COGNITION AND DEPRESSION IN CEREBELLAR AND FRONTAL LOBE STROKE PATIENTS

A Dissertation

Presented to

The Faculty of the Department

of Psychology

University of Houston

In Partial Fulfillment

Of the Requirements for the Degree of

Doctor of Philosophy

By

Kristina A. Agbayani

May, 2014

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Abstract

Contrary to prior beliefs, various case studies have shown that the cerebellum is involved in higher order cognitive functions, and the cerebrocerebellar circuitry has been implicated in subserving such functions. Specifically, cerebellar lesions are associated with a constellation of deficits termed the cerebellar cognitive affective syndrome (Schmahmann & Sherman, 1998). The purpose of the current study was to 1) compare the cognitive profile of patients with frontal lobe ($N = 28$) versus cerebellar ($N = 31$) strokes, 2) examine the effects of depression on cognition, and 3) to understand how structural and emotional factors relate to cognitive functioning. Results are consistent with previous findings of impaired executive functioning, verbal fluency, and spatial organization in patients with cerebellar strokes, which is also similar to the impairments found in patients with frontal lobe strokes. Patients with frontal lobe strokes exhibited a larger magnitude of impairment on select tests. Overall, the presence of major depressive disorder alone did not affect performance on neuropsychological measures. Laterality and stroke volume did not significantly account for performance on neuropsychological tests.

Table of Contents

List of Tables and Figures

Cognition and Depression in Cerebellar and Frontal Lobe Stroke Patients

Stroke is the third leading cause of death in the United States, with an estimated incidence of 610,000 first strokes and 185,000 recurrent strokes per year (Lloyd-Jones et al., 2009). The cognitive and emotional effects of stroke on an individual are profound. Stroke is a leading cause of disability and activity limitations, with approximately fifty percent of stroke survivors experience functional limitations and difficulty performing basic activities of daily living (NHLBI, 2009). The cognitive sequelae following a stroke vary based on the location and extent of the stroke, but may include impairments in memory, speech and language, attention, visuospatial abilities, and executive dysfunction, among others. Depression and difficulty with social adjustment are also common following stroke, affecting one- to two-thirds of survivors (Eslinger et al., 2002).

Cerebellar Stroke, Cognition, and Emotion

Historically, understanding of the functions of the cerebellum was strictly limited to modulation of balance and coordination of movement, as cerebellar lesions typically result in ataxia, which is characterized by incoordination of balance, gait, and extremity and eye movements, as well as dysarthria (Schmahmann, 2004). For example, early studies conducted by Lashley and McCarthy (1926) found that, after complete destruction of the cerebellum in rats previously trained to complete a maze task, the rats did not exhibit any retention deficits on the maze task. Specifically, the rats did not take a significantly longer amount of time to complete the maze and did not make more errors on the maze task after their cerebellums were destroyed. Lashley and McCarthy (1926) concluded that the cerebellum was not involved in retention of habitual information and, subsequently, for a significant period of time after this experiment was conducted, it was inferred that the cerebellum was only involved in motor learning and no other cognitive functions.

Over time, it has become increasingly evident that the cerebellum is involved in higher order functions. Luria was one of the first to make the connection between the cerebellum and cognition in a case report published in 1964. Specifically, he noted “pseudo-frontal” symptoms secondary to a cerebellar tumor, including disorientation to time, abulia, and numerous intrusion and interference errors during testing (Budisavljevic & Ramnani, 2012). Since that time, evidence for the cerebellum’s role beyond movement has been found in additional case studies and in small groups of patients who exhibited significant cognitive and behavioral changes following cerebellar lesions.

Schmahmann and Sherman (1998) reported a consistent constellation of deficits in patients with neurological disorders, such as stroke, that were confined to the cerebellum. These included impairments in executive functioning, such as set-shifting, planning, abstract reasoning, and verbal fluency; deficits in spatial cognition including visuospatial disorganization and impaired visual memory; and behavior and personality changes, specifically a flattening of affect and disinhibition. The authors named this unique symptom complex the cerebellar cognitive affective syndrome (CCAS). Based upon the cerebrocerebellar circuitry, Schmahmann (2004; 2010) introduced the dysmetria of thought hypothesis. This hypothesis asserts that the feedforward and feedback loops of the cerebellum modulate behavior by maintaining it around a homeostatic baseline that is appropriate to a given context. Schmahmann (2010) described how the cerebellum controls the speed, capacity, consistency, and pertinence of cognitive processes in the same way that it controls the rate, force, rhythm, and accuracy of movements. Therefore, damage to areas of the cerebellum involved in cognitive functions leads to dysmetria of thought, which is clinically manifested through the various components of CCAS.

The cerebrocerebellar circuitry has been implicated in subserving cognitive and executive processes, and a disruption of these connections likely contributes to the constellation of deficits found in CCAS. Functional imaging, behavioral, and clinical studies have pointed to a topographic organization of the cerebellum such that motor control in the anterior lobe is separated from cognitive and affective processing in the posterior lobe (Grimaldi & Manto, 2012; Stoodley & Schmahmann, 2010). The cerebrocerebullum, which is located in the lateral regions of the cerebellar hemisphere, has connections to various areas of the cerebral cortex (Purves et al., 2008). Schmahmann and Pandya (1997) and Middleton and Strick (1997) described parallel feedforward and feedback cerebrocerebellar loops in which the various cerebellar regions both receive input from and relay output to association areas in the frontal, temporal, parietal, and limbic cortices (Figure 1). The feedforward loop consists of a corticopontocerebellar pathway that originates in cerebral regions, such as the prefrontal cortex, and carries information from neurons in these regions to neurons in the ventral pons, which subsequently is directed to the cerebellum. The feedback loop consists of a cerebellothalamocortical pathway where information in the cerebellum is projected to the thalamus via the midbrain neurons of the red nucleus. This loop is completed by afferent pathways from the thalamus to the cortex (Middleton & Strick, 1998).

Animal studies have supported the notion of a topographic organization of the cerebellum, with findings of separate closed-loop circuits from the cerebellum to the motor cortex and prefrontal cortex involved in motor and cognitive operations, respectively (Kelly & Strick, 2003). Schmahmann's (1996) examination of the anatomic substrates of the cerebellum's involvement in cognitive processing in nonhuman primates found that there was a topographic organization of behavioral and cognitive functions: the vermis and fastigial nucleus are associated with emotion and affect regulation, while the lateral cerebellar hemispheres in the posterior lobe and the dentate nucleus are associated with executive functioning, visuospatial abilities, and language. Additionally, Middleton and Strick (1994) examined transport of information from the deep cerebellar nuclei and found that the dentate nuclei send information to the same areas of the prefrontal cortex that relay information to the cerebellum.

The vascular perfusion of the cerebellum allows for the study of cognitive impairment following focal lesions. The territory supplied by the superior cerebellar artery (SCA) is primarily restricted to the anterior lobe of the cerebellum, whereas the posterior inferior cerebellar artery (PICA) supplies the posterior lobe of the cerebellum and deep cerebellar nuclei (Schmahmann, 2000); as discussed above, these lobes are generally associated with motor and higher order cognitive functions, respectively. A study conducted by Tedesco et al. (2011) used structural MRI to relate areas of damage to impaired neuropsychological functioning in patients who suffered a stroke confined to the cerebellum. Patients with lesions in the territory supplied by the SCA had relatively preserved cognitive profiles, while patients whose lesions were restricted to the PICA perfusion areas, including deep cerebellar nuclei, had impaired language, executive, visuospatial, and sequencing abilities. Schmahmann and Sherman (1998) also used structural MRI to localize lesions in patient with stroke, tumor, or atrophy confined to the cerebellum. The authors found that the CCAS symptom complex was more pronounced in patients with bilateral disease and large unilateral PICA infarcts, and that the vermis was consistently involved in patients with marked behavioral and affective symptoms.

In addition to allowing for the localization and extent of stroke, structural MRI also affords the ability to quantify gray matter volumes that can be damaged after a stroke. Previous studies have related cognitive impairments to a reduction in gray matter volume in patients who had suffered a stroke. For example, a study conducted by Stebbins et al. (2008) compared gray matter volumes in patients with and without cognitive impairment following stroke. The authors found that impaired cognitive performance in one or more domains, including attention, working memory, language, visuospatial abilities, psychomotor speed, and declarative memory, was correlated with reduced gray matter volume.

Prior studies of the effects of cerebellar lesions on cognition have focused on single domains rather than an entire cognitive profile or symptom complex as encompassed by CCAS. In a review of studies examining the cerebellum's involvement in cognitive functioning by domain, differences in impairments were found according to the side of the lesion. Generally, the right cerebellum has been associated with left hemisphere functions including verbal working memory and language processing, while the left cerebellum has been found to mediate right hemispheric functions such as visuospatial skills (see O'Halloran et al., 2012 for a review). These findings are consistent with the contralateral connections between the cerebellum and cortical areas, and evidence of hypoperfusion of contralateral cortical areas following focal cerebellar lesions (Botez-Marquard et al., 1994). Additionally, there is some evidence that the right cerebellum seems to play a larger role than the left in attention and working memory tasks (O’Halloran et al., 2012). Both hemispheres of the cerebellum have been implicated in subserving executive functioning, such as planning and logical sequencing. Specifically, verbal (e.g., sorting sentences) and visuospatial sequencing (e.g., sorting drawings of behavioral sequences) have been further localized to the right and left cerebellar hemispheres, respectively (Leggio et al., 2008).

Frontal Lobe Stroke, Cognition and Emotion

The impairments found following cerebellar lesions and within the CCAS, such as impairments in executive functioning and behavior/personality change, are typically associated with frontal lobe lesions. A review of studies examining the frontal lobes described involvement of the prefrontal cortex in a variety of functions including attention, personality, maintenance of set, sequencing, behavioral modulation, and affect (O’Reilly, 2010). Major subdivisions of the prefrontal region that connect to various thalamic nuclei and other cortical and subcortical areas have been proposed, and each subdivision is thought to mediate different functions (Stuss & Benson, 1987). These subdivisions include dorsolateral, orbitofrontal, ventrolateral, ventromedial, basal, orbital, and frontopolar areas. Dorsolateral lesions are associated with deficits in control, regulation, and integration of cognitive activities; lesions in the medial frontal/anterior cingulate regions are associated with affective and emotional disturbance such as apathy; and orbital lesions often result in disinhibition and impulsivity (Lezak, Howieson, & Loring, 2004). Studies have found selective impairments on frequently administered tests of executive function, such as the Wisconsin Card Sorting Test (WCST), following focal lesions within the prefrontal regions. Specifically, Stuss et al. (2000) found that patients with superior medial lesions performed worst on the number of categories completed and perseverative responses of the WCST, patients with orbitofrontal/inferior medial lesions had the highest set loss errors and low perseveration, and patients with dorsolateral lesions showed significant perseveration. However, a meta-analysis of the relationship between executive functioning and the frontal lobes conducted by Alvarez and Emory (2006) found that the association between the frontal lobes and executive functioning by frequently used neuropsychological measures such as the WCST, phonemic fluency, and the Stroop Color-Word Interference Test, was inconsistent in the literature. Instead, the authors suggest that both frontal and non-frontal regions are essential to preserving executive functioning.

Depression and Cognition

The emotional and cognitive effects of stroke are profound, and the prevalence of post-stroke depression is relatively high. A 12-month prospective study that examined the progression of post-stroke depression found more than half of the patients, who had no prior psychiatric history, met criteria for major depressive disorder (Kauhanen et al., 1999). The study found that the frequency of depression increased within the first year following stroke. The presence of depression was related to the extent and degree of neurological and functional impairments and overall disability.

The association between depression and cognition in depressed individuals without a comorbid neurologic disorder is well documented. Depressed individuals are more likely to have impaired cognitive speed, memory, naming ability, planning, and problem-solving compared to non-depressed individuals (Austin, Ross, & Murray, 1992; Goodwin, 1997; Lezak, Howieson & Loring, 2004). In terms of localization, several studies indicated a relationship between depressed mood and reduced cognitive performance after a left cerebral hemisphere stroke, but not right hemisphere stroke (Bolla-Wilson et al. 1989; Downhill & Robinson, 1994; Robinson et al., 1986; Spalletta et al., 2002). Results indicated that greater report of depressive symptoms is associated with poorer cognitive test performance over and above impairments attributable to stroke alone. As discussed previously, lesions restricted to the cerebellar vermis consistently produced affective and emotional symptoms, such as apathy. The cognitive sequelae following brain injury, such as stroke, are thus likely to be influenced by multiple factors including the side of the lesion, structures involved, and the presence or absence of mood disturbance.

Study Goals and Hypotheses

Archival data from neuropsychological assessments, semi-structured psychiatric interview, and neuroimaging (structural MRI of the brain) will be used to investigate structural and functional relationships in individuals who sustained a stroke. To date, comparisons between frontal lobe and cerebellar lesions following stroke and their relative effects on cognition have not been reported in the literature. The current study examined the cognitive and emotional profile of patients following cerebellar stroke from a larger sample size than has been used in previous studies, and is the first to determine whether any distinctions can be made between the cognitive sequelae following frontal lobe versus cerebellar stroke.

The specific goals and hypotheses of the current study are as follows:

1. Compare the cognitive profile of patients with frontal lobe versus cerebellar strokes. When patients with frontal versus cerebellar strokes are compared, performance on tests of executive function, in particular, is expected to be similar.
2. Assess the association of clinical diagnoses of major depressive disorder with cognitive performance in patients with frontal versus cerebellar strokes. The presence of major depression is expected to be associated with poorer cognitive performance relative to that of patients without depression.
3. Examine the relationship between structural brain integrity (using gray matter volumes) and laterality of the stroke (left versus right) and cognition. It is hypothesized that a greater magnitude of cognitive impairment will be associated with larger stroke volume, and that right cerebellar lesions will be associated with worse performance on language tasks, whereas left cerebellar lesions will be associated with worse performance on visuospatial tasks.

Method

Participants

Archival data were collected by chart review from 31 patients who suffered a stroke confined to the cerebellum (9 left, 17 right, and 5 bilateral lesions) and 28 patients who suffered a stroke affecting the frontal lobes (11 left, 12 right, and 5 bilateral lesions). Participants were evaluated by the neuropsychology service of the Houston Methodist Neurological Institute at the Houston Methodist Hospital between July 1st 2009 and December 1st, 2012. The demographics and clinical characteristics of the sample by the type of stroke (cerebellar and frontal lobe) are presented in Table 1. Data included both men and women of ages 18 years and older. Patients were excluded from the study if they had a history of traumatic brain injury or other neurologic diagnoses with the exception of possible post-stroke dementia. Individuals who could not understand instructions during the cognitive evaluation were also excluded from the study.

Neuropsychological Assessment

Results of the following tests were collected from patient charts: Mini-Mental State Examination (MMSE), Repeatable Battery for the Assessment of Neuropsychological Status (RBANS); Hopkins Verbal Learning Test-Revised (HVLT-R); Benton Visual Memory Test-Revised (BVMT-R); Wechsler Memory Scale -3rd Edition (WMS-III) Logical Memory, Digit Span and Similarities subtests of the Wechsler Adult Intelligence Scale-Fourth Edition (WAIS-IV); Trail Making Test, and phonemic fluency (FAS). As this was a clinical sample, not all participants received all of the aforementioned tests or the same combinations of tests. All tests were used in the evaluation of individuals seen at the Houston Methodist Hospital who had been referred by a Physical Medicine & Rehabilitation physiatrist or neurologist. Administration and interpretation of the tests followed standardized procedures (Lezak, Howieson, & Loring, 2004; Strauss, Sherman, & Spreen, 2004).The Mini International Neuropsychiatric Inventory (MINI) was used to determine a DSM-IV-TR diagnosis of major depressive disorder (Sheehan et al., 1998).

Structural MRI

A subset of the main sample consisting of 12 patients who suffered a stroke confined to the cerebellum (3 left, 9 right), and 14 patients who suffered a stroke affecting the frontal lobes (7 left, 7 right) had stroke volume data from magnetic resonance imaging (MRI) studies. The demographics and clinical characteristics of this subset of the main sample by the type of stroke (cerebellar and frontal lobe) are presented in Table 2. Whole brain MRI image sets were routinely acquired on Siemens 3T and GE 3T MRI scanners as part of a patient's clinical work-up after stroke and admittance to The Methodist Hospital. Image data was imported into FMRIB Software Library (FSL) in order to conduct gray matter volume-based analysis. Stroke lesion volumes were obtained by manually tracing around the edges of the hyperintense lesion for each patient. Lesion volumes (in mm3) were automatically calculated by the FSL statistics feature after manual tracing was completed by the principal investigator.

Statistical Analyses

In order to compare performance among neuropsychological tests, raw scores on each test were converted to z-scores using published normative data for each of the tests administered in the clinical evaluation. Since all participants did not receive the same battery of tests, different tests measuring similar functions (e.g., RBANS List Learning subtest and HVLT-R List Learning total score) were collapsed into one variable (i.e., List Learning) to reduce the number of variables. A z-score of -1.5 was used to define impairment on a given test, based on guidelines suggested by Lezak, Howieson, & Loring (2004), for the purpose of determining frequency of impairment in the stroke subgroups. Independent variables include side of stroke (left, right, and bilateral), location of stroke (frontal versus cerebellar), psychiatric diagnosis (depressed, not depressed). Scores on neuropsychological tests were the dependent variables. Due to the large number of dependent variables, as well as previous evidence that scores for different neuropsychological tests tend to be positively correlated, conservative statistical tests and a stringent alpha level of .01 were used to determine significance in order to minimize Type I errors. The following analyses were conducted to address the goals of the study:

1. Analyses for hypothesis 1: Given the small sample sizes, Fisher's exact test was used to compare the rates of impairment on the neuropsychological measures by the type of stroke (cerebellar versus frontal lobe) and by the location of the stroke (left cerebellar versus right frontal lobe, right cerebellar versus left frontal lobe, and bilateral cerebellar versus bilateral frontal lobe). Comparisons of performance on neuropsychological measures between cerebellar and frontal lobe strokes were obtained from the type of stroke main effects analyses from the two-way between subjects analyses of variance (ANOVA) conducted for hypothesis 2 as outlined below.

2. Analysis for hypothesis 2: Two-way between subjects ANOVAs were conducted with type of stroke (frontal lobe, cerebellar) and psychiatric diagnosis (major depression, no major depression) as the independent variables and scores on each neuropsychological test as the dependent variables. Interactions were not reported when neither main effect was statistically significant, unless the data were suggestive of a crossover interaction.

3. Analysis for hypothesis 3: Hierarchical multiple regression analyses were conducted to estimate the unique contribution of laterality of the stroke (left or right) and stroke volume on performance on each neuropsychological measure for cerebellar and

frontal lobe stroke patients. Two sets of hierarchical regression analyses with and without stroke volume included as a predictor in model 2 were conducted, as only a small subset of the main sample had stroke volume data from magnetic resonance imaging (MRI) studies. Variance inflation factors (VIF) and tolerance values were examined to assess multicollinearity using the cut-off guidelines described by Myers (1990) and Menard (1995) viz., VIF < 10 and tolerance > 0.2, respectively. The analyses, conducted for cerebellar and frontal lobe stroke patient groups separately, are as follows:

a. Hierarchical multiple regression 1: In model 1, performance on a cognitive screen (MMSE) was the predictor variable of performance on each neuropsychological measure. In model 2, laterality of the stroke was entered into the equation as an additional predictor variable.

b. Hierarchical multiple regression 2: In model 1, performance on a cognitive screen (MMSE) was the predictor variable of performance on each neuropsychological measure. In model 2, laterality of the stroke and stroke volume were entered into the equation as additional predictor variables.

Results

There were no significant differences between the frontal lobe and cerebellar stroke groups on any demographic variables. Similarly, there were no significant differences between left cerebellar and right frontal lobe groups, right cerebellar and left frontal lobe groups, and bilateral cerebellar and bilateral frontal stroke groups on any demographic variables.

Rates of Impairment

The rates of impairment on each neuropsychological measure for cerebellar versus frontal lobe strokes, left cerebellar versus right frontal lobe strokes, right cerebellar versus left frontal lobe strokes, and bilateral cerebellar versus bilateral frontal lobe strokes were compared using Fisher's exact test or the *z*-test for proportions when the groups' combined sample sizes were greater than or equal to 40. A *z*-score less than or equal to -1.5 was used as the cutoff for clinical impairment.

When proportions of impairment on each neuropsychological measure were compared for patients who sustained a cerebellar versus a frontal lobe stroke, a significant result at $p < .01$ was not obtained for any of the z-tests or Fisher's exact tests. Table 3 depicts the results.

When proportions of impairment on each neuropsychological measure were compared for patients who sustained a left cerebellar versus a right frontal lobe stroke, none of the Fisher's exact tests yielded a significant result at $p < .01$. Moreover, none of the results from Fisher's exact tests trended towards significance at a level of $p < .05$. Table 4 depicts the results.

When proportions of impairment on each neuropsychological measure were compared for patients who sustained a right cerebellar versus a left frontal lobe stroke, the difference in proportions of impairment for RBANS Line Orientation was significant at $p <$

.01, with frontal lobe stroke patients performing worse on the task. The difference in proportions of impairment for RBANS Digit Span approached significance at $p < .05$. Table 5 depicts these results.

Lastly, when proportions of impairment on each neuropsychological measure were compared for patients who sustained bilateral cerebellar versus bilateral frontal lobe stroke, there were no significant results by Fisher's exact test. Table 6 depicts the results.

Analysis of Variance

To relate clinical diagnoses of major depressive disorder with cognitive performance in patients with frontal versus cerebellar strokes, a two-way between-subjects analysis of variance (ANOVA) was conducted with type of stroke (frontal, cerebellar) and psychiatric diagnosis (major depression, no major depression) as the independent variables. Scores on each neuropsychological measure were the dependent variables. Tables 7 and 8 display the results for each neuropsychological measure, by domain.

No significant Type of Stroke x Depression interaction was found for any neuropsychological measure. The Type of Stroke x Depression interaction trended towards significance for performance on three neuropsychological measures: List Learning, Story Memory, and Semantic Fluency. Each of these interactions showed a similar pattern: patients with cerebellar strokes exhibited a pattern of performance opposite what would be expected, in that mean *z*-scores were higher (better performance) in depressed patients; however, the mean *z*-scores for cerebellar stroke patients, irrespective of whether they were depressed, did not fall within the impaired range (i.e., z-score $\leq$ -1.5). Patients with frontal lobe strokes exhibited the expected pattern, with lower mean *z*-scores (worse performance) in patients who were depressed compared to those who were not. Figures 2, 3, and 4 illustrate the mean *z*-score for patients cerebellar and frontal lobe strokes as a function of depression for the List Learning, Story Memory, and Semantic Fluency tests, respectively.

There were no significant main effects of clinical depression on performance on any neuropsychological measure. There was a significant main effect for the type of stroke (cerebellar versus frontal lobe) on performance on Semantic Fluency, $F(1,50) = 12.49$, $p < .01$. On this task, patients with frontal lobe strokes performed worse (lower mean *z*-score) than patients with cerebellar strokes. The main effect for the type of stroke trended towards significance for several tests, including RBANS Digit Span, RBANS Line Orientation RBANS Copy, RBANS Naming, List Learning, and Story Recall. For each of these tests, patients with frontal lobe strokes performed worse than patients with cerebellar strokes. Mean performance on each neuropsychological measure for the two groups is presented in Figure 5.

Hierarchical Multiple Regression

The demographics and clinical characteristics of patients with left versus right cerebellar and frontal lobe strokes are presented in Tables 9-10, respectively. There was a statistically significant difference in mean performance on the MMSE between left and right frontal lobe stroke patients, $t\ (20) = -2.26$, $p = .03$. There were no significant differences in any other demographic or clinical variables between left and right cerebellar or frontal lobe stroke patients. Thus, hierarchical multiple regression analysis was used to determine the unique contribution of laterality of the stroke (left or right) and stroke volume over and above that of performance on a cognitive screen (MMSE) on performance on each neuropsychological measure for cerebellar and frontal lobe stroke groups. To ensure that multicollinearity was not confounding the regression models, variance inflation factor (VIF) and tolerance values were examined and found to be within the appropriate limits.

Cerebellar stroke patients: hierarchical multiple regression 1. Tables 11-14 depict the results of the hierarchical multiple regression analyses in which performance on the MMSE was used to predict performance on each neuropsychological test in model 1, and laterality of the stroke was added as a predictor in model 2. Performance on the MMSE was found to account for 25.2% of the variance in performance on List Learning ($R^2 = .252$, $F_{1, 26} = 8.75$, $p < .01$), 43.2% of the variance in performance on Story Memory ($R^2 = .432$, $F_{1, 20} = 15.19$, $p < .01$), and 24.3% of the variance in performance on Trails B ($R^2 = .243$, $F_{1, 26} = 8.34$, $p < .01$). When laterality of the stroke was added as a predictor in model 2, it failed to account for a significant amount of additional variance in performance on any of these neuropsychological measures.

Performance on the MMSE approached significance in accounting for the variance in performance on WAIS-IV Digit Span Backwards, RBANS Naming, FAS, List Recognition, Story Recall, Figure Recall, and WAIS-IV Similarities, all $p < .05$. Adding laterality of the stroke as a predictor in model 2 failed to account for a significant amount of additional variance in performance on any of the aforementioned tests. For the remaining neuropsychological tests, neither performance on the MMSE in model 1 nor the addition of laterality as a predictor in model 2 predicted a significant amount of the variance in performance.

Cerebellar stroke patients: hierarchical multiple regression 2. Tables 15-18 show the results of the hierarchical multiple regression analyses in which performance on the MMSE was the predictor variable of performance on each neuropsychological test in model 1, and laterality of the stroke and stroke volume were added as predictors in model 2. Performance on the MMSE was found to account for 60.2% of the variance in performance on Story Memory (R^2 = .602, $F_{1, 9}$ = 13.60, p < .01), and approached significance in accounting for the variance in performance on Trails B. When laterality of the stroke and volume were entered into the second model, they did not account for a significant amount of additional variance in performance on either neuropsychological measure.

Performance on the MMSE did not account for a significant amount of variance in performance on RBANS Digit Span. When laterality and volume of the stroke were added as predictors in the second model, they approached significance in accounting for additional variance in performance on RBANS Digit Span. For the remaining neuropsychological tests, neither performance on the MMSE in model 1 nor the addition of laterality and stroke volume as predictors in model 2 predicted a significant amount of variance in performance.

Frontal lobe stroke patients: hierarchical multiple regression 1. Tables 19-22 display the results of the hierarchical multiple regression analyses in which performance on the MMSE was the predictor variable of performance on each neuropsychological test in model 1, and laterality of the stroke was added as a predictor in model 2. Performance on the MMSE was found to account for 43% of the variance in performance on WAIS-IV Digit Span Backwards (R^2 = .430, $F_{1, 15}$ = 11.32, p < .01), 54.9% of the variance in performance on RBANS Line Orientation (R^2 = .549, $F_{1, 18}$ = 21.88, p < .01), 61.6% of the variance in performance on RBANS Copy (R^2 = .616, $F_{1, 16}$ = 25.71, p < .01) , 45.4% of the variance in performance on RBANS Naming (R^2 = .454, $F_{1, 20}$ = 16.64, p < .01), 37.3% of the variance in performance on Semantic Fluency (R^2 = .373, $F_{1, 23}$ = 13.67, p < .01), 79.3% of the variance in performance on Trails A (R^2 = .793, $F_{1, 13}$ = 49.77, p < .01), 42.8% of the variance in performance on List Learning (R^2 = .428, $F_{1, 22}$ = 16.44, p < .01), 35% of the variance in performance on Story Memory (R^2 = .350, $F_{1, 22}$ = 11.87, p < .01), 36.3% of the variance in performance on Story Recall (R^2 = .363 $F_{1, 22}$ = 12.51, p < .01), and 46.5% of the variance in performance on Figure Recall (R^2 = .465 $F_{1, 16}$ = 13.93, p < .01). When laterality of the stroke was added as a predictor in model 2, it did not account for a significant amount of additional variance in performance on any of the aforementioned neuropsychological measures.

Performance on the MMSE approached significance in accounting for the variance in performance on List Recognition and WAIS-IV Similarities, both p < .05. Adding laterality of the stroke as a predictor variable failed to account for a significant increase in variance explained for either of the two tests. For the remaining neuropsychological tests, neither performance on the MMSE in model 1 nor the addition of laterality as a predictor in model 2 significantly predicted variance in performance.

Frontal lobe stroke patients: hierarchical multiple regression 2. Tables 23-26 summarize the results of the hierarchical multiple regression analyses in which performance on the MMSE was the predictor variable of performance on each neuropsychological test in model 1, and laterality of the stroke and stroke volume were added as predictors in model 2. Performance on the MMSE significantly accounted for 67.7% of the variance in performance on RBANS Line Orientation (R^2 = .677, $F_{1, 8}$ = 16.73, p < .01), 66.7% of the variance in performance on Semantic Fluency (R^2 = .667, $F_{1, 13}$ = 26.05, p < .01), and 86.2% of the variance in performance on Trails A (R^2 = .862, $F_{1, 8}$ = 50.15, p < .01). Laterality and volume of the stroke did not significantly increase the variance accounted for by the MMSE alone.

Performance on the MMSE approached significance in accounting for the variance in performance on WAIS-IV Digit Span Backwards, RBANS Copy, RBANS Naming, List Learning, Story Recall, and Trails B, all p < .05. Adding laterality and volume of the stroke as predictors failed to account for statistically significant amounts of additional variance explained. For the remaining neuropsychological tests, neither performance on the MMSE in model 1 nor the addition of laterality and stroke volume as predictors in model 2 significantly predicted variance in performance.

Discussion

Cognitive Profile Comparisons

Comparisons of proportions of impairment and mean performance on the various neuropsychological measures within each cognitive domain revealed similar cognitive and executive profiles between patients with cerebellar and frontal lobe strokes (see Table 3 and Figure 5). Patients with cerebellar and frontal lobe strokes both showed the highest rates of impairment and lowest mean performance on tests of verbal fluency, processing speed, verbal memory for a word list, and set-switching. Given the cerebellum's crossed connections, proportions of impairment were also compared between left cerebellar versus right frontal lobe strokes, right cerebellar versus right frontal lobe strokes, and bilateral cerebellar versus bilateral frontal groups. Such comparisons again revealed similar proportions of impairment between each of the two groups. Overall, these findings are consistent with the constellation of cognitive deficits typically found as part of the cerebellar cognitive affective syndrome (CCAS) described by Schmahmann and Sherman (1998), and they further support the notion that the cerebellum is involved in “higher-order” cognitive functioning. A major difference between cerebellar and frontal lobe stroke groups’ performance on neuropsychological tests was greater impairment on a test of semantic fluency in patients with frontal lobe strokes. This finding may be due to the presence in the sample of patients with frontal lobe strokes that also impinged upon temporal areas, or it may reflect an impairment that is selective for frontal-lobe damage, such as slowed processing speed or loss of set during the task. Patients with left frontal lobe strokes exhibited a greater proportion of impairment on a visuospatial judgment task (RBANS Line Orientation). Such a difference may be due to poor attention, and/or slowed processing speed as the task included an external time constraint.

Of particular interest were comparisons in proportions of impairment and mean performance between cerebellar and frontal lobe strokes on tests of executive function. As hypothesized, there was no significant difference in performance between the two groups on any tests of executive function, including set-switching, verbal reasoning, initiation as measured through verbal fluency, and planning and organization as measured through working memory and copy tasks. Such impairments in executive functioning are typically observed following lesions to prefrontal areas (O’Reilly, 2010; Stuss & Benson, 1987; Stuss et al. 2000). Similar findings in patients with cerebellar strokes are consistent with the concept of highly integrated cerebrocerebellar circuitry, which consists of feedforward and feedback loops between the cerebellum and areas of the cerebral cortex, including the prefrontal cortex (Middleton & Strick, 1998).

Major Depressive Disorder and Cognition

Overall, in contrast to what was hypothesized based upon the literature, the presence of major depressive disorder (MDD) alone did not have a significantly negative impact on performance on the majority of the neuropsychological measures included in the study. Although no interaction between the presence of depression and the type of stroke (frontal lobe versus cerebellar) was statistically significant, several did approach significance for selected measures of language and verbal memory. Patients with frontal lobe strokes tended to be more impaired on these tests when depressed, which is consistent with previous studies' findings that depressed patients perform worse on tests of memory and naming (Austin, Ross, & Murray, 1992; Goodwin, 1997). In contrast, patients with cerebellar strokes showed the opposite and unexpected pattern: patients who were depressed tended to perform better, on average, than patients who were not depressed; however, the average z-scores for patients both with and without depression were above the cutoff for impairment on these tests. Thus, this finding in patients with cerebellar strokes may be more of a reflection of normal variation rather than the effect of depression. Furthermore, damage to the vermis has been implicated in resulting in more profound affective presentations (Schmahmann and Sherman, 1998); however, due to limitations in sample size, the current study did not distinguish involvement of the vermis within the cerebellar stroke group. Examination of differences in rates of MDD and the relationship between MDD and cognition with respect to involvement of the vermis may be more informative for future studies.

The overall lack of greater impairment on neuropsychological tests in depressed compared to non-depressed patients may be due to several factors. For example, patients who may have met diagnostic criteria for depression may have minimized their symptoms and, thus, did not meet criteria for major depressive disorder when evaluated by neuropsychology. In addition, some patients may have already been placed on antidepressant medications after sustaining their strokes, or had already been receiving long-term treatment for depression prior to the stroke. Therefore, patients may have reported being depressed but the presence of such treatment would presumably improve cognitive functioning (Fann, Uomoto, & Katon, 2001). Findings of improved cognition with antidepressant treatment are inconsistent, however, as persistent cognitive deficits following antidepressant treatment and clinically remitted depression have been reported (Nebes et al., 2003; Trivedi & Greer, 2014). Moreover, though cognitive impairment has been well documented in depressed patients, this relationship is largely inconsistent and little is understood of the factors that mediate it, such as depression severity, number of depressive episodes, and the length of the depressive episode (McClintock, Husain, Greer, & Cullum, 2010).

Prediction of Performance on Neuropsychological Measures

The MMSE significantly accounted for scores on several neuropsychological tests in the domains of memory and executive functioning for cerebellar stroke patients, and on selected tests in each domain for frontal lobe stroke patients. Examination of the beta weights of the MMSE in each regression model were positive and in the expected direction overall, suggesting that as MMSE scores increased, performance on neuropsychological measures improved (increased z-score). Poor performance on the MMSE may have reflected global cognitive impairment and greater stroke severity.

Contrary to what was hypothesized, neither laterality nor stroke volume significantly affected performance on any of the neuropsychological measures. It was hypothesized that left cerebellar strokes would be associated with worse performance on visuospatial tasks (positive laterality beta weight), right cerebellar strokes would be associated with worse performance on language tasks (negative laterality beta weight), and larger stroke volume would be associated with worse performance (negative volume beta weight). However, the valence of the beta weights for laterality and stroke volume had no consistent pattern and were relatively variable within each group. With regard to damage restricted to the frontal lobes, the literature does not suggest laterality of deficits akin to cerebellar strokes. Thus, as was found in the current study, laterality would not affect performance on neuropsychological measures.

The negative findings may suggest that the laterality or volume of the stroke may not be as important in determining impairment as the specific topographic regions of the cerebellum, frontal lobe, and prefrontal cortex that are damaged. Specifically, the lateral cerebellar hemispheres in the posterior lobe and the dentate nucleus are associated with executive functioning, visuospatial abilities, and language, whereas the anterior lobes are primarily involved in modulating motor functioning (Schmahmann, 1996).The current study did not separate strokes into specific topographic regions, such as anterior and posterior cerebellar lobe damage, cerebellar arterial blood supplies affected (e.g., posterior inferior and superior cerebellar arteries), or involvement of the vermis, as this would have led to minimal sample sizes. Moreover, for patients with MRI data, it was difficult to categorize them by the specific topographic regions damaged due to the low resolution of the images and availability of images in only one plane (horizontal). The potential utility of separation into such groups is supported by evidence from anatomical studies in non-human animals and physiological studies in humans that have demonstrated the presence of closed-loop circuits between the cerebellum and multiple cortical areas, and that specific output channels comprised of distinct clusters of neurons within the deep cerebellar nuclei are involved in specific motor and cognitive functions (Middleton & Strick, 1998).

Study Limitations

There are several major limitations to the current study. First, there was no control group in the current study with which to compare participants with cerebellar and frontal lobe strokes. This lack of a control group may reduce the generalizability of the findings of the current study. The use of standardized test norms, however, inherently provides a normal control group of individuals to which the stroke patients' performance on each neuropsychological test is compared. There was also a relatively small overall sample size within the groups compared, which reduces the statistical power and necessitated asymmetric decisions. Specifically, significant findings can be accepted, whereas negative outcomes are difficult to interpret unequivocally because of inadequate statistical power.

Another limitation to the study was that the majority of patients underwent neuropsychological evaluation as inpatients, and may have experienced changes in their sleep cycles or been on numerous medications (e.g., narcotics for pain) that could negatively affect cognition. Side effects of such medications include drowsiness and fatigue, among others, which may have negatively affected performance on neuropsychological tests.

It is also important to note that the neuropsychological measures used in the study, are not "pure" measures of functioning in their respective domains. Impairment in a given test may be due to numerous factors outside of the individual having a specific impairment in a particular domain. One such factor is the presence of external time constraints. Performance on the RBANS Line Orientation, for example, may have been impaired due to slowed processing speed rather than to a deficit in visuospatial perception and judgment, as participants only have 20 seconds to provide an answer. Additionally, performance on tests such as verbal fluency may have been affected by numerous repetition or loss of set errors that are not taken into account when determining an individual's score.

Conclusions

The results of the current study reiterate previous findings of the cerebellum's involvement in cognition. The overall cognitive profile found in patients with cerebellar strokes was consistent with that described as part of the cerebellar cognitive affective syndrome, coined by Schmahmann and Sherman (1998). The cerebellum's involvement in higher order cognitive functions has been attributed to its circuitry that consists of feedforward and feedback loops between the cerebellum and the cerebral cortex (Middleton & Strick, 1998), such as the prefrontal cortex. The results of the current study extend the literature by showing similarities in the cognitive profiles of patients with cerebellar and frontal lobe strokes, particularly in the domain of executive functioning.

Examination of the effect of major depressive disorder on cognition was not as expected. Overall, the presence of major depressive disorder did not appear to affect cognitive performance. In some instances, however, the expected pattern was found: patients who were depressed performed worse on certain tasks compared to those who were not depressed only in frontal lobe stroke patients. These findings reiterate the heterogeneity and overall inconsistency in the association between depression and cognitive impairment, but also suggest that further examination of involvement of the vermis in cerebellar strokes may be warranted. Laterality and structural integrity (measured by stroke volume) did not significantly account for performance on neuropsychological measures and, in conjunction with anatomical and physiological evidence, echoes the potential utility of separating groups by the specific topographical regions damaged. The differences between findings from the current study and previous studies of the effects of laterality, stroke volume, and major depression on cognition may suggest that the constellation of deficits seen following cerebellar stroke may be variable and depends primarily on the particular cerebro-cerebellar circuits damaged.

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Table 1. Demographic and clinical characteristics comparing patients with cerebellar and frontal lobe strokes.

Variable	Cerebellar Stroke (*N*=31) 19 Males, 12 Females	Frontal Lobe Stroke (*N*=28) 12 Males, 16 Females
	Mean (Standard Deviation)	Mean (Standard Deviation)
Age (years)	60.8 (15.1)	62.5 (16.2)
Ethnicity *N* (%)		
Caucasian	19 (61%)	14 (50%)
African American	10 (32%)	7 (25%)
Hispanic	2 (6%)	4 (14%)
Asian	0 (0%)	2 (7%)
Other	0 (0%)	1 (4%)
No. Years of Education	14.4 (3.3)	14.4 (3.3)
Interval between stroke and cognitive testing (months)	1.9 (2.0)	1.1 (0.8)
Mini-Mental State Exam (MMSE) *z*-score	-1.09 (1.8)	-2.32 (3.4)
MMSE raw score range	12-30	12-30

Table 2. Demographic and clinical characteristics of a subset of the main sample consisting of cerebellar and frontal lobe stroke patients with stroke volume data.

Variable	Cerebellar Stroke (*N*=12) 6 Males, 6 Females	Frontal Lobe Stroke (*N*=14) 7 Males, 7 Females
	Mean (Standard Deviation)	Mean (Standard Deviation)
Age (years)	56.6 (15.0)	59.7 (17.3)
Ethnicity *N* (%)		
Caucasian	7 (59%)	7 (50%)
African American	4 (33%)	4 (29%)
Hispanic	1 (8%)	1 (7%)
Asian	0 (0%)	1 (7%)
Other	0 (0%)	1 (7%)
No. Years of Education	13.9 (3.3)	13.8 (2.6)
Interval btwn stroke and cognitive testing (months)	2.1 (2.0)	1.3 (1.1)
Mini-Mental State Exam (MMSE) *z*-score	-0.72 (1.3)	-1.9 (3.0)
Stroke Volume (mm^3)	14215.1 (17060.7)	54360.8 (103017)

Table 3. Rates of impairment on neuropsychological measures for patients with cerebellar and frontal lobe strokes. There was no significant difference in proportions of impairment between the two groups for any neuropsychological measure.

	Patient Group[a]		**Statistic[b]**		
Neuropsychological Measure	**Cerebellar**	**Frontal Lobe**	***z***	***p z-test***	***p* Fisher's exact test**
Attention & Working Memory					
RBANS Digit Span	10% (2/20)	20% (4/20)			.661
WAIS-IV Digit Span Fwd	12% (3/26)	24% (4/17)			.407
WAIS-IV Digit Span Backwd	11% (3/27)	24% (4/17)			.402
Visuo-Spatial Perception & Construction					
RBANS Line Orientation	15% (3/20)	43% (9/21)			.085
RBANS Copy	21% (4/19)	32% (6/19)			.714
Language					
RBANS Naming	11% (2/19)	30% (7/23)			.149
Semantic Fluency	43% (12/28)	58% (15/26)	-1.49	.137	
FAS	45% (14/31)	54% (14/26)	-0.66	.512	
Processing Speed					
Trails A	54% (15/28)	67% (10/15)	-0.85	.395	
Verbal Memory					
List Learning	50% (15/30)	60% (15/25)	-0.75	.455	
List Recall	50% (15/30)	48% (12/25)	0.15	.883	
List Recognition	47% (14/30)	44% (11/25)	0.20	.843	
Story Memory	21% (5/24)	40% (10/25)	-1.49	.135	
Story Recall	38% (9/24)	52% (13/25)	-1.03	.302	
Visual Memory					
Figure Recall	10% (2/20)	37% (7/19)			.065
Executive Function					
Trails B	60% (17/28)	54% (7/13)	0.41	.679	
WAIS-IV Similarities	11% (3/28)	11% (2/18)			1.00

[a]Percentage indicates percent classified as impaired, based on fraction in parentheses

[b]Fisher's exact test used to assess statistical significance (alpha = .01)

Table 4. Rates of impairment on neuropsychological measures for patients with left cerebellar and right frontal lobe strokes. There was no significant difference in ratios/proportions of impairment between the two groups for any neuropsychological measure.

	Patient Group[a]		Statistic[b]
Neuropsychological Measure	**Left Cerebellar**	**Right Frontal Lobe**	***p* Fisher's exact test**
Attention & Working Memory			
RBANS Digit Span	20% (1/5)	11% (1/9)	1.00
WAIS-IV Digit Span Fwd	29% (2/7)	13% (1/8)	.569
WAIS-IV Digit Span Backwd	13% (1/8)	38% (3/8)	.569
Visuo-Spatial Perception & Construction			
RBANS Line Orientation	50% (2/4)	50% (5/10)	1.00
RBANS Copy	0% (0/4)	30% (3/10)	.505
Language			
RBANS Naming	0% (0/4)	17% (2/12)	1.00
Semantic Fluency	43% (3/7)	50% (6/12)	1.00
FAS	33% (3/9)	67% (8/12)	.198
Processing Speed			
Trails A	50% (4/8)	78% (7/9)	.335
Verbal Memory			
List Learning	44% (4/9)	45% (5/11)	1.00
List Recall	56% (5/9)	36% (4/11)	.653
List Recognition	56% (5/9)	55% (6/11)	1.00
Story Memory	20% (1/5)	33% (4/12)	1.00
Story Recall	40% (2/5)	42% (5/12)	1.00
Visual Memory			
Figure Recall	0% (0/4)	30% (3/10)	.505
Executive Function			
Trails B	63% (5/8)	57% (4/7)	1.00
WAIS-IV Similarities	11% (1/9)	0% (0/10)	.474

[a]Percentage indicates percent classified as impaired, based on fraction in parentheses
[b]Fisher's exact test used to assess statistical significance (alpha = .01)

Table 5. Rates of impairment on neuropsychological measures for patients with right cerebellar and left frontal lobe strokes.

	Patient Group[a]		Statistic[b]
Neuropsychological Measure	**Right Cerebellar**	**Left Frontal Lobe**	***p* Fisher's exact test**
Attention & Working Memory			
*RBANS Digit Span	13% (2/15)	57% (4/7)	.054
WAIS-IV Digit Span Fwd	0% (0/14)	50% (3/6)	.018
WAIS-IV Digit Span Backwd	14% (2/14)	33% (2/6)	.549
Visuo-Spatial Perception & Construction			
**RBANS Line Orientation	0% (0/15)	57% (4/7)	.005
RBANS Copy	29% (4/14)	67% (4/6)	.161
Language			
RBANS Naming	14% (2/14)	57% (4/7)	.120
Semantic Fluency	47% (8/17)	78% (7/9)	.217
FAS	35% (6/17)	44% (4/9)	.692
Processing Speed			
Trails A	53% (8/15)	60% (3/5)	1.00
Verbal Memory			
List Learning	44% (7/16)	70% (7/10)	.248
List Recall	38% (6/16)	60% (6/10)	.422
List Recognition	31% (5/16)	30%(3/10)	1.00
Story Memory	19% (3/16)	56% (5/9)	.087
Story Recall	31% (5/16)	67% (6/9)	.115
Visual Memory			
Figure Recall	20% (3/15)	67% (4/6)	.120
Executive Function			
Trails B	47% (7/15)	60% (3/5)	1.00
WAIS-IV Similarities	13% (2/15)	20% (1/5)	1.00

[a]Percentage indicates percent classified as impaired, based on fraction in parentheses

[b]Fisher's exact test used to assess statistical significance (alpha = .01)

*Trended toward significance, $p < .05$

** Statistically significant, $p < .01$

Table 6. Rates of impairment on neuropsychological measures for patients with left cerebellar and right frontal lobe strokes. There was no significant difference in ratios/proportions of impairment between the two groups for any neuropsychological measure.

	Patient Group[a]		**Statistic[b]**
Neuropsychological Measure	**Bilateral Cerebellar**	**Bilateral Frontal Lobe**	***p* Fisher's exact test**
Attention & Working Memory			
RBANS Digit Span	N/A (N = 0)	25% (1/4)	N/A
WAIS-IV Digit Span Fwd	20% (1/5)	33% (1/3)	1.00
WAIS-IV Digit Span Backwd	20% (1/5)	33% (1/3)	1.00
Visuo-Spatial Perception & Construction			
RBANS Line Orientation	100% (1/1)	25% (1/4)	.400
RBANS Copy	100% (1/1)	33% (1/3)	1.00
Language			
RBANS Naming	0% (0/1)	20% (1/4)	1.00
Semantic Fluency	50% (2/4)	60% (3/5)	1.00
FAS	100% (5/5)	60% (3/5)	.444
Processing Speed			
Trails A	60% (3/5)	0% (0/1)	1.00
Verbal Memory			
List Learning	100% (5/5)	75% (3/4)	.444
List Recall	80% (4/5)	50% (2/4)	.524
List Recognition	80% (4/5)	50% (2/4)	.524
Story Memory	33% (1/3)	25% (1/4)	1.00
Story Recall	67% (2/3)	50% (2/4)	1.00
Visual Memory			
Figure Recall	100% (1/1)	33% (1/3)	1.00
Executive Function			
Trails B	80% (4/5)	0% (0/1)	.333
WAIS-IV Similarities	0% (0/4)	33% (1/3)	.429

[a]Percentage indicates percent classified as impaired, based on fraction in parentheses

[b]Fisher's exact test used to assess statistical significance (alpha = .01)

Table 7. Results of two-way between subjects ANOVA (Type of Stroke x Depression) for domains of attention & working memory, visuo-spatial perception & construction, language, and processing speed.

DEPENDENT VARIABLE	SOURCE OF VARIATION	DF	MS	F	*p*
Attention & Working Memory					
RBANS Digit Span	Type of Stroke	1,36	8.60	6.14	*0.02
	Depression	1,36	0.03	0.02	0.88
	Type of Stroke x Depression	1,36	1.75	1.25	0.27
WAIS-IV Digit Span Forward	Type of Stroke	1,39	2.57	3.22	0.08
	Depression	1,39	0.74	0.93	0.34
	Type of Stroke x Depression	1,39	0.56	0.70	0.40
WAIS-IV Digit Span Backward	Type of Stroke	1,40	1.65	1.61	0.21
	Depression	1,40	1.31	1.28	0.27
	Type of Stroke x Depression	1,40	0.19	0.19	0.67
Visuo-Spatial Perception & Construction					
RBANS Line Orientation	Type of Stroke	1,37	18.93	6.52	*0.02
	Depression	1,37	0.29	0.10	0.76
	Type of Stroke x Depression	1,37	2.19	0.75	0.39
RBANS Copy	Type of Stroke	1,34	22.25	4.25	*0.047
	Depression	1,34	2.79	0.53	0.47
	Type of Stroke x Depression	1,34	6.60	1.26	0.26
Language					
RBANS Naming	Type of Stroke	1,38	10.12	4.95	*0.03
	Depression	1,38	0.16	0.08	0.78
	Type of Stroke x Depression	1,38	5.44	2.66	0.11
Semantic Fluency	Type of Stroke	1,50	16.05	12.49	**0.00
	Depression	1,50	3.52	2.74	0.10
	Type of Stroke x Depression	1,50	5.28	4.11	*0.047
FAS	Type of Stroke	1,53	4.79	3.68	0.06
	Depression	1,53	1.06	0.82	0.37
	Type of Stroke x Depression	1,53	0.68	0.52	0.47
Processing Speed					
Trails A	Type of Stroke	1,39	8.79	0.58	0.45
	Depression	1,39	0.15	0.01	0.92
	Type of Stroke x Depression	1,39	1.69	0.11	0.74

* Trended towards significance, $p < .05$

** $p < .01$

Table 8. Results of two-way between subjects ANOVA (Type of Stroke x Depression) for tests of memory and executive function.

DEPENDENT VARIABLE	SOURCE OF VARIATION	DF	MS	F	*p*
Verbal Memory					
List Learning					
	Type of Stroke	1,51	10.62	5.48	*0.02
	Depression	1,51	1.27	.070	0.37
	Type of Stroke x Depression	1,51	7.79	4.27	*0.04
List Recall					
	Type of Stroke	1,51	1.59	1.07	0.31
	Depression	1,51	0.39	0.26	0.61
	Type of Stroke x Depression	1,51	4.23	2.85	0.09
List Recognition					
	Type of Stroke	1,51	0.07	0.01	0.93
	Depression	1,51	9.18	1.28	0.26
	Type of Stroke x Depression	1,51	4.99	0.70	0.41
Story Memory					
	Type of Stroke	1,45	5.39	2.80	0.10
	Depression	1,45	3.49	1.81	0.19
	Type of Stroke x Depression	1,45	9.15	4.75	*0.03
Story Recall					
	Type of Stroke	1,45	8.84	4.20	*.046
	Depression	1,45	2.38	1.13	0.29
	Type of Stroke x Depression	1,45	3.89	1.84	0.18
Visual Memory					
Figure Recall					
	Type of Stroke	1,35	5.64	4.03	0.05
	Depression	1,35	0.32	0.23	0.64
	Type of Stroke x Depression	1,35	2.17	1.56	0.22
Executive Function					
Trails B					
	Type of Stroke	1,37	6.93	0.20	0.65
	Depression	1,37	15.03	0.43	0.52
	Type of Stroke x Depression	1,37	17.25	0.49	0.49
WAIS-IV Similarities					
	Type of Stroke	1,42	0.38	0.28	0.60
	Depression	1,42	0.09	0.07	0.80
	Type of Stroke x Depression	1,42	2.08	1.53	0.22

* Trended towards significance, $p < .05$

Table 9. Demographic and clinical characteristics comparing patients with left and right cerebellar strokes.

Variable	Left Cerebellar Stroke (*N*=9) 4 Males, 5 Females	Right Cerebellar Stroke (*N*=17) 12 Males, 5 Females
	Mean (Standard Deviation)	Mean (Standard Deviation)
Age (years)	55.7 (14.8)	60.3 (15.7)
Ethnicity *N* (%)		
Caucasian	7 (78%)	9 (53%)
African American	2 (22%)	6 (35%)
Hispanic	0 (0%)	2 (12%)
Asian	0 (0%)	0 (0%)
Other	0 (0%)	0 (0%)
No. Years of Education	14.1 (3.7)	14.4 (3.6)
Interval between stroke and cognitive testing (months)	1.1 (0.6)	2.3 (2.5)
Mini-Mental State Exam (MMSE) *z*-score	-1.00 (1.3)	-0.79 (1.9)

Table 10. Demographic and clinical characteristics comparing patients with left and right frontal lobe strokes.

Variable	Left Frontal Lobe Stroke (*N*=11) 5 Males, 6 Females	Right Frontal Lobe Stroke (*N*=12) 4 Males, 8 Females
	Mean (Standard Deviation)	Mean (Standard Deviation)
Age (years)	61.8 (15.4)	62.9 (17.9)
Ethnicity *N* (%)		
Caucasian	6 (55%)	6 (50%)
African American	2 (18%)	4 (33%)
Hispanic	2 (18%)	1 (8.5%)
Asian	0 (0%)	1 (8.5%)
Other	1 (9%)	0 (0%)
No. Years of Education	13.5 (2.0)	14.7 (3.0)
Interval between stroke and cognitive testing (months)	1.4 (1.2)	0.3 (0.5)
*Mini-Mental State Exam (MMSE) *z*-score	-4.29 (4.2)	-1.06 (2.4)

*Approached statistical significance, $p < .05$

Table 11. Hierarchical regression analysis assessing the relationship between performance on neuropsychological measures, by domain, and performance on the Mini-Mental State Examination (MMSE) and laterality of the stroke (left or right) for cerebellar stroke patients.

Neuropsychological Measure	**Model**	***Beta***	***t***	***F***	R^2	ΔR^2	ΔF	$p, \Delta p$
Attention & Working Memory								
RBANS Digit Span	1			.231	.013			.637
	MMSE	.116	.481					.637
	2			.138	.017	.004	.058	.872, .812
	MMSE	.108	.433					.671
	Laterality	-.060	-.242					.812
WAIS-IV Digit Span Fwd	1			.372	.016			.548
	MMSE	.126	.610					.548
	2			.377	.033	.017	.392	.690, .538
	MMSE	.099	.464					.647
	Laterality	-.134	-.626					.538
WAIS-IV Digit Span Backwd	1			7.43	.236			*.012
	MMSE	.486	2.73					*.012
	2			3.56	.237	.000	.004	*.045, .952
	MMSE	.484	2.61					*.016
	Laterality	-.011	-.060					.952
Visuo-Spatial Perception & Construction								
RBANS Line Orientation	1			.000	.000			.987
	MMSE	.004	.016					.987
	2			.194	.022	.022	.387	.826, .542
	MMSE	.046	.183					.857
	Laterality	.155	.622					.542
RBANS Copy	1			1.39	.076			.254
	MMSE	.275	1.18					.254
	2			2.07	.206	.130	2.62	.159, .125
	MMSE	.173	.745					.467
	Laterality	-.375	-1.68					.125

Table 12. Hierarchical regression analysis assessing the relationship between performance on neuropsychological measures of language and processing speed and performance on the Mini-Mental State Examination (MMSE) and laterality of the stroke (left or right) for cerebellar stroke patients.

Neuropsychological Measure	**Model**	***Beta***	***t***	***F***	R^2	ΔR^2	ΔF	***p*, Δ *p***
Language								
RBANS Naming	1			6.81	.299			*.019
	MMSE	.546	2.61					*.019
	2			3.51	.319	.020	.449	.056, .513
	MMSE	.587	2.65					*.018
	Laterality	.148	.670					.513
Semantic Fluency	1			3.96	.142			.058
	MMSE	.376	1.99					.058
	2			2.05	.152	.010	.279	.150, .603
	MMSE	.421	2.01					.057
	Laterality	.111	.528					.603
FAS	1			6.85	.202			*.014
	MMSE	.450	2.62					*.014
	2			3.55	.214	.012	.399	*.043, .533
	MMSE	.430	2.44					*.022
	Laterality	-.111	-.631					.533
Processing Speed								
Trails A	1			3.93	.131			.058
	MMSE	.362	1.98					.058
	2			1.91	.133	.002	.044	.168, .835
	MMSE	.370	1.95					.062
	Laterality	.040	.210					.835

* trended towards significance, $p < .05$

Table 13. Hierarchical regression analysis assessing the relationship between performance on neuropsychological measures of memory and performance on the Mini-Mental State Examination (MMSE), laterality of the stroke (left or right), and stroke volume for cerebellar stroke patients.

Neuropsychological Measure	**Model**	***Beta***	***t***	***F***	R^2	ΔR^2	ΔF	***p, Δ p***
Verbal Memory								
List Learning	1			8.75	.252			**.007
	MMSE	.502	2.96					**.007
	2			4.22	.252	.000	.014	*.026, .907
	MMSE	.506	2.87					**.008
	Laterality	.021	.118					.907
List Recall	1			3.32	.113			.080
	MMSE	.336	1.82					.080
	2			1.59	.113	.000	.000	.223, .988
	MMSE	.337	1.76					.091
	Laterality	.003	.016					.988
List Recognition	1			7.33	.220			*.012
	MMSE	.469	2.71					*.012
	2			3.57	.222	.002	.073	*.043, .790
	MMSE	.460	2.56					*.017
	Laterality	-.048	-.269					.790
Story Memory	1			15.19	.432			**.001
	MMSE	.657	3.90					**.001
	2			8.06	.459	.027	.959	**.003, .340
	MMSE	.731	3.95					**.001
	Laterality	.181	.979					.340
Story Recall	1			4.58	.186			*.045
	MMSE	.431	2.14					*.045
	2			2.49	.208	.021	.515	.110, .482
	MMSE	.497	2.22					*.039
	Laterality	.161	.718					.482
Nonverbal Memory								
Figure Recall	1			5.32	.228			*.033
	MMSE	.478	2.31					*.033
	2			2.66	.238	.010	.227	.099, .640
	MMSE	.449	2.05					.057
	Laterality	-.105	-.476					.640

* trended towards significance, $p < .05$

** statistically significant, $p < .01$

Table 14. Hierarchical regression analysis assessing the relationship between performance on neuropsychological measures of executive functioning and performance on the Mini-Mental State Examination (MMSE), laterality of the stroke (left or right), and stroke volume for cerebellar stroke patients.

Neuropsychological Measure	**Model**	***Beta***	***t***	***F***	R^2	ΔR^2	ΔF	p, Δp
Executive Functioning								
Trails B	1			8.35	.243			**.008
	MMSE	.493	2.89					**.008
	2			4.71	.274	.030	1.05	*.018, .316
	MMSE	.528	3.04					**.006
	Laterality	.178	1.02					.316
WAIS-IV Similarities	1			4.89	.169			*.037
	MMSE	.411	2.21					*.037
	2			2.47	.177	.007	.209	.107, .652
	MMSE	.428	2.22					*.036
	Laterality	.088	.457					.652

* trended towards significance, $p < .05$

**statistically significant, $p < .01$

Table 15. Hierarchical regression analysis assessing the relationship between performance on neuropsychological measures of attention & working memory and visuo-spatial perception & construction, and performance on the Mini-Mental State Examination (MMSE), laterality of the stroke (left or right), and stroke volume for cerebellar stroke patients.

Neuropsychological Measure	**Model**	***Beta***	***t***	R^2	***F***	ΔR^2	ΔF	***p, Δp***
Attention & Working Memory								
RBANS Digit Span	1			.008	.073			.793
	MMSE	.090	.270					.793
	2			.616	3.74	.608	5.54	.068,*.036
	MMSE	.264	1.08					.315
	Laterality	-.539	-2.18					.066
	Volume	-.787	-3.07					*.018
WAIS-IV Digit Span Fwd	1			.114	1.55			.237
	MMSE	.338	1.24					.237
	2			.143	.558	.029	.170	.654, .846
	MMSE	.346	.918					.380
	Laterality	-.157	-.485					.638
	Volume	-.040	-.105					.919
WAIS-IV Digit Span Backwd	1			.228	3.54			.084
	MMSE	.477	1.88					.084
	2			.303	1.47	.075	.537	.287, .601
	MMSE	.633	1.86					.092
	Laterality	-.301	-1.03					.328
	Volume	-.182	-.531					.607
Visuo-Spatial Perception & Construction								
RBANS Line Orientation	1			.042	.399			.543
	MMSE	-.206	-.632					.543
	2			.332	1.16	.289	1.52	.391, .284
	MMSE	-.184	-.572					.585
	Laterality	.562	1.72					.129
	Volume	-.097	-.286					.783
RBANS Copy	1			.094	.930			.360
	MMSE	.306	.964					.360
	2			.332	1.16	.238	1.25	.390, .344
	MMSE	.163	.507					.628
	Laterality	-.012	-.036					.973
	Volume	-.505	-1.49					.179

* trended towards significance, $p < .05$

Table 16. Hierarchical regression analysis assessing the relationship between performance on neuropsychological measures of language and processing speed, and performance on the Mini-Mental State Examination (MMSE), laterality of the stroke (left or right), and stroke volume for cerebellar stroke patients.

Neuropsychological Measure	**Model**	***Beta***	***t***	R^2	***F***	ΔR^2	ΔF	p, Δp
Language								
RBANS Naming	1			.189	1.63			.243
	MMSE	.434	1.13					.243
	2			.359	.933	.170	.665	.490, .555
	MMSE	.338	.910					.405
	Laterality	-.178	-.478					.653
	Volume	-.338	-.874					.422
Semantic Fluency	1			.016	.162			.696
	MMSE	.126	.403					.696
	2			.301	1.15	.285	1.63	.386, .254
	MMSE	.184	.564					.588
	Laterality	-.675	-1.75					.119
	Volume	.587	1.43					.190
FAS	1			.141	1.96			.186
	MMSE	.375	1.40					.186
	2			.244	1.08	.103	.684	.403, .527
	MMSE	.607	1.71					.117
	Laterality	-.322	-1.06					.316
	Volume	.315	.883					.398
Processing Speed								
Trails A	1			.274	4.52			.055
	MMSE	.523	2.13					.055
	2			.300	1.43	.027	.191	.291, .829
	MMSE	.518	1.52					.159
	Laterality	.149	.507					.623
	Volume	.043	.124					.904

Table 17. Hierarchical regression analysis assessing the relationship between performance on neuropsychological measures of memory and performance on the Mini-Mental State Examination (MMSE), laterality of the stroke (left or right), and stroke volume for cerebellar stroke patients.

Neuropsychological Measure	**Model**	***Beta***	***t***	R^2	***F***	ΔR^2	ΔF	***p, Δ p***
Verbal Memory								
List Learning	1			.217	3.05			.109
	MMSE	.466	1.75					.109
	2			.367	1.74	.150	1.07	.228, .383
	MMSE	.385	1.14					.285
	Laterality	-.252	-.851					.417
	Volume	-.251	-.737					.480
List Recall	1			.230	3.30			.097
	MMSE	.480	1.82					.097
	2			.454	2.49	.223	1.84	.126, .214
	MMSE	.455	1.44					.182
	Laterality	-.387	-1.41					.194
	Volume	-.196	-.618					.552
List Recognition	1			.021	.230			.641
	MMSE	.143	.480					.641
	2			.361	1.70	.341	2.40	.237, .146
	MMSE	-.157	-.461					.656
	Laterality	-.119	-.398					.700
	Volume	-.618	-1.80					.105
Story Memory	1			.602	13.60			**.005
	MMSE	.776	3.69					**.005
	2			.602	3.53	.000	.001	.077, .999
	MMSE	.776	3.12					*.017
	Laterality	-.012	-.048					.963
	Volume	.005	.019					.986
Story Recall	1			.324	4.31			.068
	MMSE	.569	2.08					.068
	2			.429	1.76	.015	.647	.243, .552
	MMSE	.636	2.14					.070
	Laterality	-.246	-.818					.441
	Volume	.314	1.06					.348
Nonverbal Memory								
Figure Recall	1			.142	1.48			.254
	MMSE	.376	1.22					.254
	2			.152	.420	.011	.045	.745, .956
	MMSE	.351	.967					.366
	Laterality	-.059	-.161					.877
	Volume	-.073	-.874					.854

* trended towards significance, $p < .05$; **statistically significant, $p < .01$

Table 18. Hierarchical regression analysis assessing the relationship between performance on neuropsychological measures of executive functioning and performance on the Mini-Mental State Examination (MMSE), laterality of the stroke (left or right), and stroke volume for cerebellar stroke patients.

Neuropsychological Measure	**Model**	***Beta***	***t***	R^2	***F***	ΔR^2	ΔF	***p, Δp***
Executive Functioning								
Trails B	1			.371	7.08			*.021
	MMSE	.609	2.66					*.021
	2			.476	3.02	.105	.997	.080, .403
	MMSE	.838	2.84					*.018
	Laterality	-.047	-.186					.856
	Volume	-.404	1.36					.204
WAIS-IV Similarities	1			.042	.478			.504
	MMSE	.204	.691					.504
	2			.153	.543	.112	.594	.665, .572
	MMSE	.416	1.06					.315
	Laterality	-.363	-1.06					.318
	Volume	.266	.675					.517

* trended towards significance, $p < .05$

Table 19. Hierarchical regression analysis assessing the relationship between performance on neuropsychological measures of attention & working memory and visuo-spatial perception & construction and performance on the Mini-Mental State Examination (MMSE) and laterality of the stroke (left or right) for frontal lobe stroke patients.

Neuropsychological Measure	**Model**	***Beta***	***t***	R^2	***F***	ΔR^2	ΔF	***p*, Δ *p***
Attention & Working Memory								
RBANS Digit Span	1			.175	3.60			.075
	MMSE	.415	1.90					.075
	2			.261	2.83	.087	1.88	.089, .189
	MMSE	.239	.951					.356
	Laterality	.344	1.37					.189
WAIS-IV Digit Span Fwd	1			.183	.3.36			.087
	MMSE	.428	1.83					.087
	2			.186	1.60	.003	.055	.237, .819
	MMSE	.443	1.77					.098
	Laterality	-.058	-.233					.819
WAIS-IV Digit Span Backwd	1			.430	11.32			**.004
	MMSE	.656	3.37					**.004
	2			.434	5.37	.004	.096	*.019, .762
	MMSE	.639	3.07					**.008
	Laterality	.064	.309					.762
Visuo-Spatial Perception & Construction								
RBANS Line Orientation	1			.549	21.88			**.000
	MMSE	.741	4.68					**.000
	2			.561	10.86	.012	.474	**.001, .500
	MMSE	.679	3.69					**.002
	Laterality	.127	.689					.542, .500
RBANS Copy	1			.616	25.71			**.000
	MMSE	.785	5.07					**.000
	2			.637	13.19	.021	.872	**.000, .365
	MMSE	.871	4.83					**.000
	Laterality	-.168	-.934					.365

* trended towards significance, $p < .05$

**statistically significant, $p < .01$

Table 20. Hierarchical regression analysis assessing the relationship between performance on neuropsychological measures of language and processing speed and performance on the Mini-Mental State Examination (MMSE) and laterality of the stroke (left or right) for frontal lobe stroke patients.

Neuropsychological Measure	**Model**	***Beta***	***t***	R^2	***F***	ΔR^2	ΔF	***p*, Δ*p***
Language								
RBANS Naming	1			.454	16.64			**.001
	MMSE	.674	4.08					**.001
	2			.460	8.10	.006	.213	**.003, .649
	MMSE	.627	3.19					**.005
	Laterality	.091	.462					.649
Semantic Fluency	1			.373	13.67			**.001
	MMSE	.611	3.70					**.001
	2			.398	7.26	.025	.907	**.004, .351
	MMSE	.685	3.74					**.001
	Laterality	-.174	-.952					.351
FAS	1			.102	2.61			.120
	MMSE	.319	1.62					.120
	2			.106	1.30	.004	.086	.293, .772
	MMSE	.337	1.60					.123
	Laterality	-.062	-.293					.772
Processing Speed								
Trails A	1			.793	49.77			**.000
	MMSE	.890	7.06					**.000
	2			.793	23.05	.001	.032	**.000, .861
	MMSE	.896	6.65					**.000
	Laterality	-.024	-.179					.861

* trended towards significance, $p < .05$
**statistically significant, $p < .01$

Table 21. Hierarchical regression analysis assessing the relationship between performance on neuropsychological measures of memory and performance on the Mini-Mental State Examination (MMSE), laterality of the stroke (left or right), and stroke volume for frontal lobe stroke patients.

Neuropsychological Measure	**Model**	***Beta***	***t***	R^2	***F***	ΔR^2	ΔF	***p, Δ p***
Verbal Memory								
List Learning	1			.428	16.44			**.001
	MMSE	.654	.654					**.001
	2			.444	8.38	.016	.611	**.002, .443
	MMSE	.710	.710					**.001
	Laterality	-.139	-.781					.443
List Recall	1			.098	2.39			.136
	MMSE	.313	1.55					.136
	2			.098	1.14	.000	.002	.338, .967
	MMSE	.317	1.40					.177
	Laterality	-.009	-.042					.967
List Recognition	1			.204	5.64			*.027
	MMSE	.452	2.38					*.027
	2			.258	3.65	.054	1.53	*.044, .230
	MMSE	.555	2.70					*.013
	Laterality	-.254	-1.24					.230
Story Memory	1			.350	11.87			**.002
	MMSE	.592	3.45					**.002
	2			.366	6.05	.015	.498	**.008, .488
	MMSE	.658	3.34					**.003
	Laterality	-.139	-.706					.488
Story Recall	1			.363	12.51			**.002
	MMSE	.602	3.54					**.002
	2			.423	7.70	.061	2.21	**.003, .152
	MMSE	.734	3.90					**.001
	Laterality	-.279	-1.49					.152
Nonverbal Memory								
Figure Recall	1			.465	13.93			**.002
	MMSE	.682	3.73					**.002
	2			.469	6.62	.004	.100	**.009, .757
	MMSE	.717	3.29					**.005
	Laterality	-.069	-.316					.757

* trended towards significance, $p < .05$; **statistically significant, $p < .01$

Table 22. Hierarchical regression analysis assessing the relationship between performance on neuropsychological measures of executive functioning and performance on the Mini-Mental State Examination (MMSE), laterality of the stroke (left or right), and stroke volume for frontal lobe stroke patients.

Neuropsychological Measure	**Model**	***Beta***	***t***	R^2	***F***	ΔR^2	ΔF	p, Δp
Executive Functioning								
Trails B	1			.268	4.02			.070
	MMSE	.517	2.01					.070
	2			.337	2.54	.069	1.04	.128, .331
	MMSE	.642	2.25					*.048
	Laterality	-.291	-1.02					.331
WAIS-IV Similarities	1			.322	7.13			*.018
	MMSE	.567	2.67					*.018
	2			.365	4.02	.043	.946	*.042, .347
	MMSE	.589	2.75					*.016
	Laterality	-.208	-.973					.347

* trended towards significance, $p < .05$

Table 23. Hierarchical regression analysis assessing the relationship between performance on neuropsychological measures of attention & working memory and visuo-spatial perception & construction, and performance on the Mini-Mental State Examination (MMSE), laterality of the stroke (left or right), and stroke volume for frontal lobe stroke patients.

Neuropsychological Measure	**Model**	***Beta***	***t***	R^2	***F***	ΔR^2	ΔF	***p*, Δ *p***
Attention & Working Memory								
RBANS Digit Span	1			.034	.315			.588
	MMSE	.184	.561					.588
	2			.230	.699	.197	.894	.582, .451
	MMSE	-.101	-.256					.805
	Laterality	.304	.867					.415
	Volume	.422	1.12					.300
WAIS-IV Digit Span Fwd	1			.078	.766			.404
	MMSE	.280	.875					.404
	2			.092	.237	.014	.053	.868, .949
	MMSE	.273	.753					.476
	Laterality	-.079	-.213					.837
	Volume	.105	.285					.784
WAIS-IV Digit Span Backwd	1			.400	5.99			*.037
	MMSE	.632	2.45					*.037
	2			.458	1.97	.058	.376	.207, .700
	MMSE	.632	2.26					.058
	Laterality	.004	.013					.990
	Volume	-.242	-.851					.423
Visuo-Spatial Perception & Construction								
RBANS Line Orientation	1			.677	16.73			**.003
	MMSE	.823	4.09					**.003
	2			.695	4.55	.018	.177	.055, .842
	MMSE	.835	3.69					*.010
	Laterality	-.108	-.474					.652
	Volume	-.070	-.310					.767
RBANS Copy	1			.489	8.62			*.017
	MMSE	.699	2.94					*.017
	2			.579	3.21	.090	.748	.092, .508
	MMSE	.720	2.47					*.043
	Laterality	-.274	-1.06					.326
	Volume	.133	.478					.648

* trended towards significance, $p < .05$

**statistically significant, $p < .01$

Table 24. Hierarchical regression analysis assessing the relationship between performance on neuropsychological measures of language and processing speed, and performance on the Mini-Mental State Examination (MMSE), laterality of the stroke (left or right), and stroke volume for frontal lobe stroke patients.

Neuropsychological Measure	**Model**	***Beta***	***t***	R^2	***F***	ΔR^2	ΔF	***p*, Δ*p***
Language								
RBANS Naming	1			.335	5.03			*.049
	MMSE	.578	2.24					*.049
	2			.358	1.49	.023	.144	.290, .868
	MMSE	.546	1.84					.103
	Laterality	.069	.233					.822
	Volume	.130	.456					.661
Semantic Fluency	1			.667	26.05			**.000
	MMSE	.817	5.10					**.000
	2			.730	9.93	.063	1.29	**.002, .314
	MMSE	.832	5.23					**.000
	Laterality	-.175	-1.10					.296
	Volume	.196	1.25					.238
FAS	1			.110	1.73			.209
	MMSE	.332						.209
	2			.135	.625	.025	.173	.613, .843
	MMSE	.343	1.27					.228
	Laterality	-.074	-.274					.789
	Volume	-.132	-.488					.635
Processing Speed								
Trails A	1			.862	50.15			**.000
	MMSE	.929	7.08					**.000
	2			.900	18.01	.038	1.13	**.002, .384
	MMSE	.922	7.13					**.000
	Laterality	.043	.305					.770
	Volume	-.208	-1.47					.193

* trended towards significance, $p < .05$

**statistically significant, $p < .01$

Table 25. Hierarchical regression analysis assessing the relationship between performance on neuropsychological measures of memory and performance on the Mini-Mental State Examination (MMSE), laterality of the stroke (left or right), and stroke volume for frontal lobe stroke patients.

Neuropsychological Measure	**Model**	***Beta***	***t***	R^2	***F***	ΔR^2	ΔF	***p, Δ p***
Verbal Memory								
List Learning	1			.410	8.34			*.014
	MMSE	.640	2.89					*.014
	2			.608	5.18	.198	2.53	*.020, .129
	MMSE	.677	3.40					**.007
	Laterality	-.394	-1.94					.081
	Volume	.304	1.51					.163
List Recall	1			.012	.142			.713
	MMSE	.108	.377					.713
	2			.018	.062	.007	.033	.979, .967
	MMSE	.114	.363					.724
	Laterality	-.050	-.155					.880
	Volume	-.055	-.171					.868
List Recognition	1			.177	2.60			.134
	MMSE	.421	1.61					.134
	2			.564	4.32	.387	4.44	*.034, *.042
	MMSE	.480	2.29					*.045
	Laterality	-.503	-2.34					*.041
	Volume	-.284	-1.33					.212
Story Memory	1			.223	3.44			.088
	MMSE	.472	1.86					.088
	2			.361	1.88	.138	1.08	.197, .376
	MMSE	.564	2.15					.057
	Laterality	-.382	-1.44					.181
	Volume	.132	.515					.618
Story Recall	1			.311	5.41			*.038
	MMSE	.557	2.33					*.038
	2			.478	3.05	.167	1.60	.079, .250
	MMSE	.660	2.79					*.019
	Laterality	-.423	-1.76					.108
	Volume	.132	.569					.582
Nonverbal Memory								
Figure Recall	1			.218	2.52			.147
	MMSE	.467	1.59					.147
	2			.418	1.67	.199	1.20	.259, .357
	MMSE	.659	1.92					.096
	Laterality	-.469	-1.54					.167
	Volume	-.112	-.341					.743

* trended towards significance, $p < .05$; **statistically significant, $p < .01$

Table 26. Hierarchical regression analysis assessing the relationship between performance on neuropsychological measures of executive functioning and performance on the Mini-Mental State Examination (MMSE), laterality of the stroke (left or right), and stroke volume for frontal lobe stroke patients.

Neuropsychological Measure	**Model**	***Beta***	***t***	R^2	***F***	ΔR^2	ΔF	***p*, Δ*p***
Executive Functioning								
Trails B	1			.605	9.18			*.023
	MMSE	.778	3.03					*.023
	2			.663	2.62	.058	.343	.188, .729
	MMSE	.594	1.61					.183
	Laterality	.378	.818					.459
	Volume	-.204	-.491					.649
WAIS-IV Similarities	1			.252	2.69			.139
	MMSE	.502	1.64					.139
	2			.377	1.21	.125	.601	.384, .578
	MMSE	.343	.967					.371
	Laterality	-.390	-1.09					.316
	Volume	.017	.053					.960

* trended towards significance, $p < .05$

Figure 1. Cerebrocerebellar circuitry.

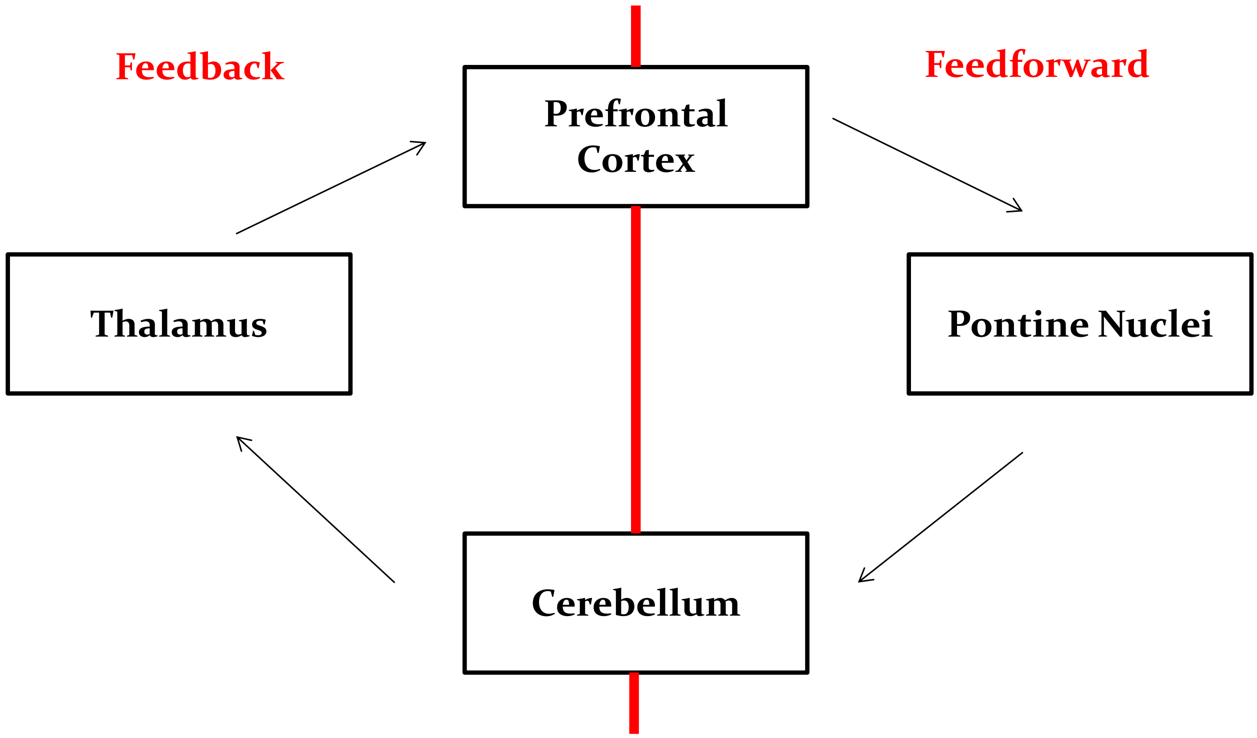


Figure 2. Effects of the presence of major depressive disorder (MDD) and type of stroke (frontal lobe versus cerebellar) on performance on List Learning.

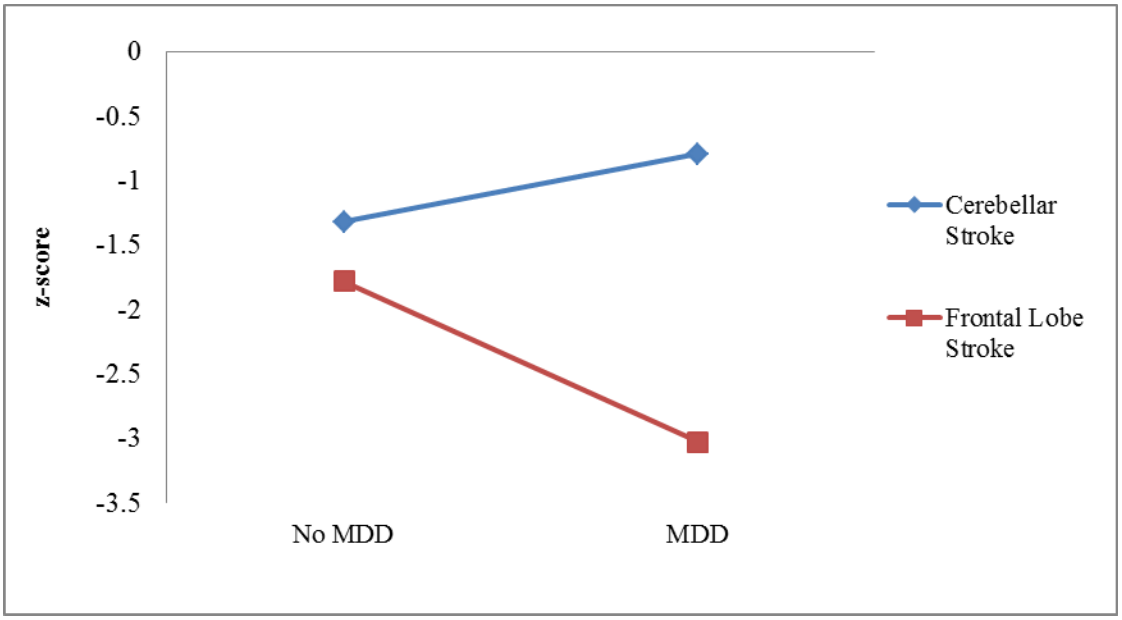


Figure 3. Effects of the presence of major depressive disorder (MDD) and type of stroke (frontal lobe versus cerebellar) on performance on Story Memory (immediate recall).

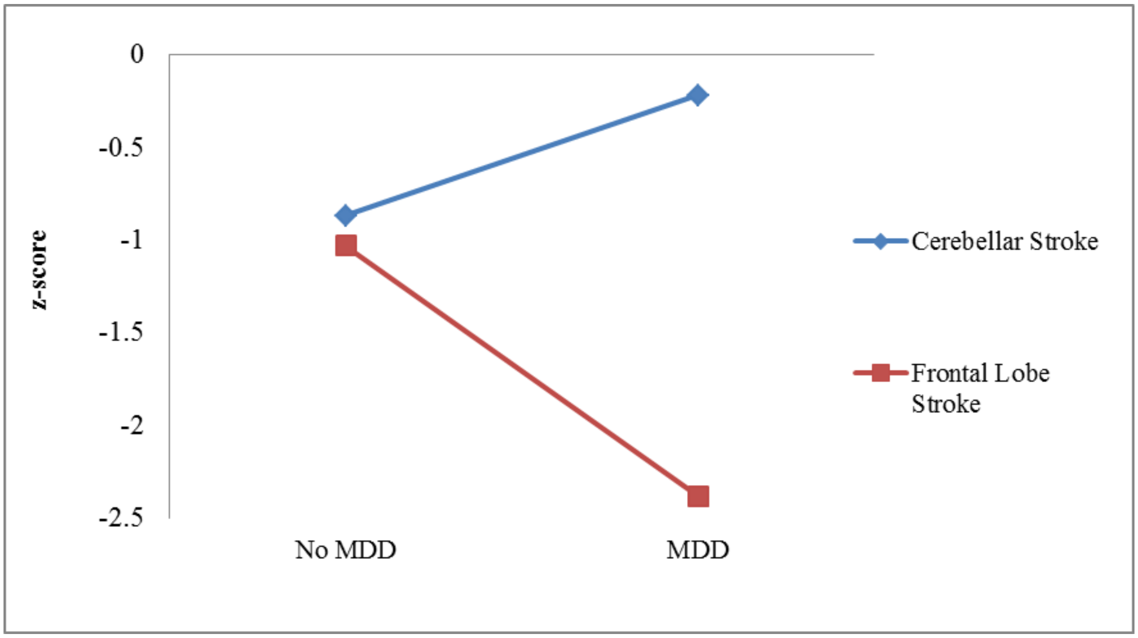


Figure 4. Effects of the presence of major depressive disorder (MDD) and type of stroke (frontal lobe versus cerebellar) on performance on Semantic Fluency.

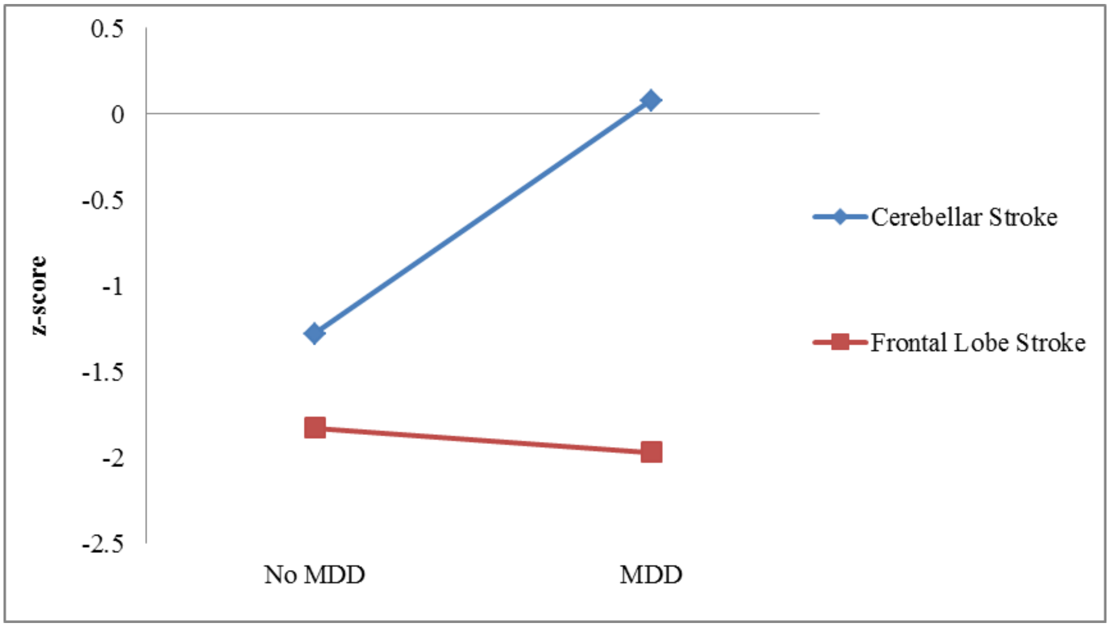
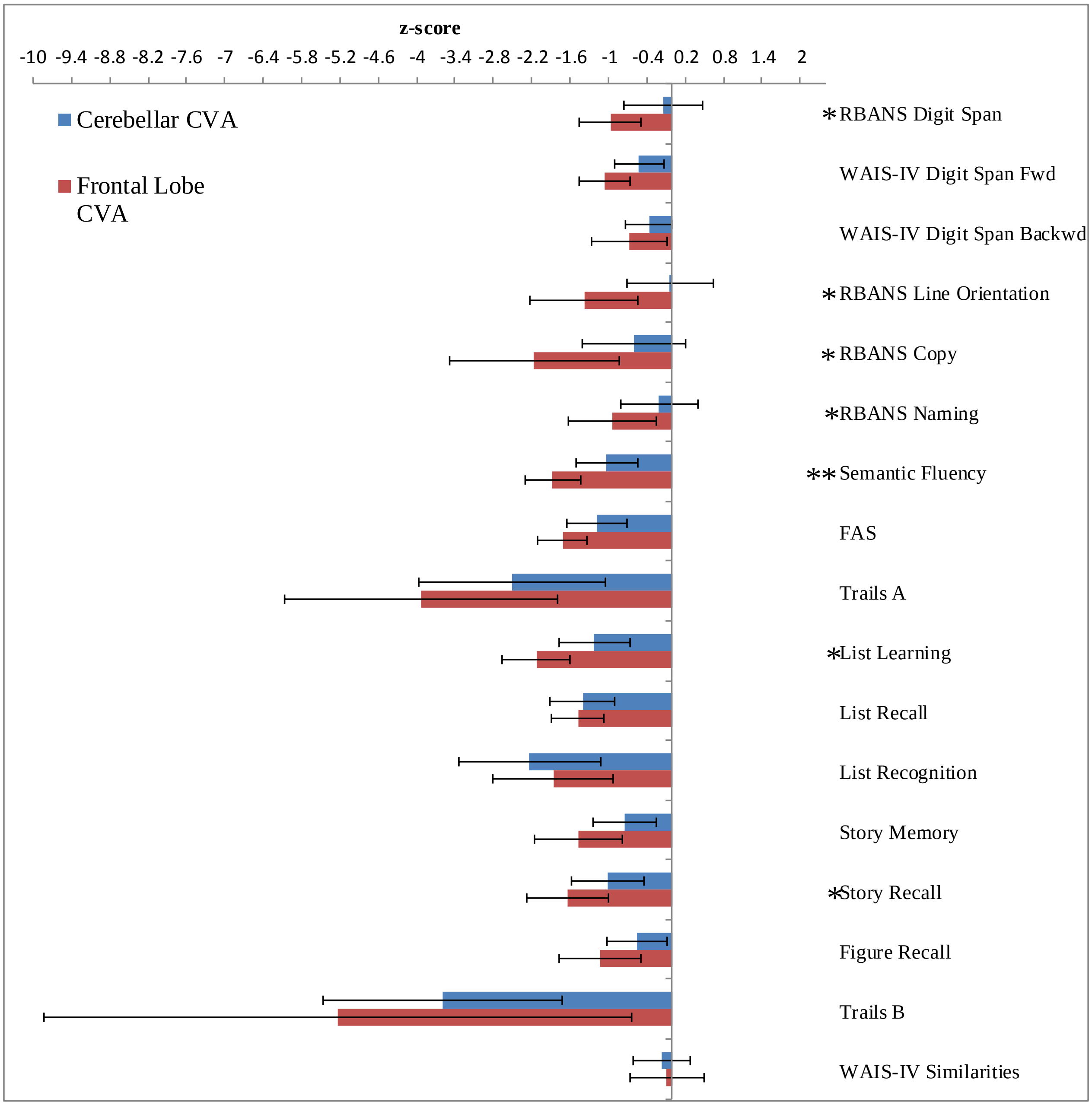


Figure 5. Comparison of the magnitude of impairment (in mean z-score) for each neuropsychological measure between patients with cerebellar and frontal lobe strokes. Error bars depict the 95% confidence interval.



* trended towards significance, $p < .05$

** $p < .01$