variables. Hotelling *T*-squared is similar to completing repeated measures multivariate analysis of variance. Reliable change scores were used to identify patients that showed a statistically significant change or stable performance at the 90% CI as indicated by the following scores: decline (change score < -1.64), stable performance (-1.65 < change score < 1.65), or gain (change score > 1.64). Exploratory analysis, using ANOVA, compared rates of impaired scores (>1 SD from the normative mean) between right and left SAH groups on the BVMT-R Learning and Delay as well as the RAVLT-Learning and Delay.

#### 3. Results

#### 3.1. Demographics

There were no significant demographic differences between right and left SAH groups with the exception of ethnicity (Table 1). There were a significantly higher number of Hispanic patients in the left compared to right SAH group. In this sample, most of the patients were female and right handed with half of the patients employed. On average, postoperative follow-up neurocognitive evaluations were conducted approximately 7 months post-surgery (M = 6.9, SD = 1.9) with a range of 3–11 months. By far, the majority

#### Table 1

Post-operative demographics by seizure group.

Demographic	Right SAH (n=22)	Left SAH ( <i>n</i> =25)	$F/\chi^2$	р
Age	34.6 (11.6)	39.9 (12.8)	2.14	0.15
Education (years)	13.3 (2.2)	13.2 (2.6)	0.00	0.92
Gender				
Female	13 (59.1%)	18 (72%)	0.87	0.35
Male	9 (40.9%)	7 (28%)		
Ethnicity				
Caucasian	21 (95.5%)	15 (60%)	8.24	0.02
Hispanic	1 (4.5%)	9 (36%)		
African American	0 (0%)	1 (4%)		
Handedness				
Right	20 (90.9%)	23 (92%)	0.02	0.89
Left	2 (9.1%)	2 (8%)		
Employment				
Unemployed/disability	9 (40.9%)	10 (40%)	0.02	0.99
Employed	12 (54.5%)	14 (56%)		
School	1 (4.5%)	1 (4%)		
Age at first seizure	14.4 (10.6)	15.3 (15.7)	0.05	0.82
Years since first seizure	20.2 (13.1)	24.9 (14.1)	1.33	0.25
Number of AED's	1.7 (0.6)	1.8 (0.5)	0.04	0.85
Number of AED's	1.7 (0.6)	1.8 (0.5)	0.04	0.85

*Note*: Means (SD) or frequencies (%) are reported for each variable. AEDs refers to antiepileptic drugs.

of patients (n = 37, 78.7%) were seen around 7 months ( $\pm 2$  months) post-operatively.

#### 3.2. Pathology and seizure freedom

Evidence of MTS based on combined MRI results and histopathology ipsilateral to side of SAH was non-significant (see Table 2). Based on MRI, there were no patients with MTS contralateral to SAH and there were no patients with bilateral MTS or other pathologies.

Seizure freedom at an average of 7 months post SAH was obtained in 74.5% of patients (right SAH n = 15 [68.2%]; left SAH n = 20 [80%]) and did not statistically differ between SAH groups ( $\chi^2 = .0860, p = 0.354$ ). A portion of the patients classified as having recurrent seizures may in fact still be classified as Engle class 1 depending on the frequency of seizures and their diurnal variation; however, these details were not available for all patients. Postoperative seizure control did not statistically differ based on presence or absence of MTS (F = 0.038, p = 0.846).

#### 3.3. Mean group differences on neuropsychological tests

Descriptive statistics for pre and post operative neuropsychological test performance by side of SAH are presented in Table 3. Based on Hotelling *T*-squared, there were no significant pre and post-operative differences on neuropsychological measures at the omnibus level when compared by side of SAH (F = 1.095; p = 0.449), presence/absence of MTS (F = 0.255; p = 0.992), and presence/absence of post operative seizures (F = 1.874; p = 0.148). Results indicated at the group level there were no significant changes in pre to post operative neuropsychological performance

Table 2			
Mesial temporal path	nology based on brain	MRI and/or histo	pathology.

Variable	Right SAH $(n=22)$	Left SAH ( $n = 25$ )
MTS Laterality Right Left No MTS	20 (90.9%) 0 (0%) 2 (9.1%)	0 (0%) 20 (80%) 5 (20%)

Note: MTS = mesial temporal sclerosis based on brain MRI or post-operative histopathology.

Table 3

Tuble 5				
Pre and post-o	operative n	neuropsy	chological	results.

Test	Right SAH $(n=22)$	Right SAH $(n=22)$		
	Pre-operative	Post-operative	Pre-operative	Post-operative
WASI (SS)				
FSIQ	91.6 (14.1)	94.6 (14.2)	98.2 (10.0)	96.5 (8.4)
VIQ	88.3 (11.9)	90.7 (12.8)	93.1 (11.9)	87.0 (9.6)
PIQ	93.7 (17.4)	97.3 (18.3)	104.0 (9.0)	106.6 (8.3)
WAIS-III (ACSS)				
Digit Span	8.4 (3.0)	8.2 (2.8)	9.2 (3.5)	9.3 (3.0)
Coding	9.0 (1.9)	8.9 (3.7)	8.2 (2.7)	8.6 (3.0)
Trail Making Test (T-score)				
Trails A	41.5 (11.7)	48.2 (13.6)	43.7 (13.9)	44.6 (12.6)
Trails B	40.0 (13.4)	44.4 (14.8)	47.3 (14.8)	48.6 (11.3)
BNT (T-score)	37.0 (11.4)	41.3 (12.7)	34.8 (11.0)	31.2 (9.6)
BVMT-R (T-score)				
Learning	34.9 (13.7)	35.6 (13.7)	45.0 (12.3)	42.7 (12.6)
Delay	36.0 (14.9)	34.8 (15.4)	45.1 (12.7)	42.5 (14.4)
RAVLT (T-score)				
Learning	43.4 (11.8)	46.2 (11.4)	40.0 (13.6)	38.3 (12.0)
Delay	44.6 (13.2)	46.1 (14.7)	39.9 (15.0)	37.4 (15.7)
Finger Tapping Test (T-score)				
Right	45.5 (7.2)	41.6 (8.7)	47.6 (11.6)	48.9 (11.1)
Left	46.1 (9.5)	43.4 (9.7)	47.2 (12.2)	50.3 (11.8)
BDI-2 (raw score)	9.1 (7.8)	5.9 (5.6)	15.5 (11.7)	12.0 (10.7)

*Note*: Mean and standard deviation (SD) are provided for each variable.

when compared by right or left SAH, presence or absence of MTS, or presence or absence of postoperative seizures.

#### 3.4. Reliable change scores

Distribution of reliable change scores using a 90% CI were qualitatively compared between right and left SAH groups (Table 4). By far, the majority of patients showed no decline on neurocognitive measures post-operatively in either SAH group. The highest proportion of patients demonstrating decline in the right SAH group was on the BVMT-R Delay (nonverbal memory) (~36% of patients). The highest proportion of patients with decline in the left SAH group was noted on the WASI VIQ (verbal intellect), Trails A (processing speed), BNT (naming), and the BVMT-R Learning and Delay (nonverbal) which occurred in approximately 21–39% of patients. A notable proportion of patients experienced a statistically significant decline on a measure of nonverbal memory

(BVMT-R Delay) following both right and left SAH but minimal decline on a test of verbal learning and memory (RAVLT). Time post surgery in months did not significantly correlate with any of the neuropsychological change scores.

#### 3.5. Exploratory analysis

The percentage of patients with impaired scores ( $\geq$ 1 SD below the normative mean) on learning and memory tests was evaluated by ANOVA (Table 5). A significantly higher proportion of right SAH compared to left SAH patients had preoperative impaired scores on BVMT-Learning and Delay. A significantly higher proportion of left compared to right SAH patients had preoperative impaired scores on the RAVLT-Learning and Delay. Postoperatively, rates of impaired BVMT-Learning and Delay did not significantly differ between groups; however, more than half of right SAH patients and less than half of left SAH patients had impaired scores.

#### Table 4

90% confidence interval reliable change results for neuropsychological tests.

Test	Right SAH 90% CI Left SAH 90% CI					
	Decline	Stable	Improved	Decline	Stable	Improved
WASI						
FSIQ	10%	75%	15%	18.2%	81.8%	0%
VIQ	10%	80%	10%	38.1%	61.9%	0%
PIQ	10%	80%	10%	9.5%	90.5%	0%
WAIS-III						
Digit Span	5.6%	94.4%	0%	4.2%	91.7%	4.2%
Coding	11%	78%	11%	8.7%	91.3%	0%
Trail Making Test						
Trails A	9.5%	66.7%	23.8%	24%	52%	24%
Trails B	5.3%	84%	10.5%	4%	92%	4%
BNT	10%	75%	15%	39.1%	52.2%	8.7%
BVMT-R						
Learning	4.5%	90.9%	4.5%	20.8%	75%	4%
Delay	36.4%	59.1%	4.5%	29.2%	66.7%	4.2%
RAVLT						
Learning	0%	100%	0%	4.1%	91.7%	4.2%
Delay	0%	100%	0%	8%	88%	4%
Finger Tapping Test						
Right	15%	75%	10%	5.3%	89.5%	5.3%
Left	15%	80%	5%	0%	90%	10%

Note: Percentage of cases is reported for each variable.

#### Table 5

Frequency of preoperative and postoperative learning and memory impaired scores ( $\geq 1$  SD).

Variable	Right SAH (n=22)	Left SAH ( <i>n</i> =25)	χ <sup>2</sup>	р
Preoperative				
BVMT-R Learning	15 (68.2%)	7 (28%)	7.59	0.01
BVMT-R Delay	14 (63.6%)	6 (24%)	7.52	0.01
RAVLT-Learning	7 (31.8%)	14 (58.3%)	3.25	0.07
RAVLT-Delay	5 (22.7%)	12 (50%)	3.66	0.06
Postoperative				
BVMT-R Learning	14 (63.6%)	11 (44%)	1.81	0.18
BVMT-R Delay	13 (59.1%)	9 (36%)	2.51	0.11
RAVLT-Learning	6 (27.3%)	13 (52%)	2.97	0.09
RAVLT-Delay	6 (27.3%)	14 (56%)	3.95	0.05

Note: Frequency and percentages are presented.

Postoperatively, impaired scores were noted in half of left SAH patients and approximately one quarter of right SAH patients for the RAVLT-Learning and Delay. The high rates of preoperative impairment on the RAVLT may in part explain low rates of significant post-operative change on this measure.

#### 4. Discussion

The aim of the present study was to evaluate post-surgical neurocognitive outcome using reliable change scores at the 90% confidence interval and to identify rates of decline following subtemporal SAH in the largest sample to date. Use of reliable change scores indicated a significant number of patients experienced post-operative neurocognitive decline following subtemporal SAH which is in contrast to previous studies group level analyses. Dominant hemisphere surgery presented the greatest risk for neurocognitive decline across the highest number of domains with one-third of patients showing decline in memory, verbal intellect, and naming. Visuospatial memory decline was noted in 36% of non-dominant SAH patients, but there were low rates of decline in other cognitive domains. Postoperative gain was most common following non-dominant SAH including better performance on measures of global intellect, processing speed, and naming. In contrast, significant gain following dominant SAH was primarily noted on one of two measures of processing speed. At the group level, there was no significant neurocognitive changes based on side of SAH, presence/absence of MTS, or presence/absence of post-operative seizure. In this sample, approximately 75% of patients were seizure free at an average of 7 months following surgery, which is similar to seizure control rates noted by other studies.<sup>4,42,43</sup> However, based on the archival nature of these data, Engle class could not be reliably rated. Overall, findings indicated subtemporal SAH can produce good short-term post-operative seizure control and high rates of stable post-operative neurocognitive performance with the greatest risk for neurocognitive decline associated with dominant hemisphere surgery.

Conflicting findings have been obtained by prior studies comparing neuropsychological outcome following ATL and SAH.<sup>14,44–50</sup> Some evidence suggests more extensive resections may result in greater memory impairment at least in regards to verbal memory and left hemisphere resections.<sup>14,44–47</sup> For example, Helmstaedter et al.<sup>47</sup> noted better verbal memory outcome in left resection when the temporal stem was spared by combined temporo-polar and amygdalohippocampectomy resection as compared to a standard ATL. In the case of a right resection, the lowest decline in nonverbal memory was obtained by sparing neocortical tissue through a transsylvian SAH. In regards to short-term group level outcomes (<12 months post surgery), a decline in

verbal memory is often noted at least for left sided resections.<sup>10,15,26,28,43</sup> Longitudinal data generally suggests there may be a post-operative decline in verbal memory, and in some cases intellect, but typically neurocognitive functions remain fairly stable and in some cases show mild improvement 2 or more years post surgery.<sup>51,52</sup> Use of a transsylvian or transcortical SAH has shown a similar pattern of performance with a group level decline in verbal memory for left SAH patients but otherwise generally stable performance for attention, executive, and nonverbal memory at a short-term follow-up without a significant difference by surgical approach.<sup>15</sup> Unfortunately, a direct comparison has not been made between subtemporal, transsylvian, and transcortical SAH. Short-term outcome following subtemporal SAH has shown a similar pattern to findings with other approaches to SAH or ATL. Hori et al.<sup>28</sup> noted stable or improved intellect and verbal memory at 2 and 24 months post SAH with the exception of a verbal memory decline following dominant subtemporal SAH. Robinson et al.<sup>26</sup> showed stable or improved performance for intellect, naming, and story memory. However, a decline was noted for rote verbal memory following dominant subtemporal SAH and a small decline in design memory following non-dominant subtemporal SAH. In the present study, stable group level performance across neurocognitive functions but notable decline in aspects of neurocognitive functions based on reliable change scores was observed following left more than right subtemporal SAH. However, it is possible the post-operative decline based on reliable change scores for VIQ, naming, and memory may resolve by 2 years post surgery as was noted by other researchers. Other subtemporal SAH studies however did not use reliable change scores and consequently, long-term outcome regarding individual change was not available.

Although nonverbal memory decline was noted in 36% of patients that underwent right SAH, performance deficits were essentially limited to this one cognitive domain. In contrast, patients with a dominant hemisphere surgery appeared to be at the greatest risk for cognitive decline across multiple neurocognitive domains including memory (nonverbal), verbal intellect, and naming (29-38% of patients). These results are generally consistent with risk for cognitive decline reported by prior research with other surgical approaches for SAH. In addition, presence of greatest risk for cognitive decline following dominant hemisphere surgery was also consistent with prior research. There has only been one prior study<sup>8</sup> investigating outcome by use of a reliable change approach in patients with a subtemporal SAH; however, that sample was less than half the size (n = 18) of the present sample (n = 47). The current findings expand on the previous study by suggesting a greater risk for memory decline following subtemporal SAH than was previously reported by Little et al.<sup>8</sup> However, differences in obtained results may be multifactorial and may include the differences in sample size and memory tests used. For example, the Little et al.<sup>8</sup> study used either the RAVLT (as in the present study) or the California Verbal Learning Test-2 (CVLT-2) to measure verbal memory and either the BVMT-R (as in the present study) or the Rey-Osterrieth Complex Figure Test (RCFT) to measure non-verbal memory but it was not clear what proportion of patients were given which verbal or non-verbal memory test. The present study used the same verbal memory and the same non-verbal memory test for all patients and consequently, differences in test stimuli, psychometric properties, and normative data were less likely to introduce error into the obtained results. Finally, in regards to memory, the present study suggested a notable proportion ( $\sim$ 30%) of patients experienced a post-operative decline when reliable change scores were used and, therefore, subtemporal SAH is not without risks to memory, naming, and verbal intellectual functioning in individual patients depending on side of surgery.

Both right and left SAH groups showed a decline in nonverbal memory in approximately one third of patients but only a small number of patients showed decline in verbal learning and memory. Decline in nonverbal memory following both dominant and nondominant SAH has been noted by prior studies;<sup>12,13,53–55</sup> however, use of the BVMT-R as a measure of nonverbal memory may at least in part account for this finding. Nonverbal memory tests have been criticized in the past because the stimuli may be encoded and recalled by both verbal and visual means resulting in poor sensitivity to unilateral temporal lobe dysfunction. Consequently, surgical intervention in either temporal lobe may reduce encoding and recall for information that can be stored by either modality. In the only prior study using the BVMT-R in an epilepsy sample,<sup>59</sup> this test was found to be a poor predictor of unilateral TLE and consequently may function as a general as opposed to material specific test of memory. Still, the prior study did not use reliable change scores and compared groups rather than individuals. The reason for very limited verbal memory decline but notable nonverbal memory decline following SAH in the present study was unclear. However, psychometric differences between these tests (e.g., standard deviation, test-retest reliability) may have made it more difficult to reach statistically significant change on the RAVLT. In addition, high rates of baseline impairment on the RAVLT may also be a contributing factor. Since rates of unilateral MTS ipsilateral to surgical resection and recurrence of seizures did not significantly differ between SAH groups these factors were unlikely to explain limited verbal memory decline but notable non-verbal memory decline in both seizure groups.

Specific to the subtemporal approach, statistical comparisons at the group level were generally consistent with prior neurocognitive outcome research.<sup>8,25–29</sup> Although there was no evidence of cognitive decline at the group level, unlike prior outcome studies, there was no evidence of significant post-operative improvement either.<sup>15,47,56-58</sup> The disparity in findings between group level analyses and reliable change analyses were important to note. Group level analyses are commonly employed; however, unlike reliable change analyses, they make no correction for each patient's individual baseline (preoperative) performance, practice effects from taking the tests more than once, and the specific amount of measurement error inherent to each individual cognitive test. Consequently, individual post-operative changes are likely to be attenuated at the group level given the lack of accounting for the prior confounds whereas reliable change analyses are likely to provide a more accurate estimate of postoperative change. In the present study it was clear that although group level analyses showed non-significant pre to postoperative change, substantial individual change was noted in a subset of patients when baseline performance, practice effect, and measurement error were accounted for.

Presence of notable confrontation naming and verbal intellect decline following dominant hemisphere surgery was not a new finding; however, use of a subtemporal approach with preservation of lateral neocortical tissue and the temporal stem was expected to limit changes in language and executive functions. Current findings indicate that despite no resection of lateral neocortical tissue and preservation of the temporal stem, language disturbance still may occur in approximately one third of patients that undergo dominant temporal lobe SAH. Disruption of the "basal temporal language area" (which includes the inferior temporal, fusiform, and parahippocampal gyri) may be one mechanism by which post-operative naming decline occurs.<sup>29,59</sup> Studies have indicated intraoperative cortical stimulation of the ventral temporal lobe can disrupt language functions (including naming)<sup>29,60–62</sup> and their disruption may underlie post-operative naming impairment. Alternatively, neurocognitive functioning, including language and memory, involve various neural networks<sup>63-65</sup> and disruption of these networks may result in decline in neurocognitive function.<sup>66</sup> Further, presence of a postoperative decline in VIQ was somewhat unexpected since this score was based primarily on knowledge based tests. However, the observed VIQ decline may be related to reduced naming ability as evidenced by a significant correlation between the postoperative BNT score and the VIO reliable change score (r = 0.436, p < .01). This finding may be explained by findings from prior studies<sup>67,68</sup> which noted post-operative language decline accounted for post-operative verbal memory decline. Alternatively, in a small sample of patients post subtemporal SAH at our center,<sup>69</sup> cortical thinning was noted postoperatively in the ipsilateral inferior temporal gyrus in the area of postoperative edema following retraction. It is possible that even with minimal retraction used in subtemporal SAH, postoperative cognitive decline may be associated with cortical thinning as opposed to hippocampal resection alone. In the present study, it appears that resection of mesial temporal structures or possibly retraction, even with minimal cortical disruption, may sufficiently interfere with language networks to produce postoperative language decline.

Limitations of the present study include fewer right SAH compared to left SAH patients, insufficient data to establish Engle classification, and multiple statistical comparisons. Fewer right SAH cases were included in this study which has the potential of influencing obtained results. This was not due to inequality in case exclusion but rather a product of the patients that returned for postoperative evaluation. It is possible a greater number of left SAH patients returned for follow-up evaluation due to greater concern regarding postoperative decline: although, rates of cognitive decline in right and left SAH from the present study were generally commensurate with other studies using reliable change scores. Another limitation of the present study, and directly related to its archival nature, was the inability to assign Engle class which significantly limits comments on seizure outcome. Consequently, patients were identified as either seizure free or having presence of recurrent seizures (1 or more seizures) and it is possible a portion of those identified as having recurrent seizures would still be classified as Engle class 1.

In conclusion, the present study, which measured changes in cognition via reliable change scores and expanded on previous findings in the largest sample to date, indicated the majority of patients that underwent subtemporal SAH experienced no significant cognitive decline and most experienced good shortterm seizure control. However, through use of reliable change analyses, memory decline was found in approximately 30% of patients which is in marked contrast to prior studies using only group level analyses in subtemporal SAH. These findings highlight the importance of using reliable change procedures in outcome research. Further, despite the preservation of the temporal stem and minimal neocortical resection in subtemporal SAH, there remains a naming decline in more than one third of patients that undergo dominant hemisphere SAH. Together, these results indicate that a notable proportion of subtemporal SAH patients experience post-operative memory and naming decline with rates similar to other reported surgical approaches. Dominant subtemporal SAH patients appear to be at the greatest risk for cognitive decline in multiple cognitive domains. Direct comparison between subtemporal SAH and another surgical approach (e.g., anterior temporal lobectomy, transsylvian SAH, or transcortical SAH) is an important area for future research in order to assess if rates of neurocognitive decline vary as a function of surgical approach.

#### **Conflicts of interest**

There are no conflicts of interest to disclose.

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