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## Neuropsychological outcome following thalamic stroke in adolescence: an identical twin comparison

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### ABSTRACT

**Objective:** Medial thalamic stroke in adults commonly results in severe learning and memory impairments and executive dysfunction, particularly during the acute phase. However, there is limited research on the cognitive recovery from thalamic stroke in physically healthy adolescents. This study aimed to fill this gap in the literature by utilizing a monozygotic twin control to investigate the neuropsychological outcomes of bilateral thalamic stroke in adolescence.

**Method:** We evaluated an otherwise healthy 17-year-old male with a history of premature birth, developmental delay, and learning disability 2 and 7 months after he sustained a bilateral medial/anterior thalamic stroke of unknown etiology. His identical twin brother served as a case control.

**Results:** The patient presented with improvements in many cognitive skills between assessments, most notably processing speed. Despite some mild improvement, however, he presented with significant deficits in fine motor speed/coordination, spatial perception, and rapid naming. Additionally, he exhibited persistent, severe deficits in verbal learning and memory. Relative sparing of executive functions (i.e., planning and set-shifting) and attention on standardized measures in this case may be explained by good underlying health, limited extra-thalamic damage, and/or recovery of function. The effects of thalamic injury resulted in minimal adaptive dysfunction or deterrence from academic or athletic success for the presented case.

**Conclusions:** These results suggest risk for deficits in encoding of new verbal information following bilateral thalamic stroke in adolescence, as well as risk for persistent cognitive deficits despite initial improvements. This is consistent with descriptions of anterograde memory impairments in adults with similar lesions.

### ARTICLE HISTORY

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### KEYWORDS

Thalamus; memory; adolescence; stroke; amnesia; recovery

## 1. Introduction

### 1.1. Background

Ample literature has consistently demonstrated significant acute and long-term cognitive deficits associated with thalamic stroke in adults (Carrera et al., 2004). Despite the multitude of studies examining thalamic stroke in adulthood, however, the neuropsychological and functional outcomes of adolescent thalamic stroke have not been well-studied. Adolescents and young adults make up approximately 15% of stroke cases annually (Putala et al., 2009), with higher prevalence in boys (Jacobs et al., 2002). Consequently, the current study aims to examine the cognitive effects of medial thalamic stroke in an adolescent male.

The thalamic nuclei are commonly categorized into four territories: anterior, paramedian, inferolateral, and posterior (Amici, 2012; Carrera & Bogousslavsky, 2006; Freeland, Levi, & Hunter, 2014). The anterior region includes the anterior nuclei, which are connected to the mammillothalamic tract, the anterior limbic system, and the medial and prefrontal cortex (Schmahmann, 2003). This region is supplied by the tuberothalamic artery, which originates from the posterior communicating artery (Carrera & Bogousslavsky, 2006). The paramedial thalamic region includes the dorsomedian and intralaminar nuclei and is supplied by the thalamoperforating arteries, coming from the first region of the posterior cerebral artery (Carrera & Bogousslavsky, 2006; Schmahmann, 2003). Thalamic strokes impacting the anterior and paramedian regions are consistently associated with learning and memory impairments (Schmahmann, 2003). The inferolateral territory is supplied by the thalamogeniculate arteries, originating from the second region of the posterior cerebral artery (Carrera & Bogousslavsky, 2006). The inferolateral territory includes the ventrolateral nucleus, ventroposterior nuclei, and the ventromedian nucleus, which connects to the cerebellum, motor cortex and prefrontal cortex (Schmahmann, 2003). Strokes impacting the interolateral territory are commonly associated with sensory loss and motor impairment. Lastly, the posterior territory is supplied by the medial and lateral regions of the posterior choroidal artery (Carrera & Bogousslavsky, 2006). This region includes the pulvinar, which connects to the parieto-occipital cortex, prefrontal cortex, cingulum, parahippocampal cortex, and temporal lobes (Schmahmann, 2003). Stroke impacting the posterior territory often results in visual field deficits, sensory loss, and motor deficits (Schmahmann, 2003).

Numerous neurocognitive deficits result from thalamic stroke, although the nature of these deficits often depends on the time since injury and the specific location of the injury. Common neurocognitive deficits during the acute phase in adulthood include attention deficits and neglect (Kraft et al., 2015; Kuljic-Obradovic et al., 2007), language disturbances (Kuljic-Obradovic et al., 2007), spatial deficits (Kraft et al., 2015; Rusconi, Rusconi, Carelli, Stampatori, & Mattioli, 2014), behavioral dysfunction (Liebermann et al., 2013; Rusconi et al., 2014), and executive dysfunction, such as planning, inhibition, set-shifting, working memory, and problem-solving skills (Kuljic-Obradovic et al., 2007; Liebermann et al., 2013; Sagnier et al., 2015; Shim et al., 2008; Van der Werf et al., 2000, 2003). Learning and memory deficits are consistently reported during the acute phase as well, including impaired long-term and short-term

memory on both visual and verbal tasks (Hampstead & Koffler, 2009; Kuljic-Obradovic et al., 2007; Rusconi et al., 2014; Shim et al., 2008; Van der Werf et al., 2000, 2003). Longstanding impairments generally depend on the severity and location of the thalamic insult, although research has most consistently demonstrated lasting deficits in executive function and memory (Kuljic-Obradovic et al., 2007; Van der Werf et al., 2003).

Regarding memory deficits, lesions in the anterior and medial thalamic nuclei are thought to underlie memory impairment because of the connectivity between these nuclei and medial temporal lobe structures that are known to be involved in memory encoding, consolidation, and retrieval (Rusconi et al., 2014; Van der Werf et al., 2000, 2003). Specifically, the medial nuclei of the thalamus are responsible for processing information to be stored and have connections to the amygdala and the prefrontal cortex, and the anterior nuclei of the thalamus select information to be stored and have connections to the hippocampus (Graff-Radford, Tranel, & van Hoesen, 1990; Mishkin, 1978; Van der Werf et al., 2003). Damage to the medial nuclei commonly results in persisting anterograde amnesia (i.e., difficulty learning new information), and some studies have reported retrograde amnesia as well, although this finding is inconsistent (Hampstead & Koffler, 2009; Kuljic-Obradovic et al., 2007). Additionally, damage to the medial nuclei commonly results in impaired spontaneous recall and forced recognition (Edelstyn, Mayes, Denby, & Ellis, 2012). In contrast to individuals with medial nuclei damage, individuals with damage to the anterior nuclei demonstrate greater declarative memory deficits, similar to deficits observed in individuals with hippocampal lesions (Van der Werf et al., 2000, 2003). The severity and duration of memory deficits, however, also depend on lesion lateralization (Carota et al., 2015). Bilateral paramedian strokes typically result in more persisting cognitive deficits, particularly memory impairment (Hermann et al., 2008).

Although the neurocognitive deficits associated with thalamic stroke in adulthood are well documented, very few studies have examined outcomes in physically healthy youth with thalamic stroke. The limited number of case series or small studies available report general neurological findings without detailed description of cognitive or adaptive functioning. Reported neurological findings include disruptions of consciousness, disturbances in language and movement, and sensory deficits (Garg & DeMyer, 1995; Gout et al., 2005; Kothare et al., 1998; Lascelles, Hewes, & Ganesan, 2001; Micheli et al., 1998). In addition, these reports indicate recovery of many neurological functions within 6 months. The presence and resolution of cognitive deficits, however, is not well described. Although it may be reasonable to hypothesize that long-term cognitive sequelae in adolescence is comparable with adulthood, childhood stroke is not equivalent to adult stroke, and therefore deserves separate analyses which consider age and development (Kossorotoff, 2013). In fact, age has been found to significantly impact stroke recovery and has a non-linear effect on cognitive recovery, particularly throughout development (Allman & Scott, 2013; Liman et al., 2011; Max et al., 2010). In other words, we cannot assume there will be greater cognitive recovery when age of insult is younger, or vice versa. Furthermore, stroke in older age is more commonly associated with comorbid health conditions, such as cardiac disease, hypertension, and diabetes (Deng et al., 2012). Consequently, cognitive outcomes following adult

stroke may be influenced by other health factors. Examining the cognitive outcomes of stroke in adolescence may provide insight into consequences of the injury in the absence of other vascular and health-related problems that often exist in adults who sustain stroke (Deng et al., 2012). Thus, long-term cognitive recovery from thalamic stroke in adolescence deserves further investigation.

Moreover, stroke during adolescence can result in functional impairments unique to this developmental stage. Specifically, stroke at a young age is associated with significantly reduced quality of life and adaptive functioning, such as reduced autonomy, social participation, and family relations, and increased frequency of internalizing and externalizing behavioral problems (Everts et al., 2008; Greenham et al., 2015; Lo et al., 2014). In addition, greater cognitive impairment is associated with poorer quality of life following stroke (Cumming, Brodtmann, Darby, & Bernhardt, 2014). Thus, stroke can significantly alter an adolescent's developmental trajectory at a crucial time when most typically developing adolescents are preparing for college, work, and independent living. Therefore, further examination of the long-term outcome of thalamic stroke in adolescence is relevant in supporting cognitive and functional recovery, as well as quality of life.

The current case study examines cognitive and behavioral functioning and recovery in TC, an adolescent male, following bilateral thalamic stroke affecting the medial and anterior nuclei. We assessed neuropsychological outcome at 2 months and 7 months post-stroke, and also evaluated his monozygotic twin brother, which allowed a surrogate estimation of functional trajectory for this patient. The aim of this study was (1) to examine the pattern of cognitive recovery following pediatric thalamic stroke, (2) to consider whether bilateral thalamic stroke in an adolescent patient results in long-standing anterograde memory deficits similar to what is observed in adults, and (3) to identify whether other long-term cognitive deficits are present following this kind of injury in a young brain.

## 1.2. *Patient history*

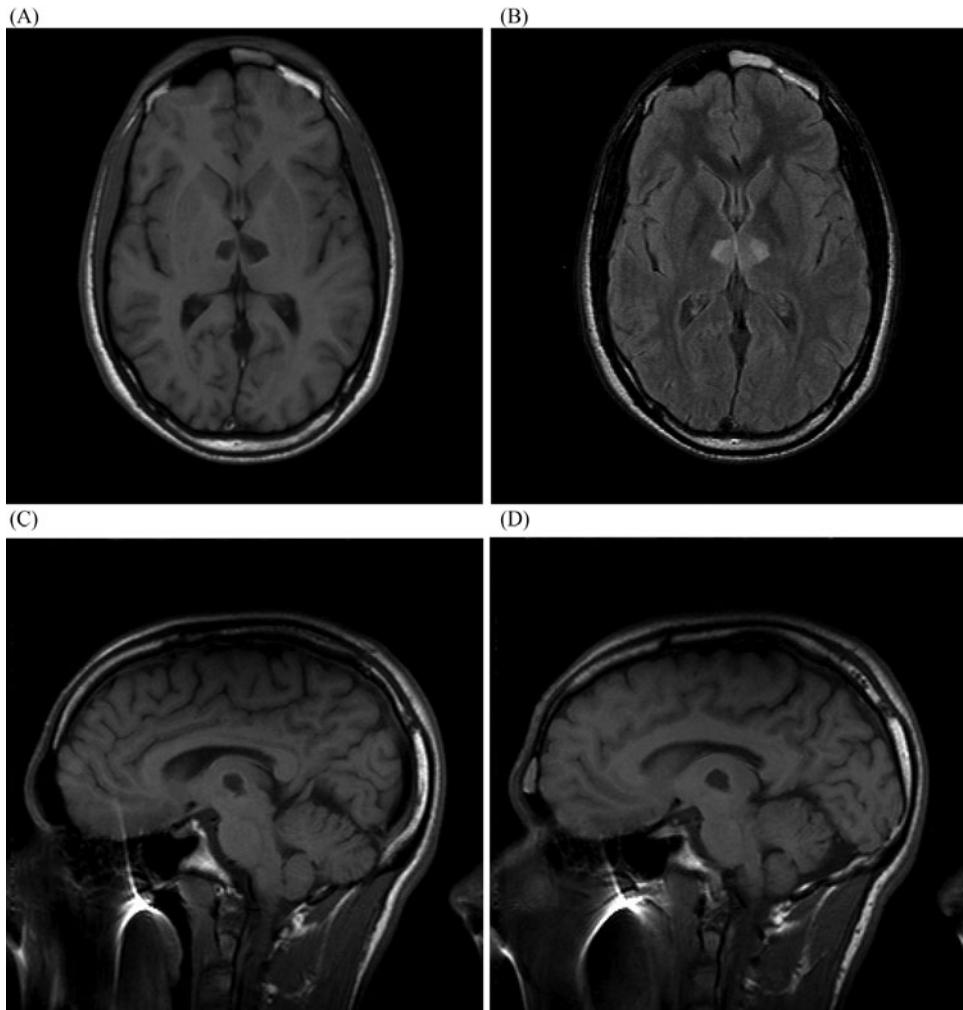
At the time of his initial evaluation, TC was a 17-year-old, African-American, right-handed male who lived with his biological parents, monozygotic twin brother, and an older brother. His father graduated from high school and his mother earned a college degree. TC was born via uncomplicated, vaginal delivery at 32 weeks' gestation following premature labor. He weighed 3 pounds, 2 ounces and remained in the neonatal intensive care unit (NICU) for approximately one month with no reported neurological complications. No problems were reported with growth or feeding but his early language development was delayed. TC received Early Intervention services, including speech and language and occupational therapies, for approximately 2 years.

TC attended a special education preschool for children with disabilities. Although he initially qualified for an autistic support class due to a diagnosis of pervasive developmental disorder (PDD) and global developmental delay, a re-evaluation completed before he entered Kindergarten concluded that he no longer met criteria for PDD. He continued to qualify for an Individualized Education Program and received learning support and speech and language therapy for many years. At the time of his injury,

TC had recently completed the 11th grade and was scheduled to transition to general education classes with no services for 12th grade, despite some persisting weaknesses with speech articulation. He excelled at Track and Field and had developmentally typical adaptive skills, per his caregivers. Regarding long-term goals, TC expressed an interest in attending a 4-year college.

TC's medical history prior to the stroke was unremarkable, other than his birth history. On the day of the stroke, TC came home from a carnival and reported that he did not feel well and presented with facial twitching. He went to sleep, waking the next day feeling ill and tired, complaining of headache, and stating that he could not see or walk normally. Over the course of several hours, he became increasingly lethargic and difficult to arouse. His mother took him to a local hospital, where he became unresponsive. A head computed tomography (CT) scan completed at that time was remarkable for a small hypodense focus in the right thalamus, and a small hypodense focus in the right cerebellar hemisphere with no evidence of intracranial hemorrhage. Findings of brain magnetic resonance imaging (MRI) completed the same day included non-enhancing foci of restricted diffusion of the upper brainstem/thalami bilaterally, suggestive of acute cerebral infarcts. Small chronic infarcts were also observed in the right cerebellar hemisphere. Three days later, electroencephalography (EEG) revealed abnormal excessive slowing. On a follow-up MRI completed 1 week later, a left thalamic infarct was observed and was larger and more ill-defined, and the right thalamic and right cerebellar infarcts were not as well seen. Magnetic resonance angiography (MRA) was unremarkable and magnetic resonance venography (MRV) revealed marked attenuation of the proximal third of the left transverse sinus, which was thought to be a developmental anomaly. Medical work-up did not reveal an etiology for the strokes. TC did not recall the events of his injury or much of his hospital stay. Results of a follow-up MRI completed approximately five weeks post-injury at our institution are presented in [Figure 1](#) and revealed bilateral paramedial/anterior thalamic infarcts, with greater involvement on the left than the right. Signal analysis suggests that these lesions occurred around the same time. The cerebellar abnormality was only seen in retrospect and was thought to be consistent with mild volume loss. The images described here were obtained for the purposes of diagnosis and clinical management and read and reported by clinical radiologists, and were not part of a research protocol. Artifact from braces affected the integrity of the studies to some degree, as well as the ability to obtain sequences that could provide additional information.

Three days following his stroke, TC could follow simple commands and produce minimal speech. During his acute hospitalization, he received speech and language therapy. Two weeks following the injury, at the time of hospital discharge, he presented with intact orientation, good attention, and grossly intact receptive and expressive language skills despite some dysarthria and mild difficulty following multi-step directions. He received outpatient physical, speech/language, and occupational therapies to address poor speech articulation and volume, supranuclear downgaze deficit, disinhibited behaviors, and fatigue, as well as poor memory, attention, initiation of activities of daily living, visual-perceptual functioning, and information processing.



**Figure 1.** Brain MRI results 5 weeks post-injury showing subacute lesion in the anterior/medial aspects of the thalamus bilaterally: (A) axial T1-weighted, (B) axial FLAIR, (C) sagittal T1-weighted right paramedian slice, and (D) sagittal T1-weighted left paramedian slice.

TC's monozygotic twin, CC, was used as a control to provide a surrogate estimation of TC's baseline performance, given similarities in their genetic, environmental, developmental, educational, and social histories. CC has a similar history related to premature birth, mild developmental delays, and need for early intervention and special education support through middle school, as well as a high level of athletic success and typical adaptive functioning. CC's medical history is also unremarkable other than his birth history.

### 1.3. Previous evaluations

TC was evaluated several times by his county and school district prior to his injury. At four years of age, he presented with borderline intellectual functioning (with

comparable verbal and non-verbal abilities) and deficits in visuomotor integration. In the fourth grade, TC's performances on tests of academic achievement were generally at a late second grade to late third grade level, with relative weaknesses noted in math application skills. During his seventh grade year, TC performed in the average range on many standardized achievement measures, but presented with weaknesses in reading comprehension. A speech and language evaluation revealed low average receptive language skills and average expressive language skills at that time.

CC's level of intellectual functioning, also assessed very early in life, was comparable to TC's intellectual functioning. An evaluation during CC's sixth grade year indicated his math and reading skills were at or close to grade level and he no longer qualified for special education services.

## 2. Methods

TC completed a comprehensive protocol of neuropsychological assessments during his first clinical evaluation (Time 1), which occurred two months following his injury. The same protocol was administered to CC. Seven months following his stroke, TC returned for a clinical re-evaluation (Time 2). Detailed clinical interview was conducted at both evaluations. Due to research indicating that much of cognitive recovery occurs within the first 6 months following a stroke, TC's re-evaluation at seven months following his stroke was believed to be a general indicator of long-term sequelae (Rasquin et al., 2004; Wagle et al., 2011). A complete list of the neuropsychological tests and behavioral questionnaires administered can be found in [Table 1](#).

To evaluate TC's recovery, his scores at Time 2 were compared to (a) his scores at Time 1, and (b) CC's scores. To determine if the difference in TC's scores across time points was statistically significant, the Reliable Change Index (RCI) method was used (Jacobson & Truax, 1992). The RCI method can be used to determine whether a change in scores at Time 1 and Time 2 is due to chance variation or is clinically meaningful. This empirical method has been consistently used to evaluate change in individual cognitive performance across time points (Duff, 2012; Heaton et al., 2001). The RCI was calculated for assessments that were administered at Time 1 and Time 2, and that provided sufficient technical information (i.e. standard error of measurements or standard deviations of the normative sample and test-retest reliability). To calculate the RCI, the difference score between time points was divided by the standard error of differences (Jacobson & Truax, 1992). The standard error of differences ( $S_{diff}$ ) was determined using the standard error of measurement ( $SEM$ ) for tests that provided  $SEM$  data. For assessments that did not provide  $SEM$  data, the  $SEM$  was calculated using standard deviation (SD) and test-retest reliability coefficient values ( $r_{xx}$ ). If the RCI value is larger than the z-score value of 1.96 (representing a 95% significance level), then the change is considered statistically significant.

Because we do not have a true baseline for TC, as he did not participate in neuropsychological evaluation prior to his stroke, CC's cognitive performance served as a surrogate baseline to represent an estimate of TC's cognitive function prior to injury. The comparison between TC's Time 2 cognitive profile and CC's performance allows for some analysis of areas of long-standing impairment due to the stroke. To

**Table 1.** Assessments administered at Time 1 and Time 2.

Domain	Test
Academics	<i>WJ-III Letter Word Identification</i> <i>WJ-III Calculation</i> <i>WJ-III Math Fluency</i> <i>WJ-III Reading Fluency</i>
Verbal Knowledge	<sup>a</sup> <i>WASI / WAIS-III Vocabulary</i> <sup>a</sup> <i>WASI / WAIS-III Similarities</i>
Nonverbal Processing	<sup>a</sup> <i>WASI / WAIS-III Block Design</i> <sup>a</sup> <i>WASI / WAIS-III Matrix Reasoning</i>
Processing Speed	<i>Benton Judgement of Line Orientation</i> <i>WAIS-III Digit Symbol Coding</i> <i>WAIS-III Symbol Search</i>
Attention/Working Memory	<i>WAIS-III Digit Span</i> <i>WMS-III Spatial Span</i> <i>WAIS-III Letter Number Sequencing</i> <i>WMS-III Mental Control</i> <i>Connor's Continuous Performance Test (CPT)</i>
Motor Memory	<i>Grooved Pegboard Test</i> <i>CVLT-II</i> <i>WMS-III Logical Memory</i> <i>WMS-III Faces</i>
Executive Functioning	<i>RCFT/Taylor Figure</i> <i>D-KEFS Trail Making Test</i> <i>D-KEFS Verbal Fluency</i> <i>D-KEFS Color Word Interference</i> <i>D-KEFS Tower Test</i> <i>D-KEFS Twenty Questions</i> <i>Wisconsin Card Sorting Test (WCST)</i>
Emotional and Behavioral Functioning	<i>Child Behavior Checklist (CBCL) and Youth Self Report (YSR)</i>

<sup>a</sup>Indicates these tests were derived from the WASI at Time 1 and from the WAIS-III at Time 2. CVLT-II: California Verbal Learning Test, 2nd ed.; D-KEFS: Delis – Kaplan Executive Function System; RCFT: Rey Complex Figure Test; WASI: Wechsler Abbreviated Scale of Intelligence; WAIS-III: Wechsler Adult Intelligence Scale, 3rd ed.; WJ-III: Woodcock–Johnson Test of Academic Achievement, 3<sup>rd</sup> Edition; WMS-III: Wechsler Memory Scale, 3rd ed.

determine clinically-meaningful differences based on standard scores, research methods have varied, with thresholds ranging from 1.0 to 1.5 standard deviations difference. We employed a conservative approach in the current study, using a cut off of at least 1.5 standard deviations to represent clinically significance differences between TC's Time 2 performance and CC's performance.

### 3. Results

#### 3.1. Time 1: initial neuropsychological evaluation

Two months post-injury, TC and his mother reported improvement of physical symptoms (e.g. fatigue and eye movement abnormalities), along with significantly improved memory and cognitive function, other than persisting voice/speech abnormalities and slowing of physical movements. At that time, TC was routinely taking aspirin. TC presented as cooperative, polite, respectful, and pleasant. He did not engage in spontaneous conversation and his affect was very restricted in range, but not inappropriate. Speech was labored and notable for poor articulation and low voice. He swallowed frequently. For many tasks that required a verbal response, he provided sparse information, requiring cuing to elaborate or persist in verbal responding. There was no observed disturbance of language content. Results of standardized testing are presented in Table 2.

Performance across many tasks fell within the low average to borderline ranges compared to age expectations (see [Table 2](#)). This included TC's verbal/language skills, such as verbal knowledge, rapid generation of words, verbal concept formation, and repetition of verbal information. TC demonstrated specific strengths in attention, working memory, and non-verbal pattern reasoning, performing in the average range or better on tasks assessing these skills. However, aspects of executive functioning fell within the borderline range, including problem-solving and set-shifting. In addition, TC's fine motor speed/dexterity was very poor and he presented with overall psychomotor slowing, slow speech, and poor visual scanning of information arranged in a random array, as well as a weakness in visuoconstruction.

Moreover, TC presented with significant deficits in new learning and memory. Although his ability to learn and remember faces was within the normal range for age, his ability to learn and remember a list of words, stories, and an abstract design was well below normal. He seemed to learn and remember "big picture" information, but was not able to encode and/or recall details and made intrusion errors. He did not benefit much from repetition or testing in a recognition format, suggesting that problems with learning/memory primarily occurred at the level of encoding.

Despite his medical event and cognitive deficits, TC and his mother denied clinically significant internalizing or externalizing symptoms on standardized rating scales (i.e. the YSR and CBCL). During a clinical interview, TC denied any significant change in emotional or behavioral functioning since his injury.

### ***3.2. Time 2: neuropsychological follow-up***

Seven months after his injury and 5 months following the initial evaluation, TC reported resolution of fatigue and a recent neuro-ophthalmology evaluation indicated moderate improvement of a supranuclear gaze deficit. TC had returned to school (12th grade) where he remained enrolled in all general education classes with some new accommodations and modifications. He reportedly completed homework independently and his teachers quickly transitioned from a pass/fail to letter-grading system. Despite success in this transition back to school, his teachers reported persisting behavioral changes including disinhibition and disorganization, as well as poor encoding and retention of new information. TC, in contrast, stated that he returned to his pre-injury level of function, suggesting limited insight. TC rejoined Track and Field, where he was again performing at a very high level in comparison to his typically developing, healthy peers. His mood and level of independence in daily activities were reportedly back to baseline. Despite recommendations, TC rejected the idea of attending community college and planned to apply to 4-year colleges.

A shortened battery was administered to replicate a significant portion of the initial assessment, employing alternative versions of tests administered at Time 1, when possible, to minimize concern for practice effects influencing TC's performance (see [Table 2](#)). TC again did not initiate conversation and presented with restricted, but appropriate, affect. He spoke with a low volume and immature articulation, but with no observed disturbance of language content.

**Table 2.** Neuropsychological test results of patient (Time 1 and Time 2) and control.

Age at testing	Patient: Time 1	Patient: Time 2	Time 1 versus Time 2 RCI	Twin CC
	17 years, 4 months	17 years, 9 months	Significant yes/no	18 years, 3 months
WASI /WAIS-III Vocabulary	−1.33	0.00	−	+0.33
WASI /WAIS-III Similarities	1.00	−0.33	−	0.00
WASI /WAIS-III Block Des	−2.00	−1.00	−	−0.67
WASI /WAIS-III Matrix Reas	−0.33	−0.67	−	−0.67
WAIS-III Digit Symbol Coding	−2.33	−1.00	Y	+0.67 <sup>a</sup>
WAIS-III Symbol Search	−1.00	+0.33	Y	−0.33
WAIS-III/WMS-III Digit Span	−1.00	−0.67	N	−0.33
WMS-III Spatial Span	−0.33	+0.33	N	+1.00
WAIS-III/WMS-III Letter Number Sequencing	−2.00	−1.00	N	+0.33
WMS-III Mental Control	−1.00	+0.33	Y	0.00
CPT-II				
Omissions	−0.50	−	−	0.00
Commissions	+0.25	−	−	+0.33
Hit RT	−0.40	−	−	−1.40
Hit RT Standard Error	−0.33	−	−	0.00
Grooved Pegboard Test				
Dominant	−7.78	−8.00	−	−1.63 <sup>a</sup>
Non-Dominant	−8.60	−6.32	−	−2.93 <sup>a</sup>
Benton JLO	−1.67	−2.33	−	0.00 <sup>a</sup>
D-KEFS Trail Making Test				
Visual Scanning	−2.67	0.00	Y	+0.67
Number Sequencing	−2.67	−0.33	Y	+0.33
Letter Sequencing	−3.00	−1.33	Y	+0.67 <sup>a</sup>
Number Letter Switch	−3.00	−1.00	Y	0.00
Motor Speed	−2.33	0.00	Y	0.00
D-KEFS Verbal Fluency				
Letter Fluency	−2.00	−0.67	Y	−1.00
Category Fluency	−1.33	−1.67	N	+0.33 <sup>a</sup>
Switching Total	−2.00	−0.33	N	0.00
Switching Accuracy	−1.67	−0.33	N	+0.33
D-KEFS Color Word Interfer.				
Color Naming	−3.00	−2.67	N	0.00 <sup>a</sup>
Word Reading	−3.00	−3.00	N	0.00 <sup>a</sup>
Inhibition	−3.00	−2.33	N	0.00 <sup>a</sup>
D-KEFS Tower Test: Total Achievement	−	−0.67	−	0.00
D-KEFS Twenty Questions Total Weighted Achievement	−	+0.67	−	−0.67
WCST				
Categories Completed	4 (raw)	−	−	6 (raw)
Failure to Maintain Set	0 (raw)	−	−	1 (raw)
Perseverative Errors	−1.67	−	−	+0.60
Nonperseverative Errors	−1.33	−	−	+0.30
CVLT-II				
Trials 1-5	−2.67	−1.33	−	−0.67
List A Free: Trial 1	−2.50	−1.00	N	−1.50
List A Free: Trial 5	−3.00	−1.50	N	0.00 <sup>a</sup>
List B	−2.00	−1.50	N	0.00 <sup>a</sup>
List A Short Delay Free	−3.00	−2.00	N	−0.50 <sup>a</sup>
List A Short Delay Cue	−3.00	−3.50	−	−2.00 <sup>a</sup>
List A Long Delay Free	−3.00	−4.50	N	−1.00 <sup>a</sup>
List A Long Delay Cue	−3.00	−4.50	−	−1.50 <sup>a</sup>
Recognition Discrimin.	−2.50	−2.50	N	−0.50 <sup>a</sup>
WMS-III Logical Memory				

(Continued)

**Table 2.** Continued.

	Patient: Time 1	Patient: Time 2	Time 1 versus Time 2 RCI	Twin CC
	17 years, 4 months	17 years, 9 months		18 years, 3 months
Age at testing			Significant yes/no	
	Z-Score	Z-Score		Z-Score
Logical Memory I	−1.67	−1.67	N	0.00 <sup>a</sup>
Logical Memory II	−2.67	−1.67	N	+0.67 <sup>a</sup>
Percent Retention	41%	74%	—	—
Recognition Raw	19/30	23/30	—	—
WMS-III Faces				
Faces I	−1.00	—	—	+0.33
Faces II	−1.00	—	—	0.00
RCFT/Taylor Figure				
Copy Raw (Z-score)	30/36 (−2.01)	30/36 (−1.90)	—	32/36 (−1.26)
Delayed Recall Raw (Z-score)	9.5/36 (−3.00)	18.5/36 (−0.33)	—	13/36 (−1.00)
WJ-III				
Letter Word Identification	−0.70	—	—	−0.50
Calculation	−0.33	—	—	+0.80
Math Fluency	−2.35	−0.25	Y	0.00
Reading Fluency	−2.25	−1.67	N	−0.67

<sup>a</sup>Indicates CC's z-scores that are more than 1.5 SD above TC's Time 2 scores. Benton JLO: Benton Judgment of Line Orientation; CPT-II: Continuous Performance Task, 2nd ed.; CVLT-II: California Verbal Learning Test, 2nd ed.; D-Kefs: Delis-Kaplan Executive Function System; RCFT: Rey Complex Figure Test; WASI: Wechsler Abbreviated Scale of Intelligence; WAIS-III: Wechsler Adult Intelligence Scale, 3rd ed.; WCST: Wisconsin Card Sorting Test; WJ-III: Woodcock-Johnson Test of Academic Achievement, 3rd ed.; WMS-III: Wechsler Memory Scale, 3rd ed.

At 7 months post-injury, verbal/language skills fell in the average range, non-verbal reasoning skills and visuoconstruction ranged from average to low average, and performance on several processing speed tasks improved to the average to low average range. Moreover, TC's attention and executive functioning skills, including immediate attention, working memory, non-verbal problem-solving skills, set-shifting, and planning, were average to low average. TC demonstrated persistent weakness in basic visual perceptual processing, however, which may have been a consequence of his mild visual gaze deficit considering his adequate performance on other visually-mediated tasks. Moreover, he continued to show weakness in some aspects of executive functioning, including self-monitoring and inhibition. TC again scored below age expectations across verbal learning and memory tasks, although he made relative improvements in his ability to retain stories and an integrated design. TC again tended to recall "big picture" or gist information, but had difficulty encoding or retaining details. He made numerous semantically related intrusion errors. Again, repetition and testing in a recognition format were not beneficial for TC, indicating that memory difficulties reflected problems with encoding.

TC presented with significant improvement across many tasks between 2 and 7 months post-injury. Tasks assessing sustained attention, face memory, and word reading and math calculation were not repeated, as scores on these tests were within normal expectations at the initial evaluation. Simple examination of z-scores revealed improvement on tasks assessing verbal knowledge, phonemic fluency, processing speed, brief attention, working memory, visual scanning, set-shifting, retention of some kinds of information, and academic fluency. Z-scores remained stable or

declined on tasks assessing fluid reasoning, spatial perception, complex visuomotor integration, fine motor speed/coordination, and verbal learning and memory.

Based on an RCI of 1.96 or higher for tasks in which this statistic could be calculated, significant improvement emerged on tasks assessing fluency, attention, and processing speed between assessments. In general, significant improvement in information processing/retrieval speed seemed to account for significantly better performance on a number of timed tasks. In addition, retention of visual information improved significantly. Despite this, fine motor speed/coordination, rapid naming, and encoding of verbal information did not appear to improve over the 5-month interval.

### **3.3. Case control comparison**

CC participated in a neuropsychological evaluation for the purposes of this study at the age of 18 years, 3 months. CC performed solidly in the average range across the majority of tasks, including those assessing verbal skills (word knowledge, rapid naming, and ability to identify abstract concepts), fluid reasoning, visual perception, visuoconstruction, visuomotor integration, and information processing speed. His attention and executive functioning skills were primarily average, including his brief and sustained attention, set-shifting, fluency, problem-solving skills, and inhibition. His learning and memory performances were variable. That is, his ability to encode and retrieve contextual information was average, including stories and faces. Despite adequate learning, retention/retrieval of a word list was relatively weaker, and he displayed a weakness in his ability to retain/recall a complex figure that he copied.

Using CC's profile as a case control, comparisons were made between TC's Time 2 performances and CC's performances, with a difference of at least 1.5 standard deviations used to represent significant differences. Using this criteria, TC's verbal knowledge and verbal reasoning, fluid reasoning, and visuoconstruction skills were comparable to those of his brother. Additionally, a number of TC's scores on executive functioning tasks indicated comparable abilities to CC, including brief attention and working memory, set-shifting, planning, and problem-solving. Cognitive inhibition was affected by processing speed, so a direct comparison is challenging. In contrast, TC performed significantly poorer than his brother on tasks assessing naming and reading speed, processing speed, visual-spatial perception (despite comparable complex visuomotor integration), and fine motor speed/dexterity. Moreover, TC exhibited poorer performance than CC on tasks of verbal learning and memory, particularly encoding and retention of a word list.

### **3.4. Long-term follow-up**

Despite TC's long-term cognitive deficits following his stroke, he responded well to outpatient rehabilitation and benefited from support from caregivers, treatment providers, and educators. Although he no longer qualified for an Individualized Education Program at the end of 11th grade and was planning to return to school without any specialized support or accommodations, following his stroke, his school district provided formal accommodations and modifications in a general-education setting. TC

completed high school in good academic standing and competed in the state's Track and Field meet. Although TC was not initially accepted into a four-year undergraduate program, he received a scholarship to attend a local, two-year associate's program and to compete on the college's Track and Field team. As he had planned, TC graduated from the program within 2 years and was then accepted into a 4-year university away from home. TC graduated after 4 years with a bachelor's degree in Human Performance (i.e. Exercise Science).

## 4. Discussion

### 4.1. Summary of results

The current investigation examined the long-term cognitive outcome of a 17-year-old patient with bilateral thalamic stroke. This study specifically aimed (1) to examine the pattern of cognitive recovery following pediatric thalamic stroke, (2) to determine if this injury results in anterograde memory deficits similar to that seen in adulthood, and (3) to identify other long-term cognitive deficits.

To address our aims, we analyzed performance on neuropsychological evaluation two and seven months post-injury in our patient, TC. TC's monozygotic twin, CC, served as a case control. Two months post-injury, skills that appeared minimally affected by TC's injury included fluid reasoning, brief attention, sustained attention, face recognition, visuomotor integration, and untimed word reading and calculation skills. Nonetheless, a number of skills appeared to be compromised, including processing and retrieval speed across many timed tasks, fine motor speed/dexterity, language formulation, visuoconstruction, aspects of working memory, and spatial perception. Deficits in encoding were notable across all learning and memory tasks (verbal and visual), except face recognition. This subacute profile is consistent with findings in adult patients with thalamic stroke. Specifically, deficits of learning and memory, language, spatial abilities, processing speed, and working memory skills are commonly observed shortly after thalamic stroke in adulthood (Kraft et al., 2015; Kuljic-Obradovic et al., 2007). In TC's case, however, there was also some evidence of right cerebellar involvement, although the cerebellar abnormalities were less conspicuous than the thalamic injuries and analysis of the brain MRI completed 5 weeks post-injury suggests that the cerebellar abnormalities could be described as mild volume loss. Nonetheless, it is important to note that weaknesses in fine motor speed/dexterity, visual spatial skills, and expressive language following TC's neurological event could potentially be explained by cerebellar involvement (Koziol et al., 2014).

By 7 months post-injury, TC exhibited evidence of further cognitive recovery in many areas and, based on control comparison, are presumed to have returned to or approached baseline performance. Specifically, phonemic fluency, math fluency, some aspects of processing and retrieval speed and executive function (set-shifting/mental flexibility, working memory, problem-solving), language formulation, visuoconstruction, and recall/recognition of visual information significantly improved by seven months post-injury. TC and his mother also reported a return to baseline in many aspects of functioning and his level of participation in his school and community and his adaptive functions were reportedly at baseline.

Despite cognitive recovery, TC presented with persisting weaknesses in semantic fluency, reading fluency, rapid naming, spatial perception, and fine motor speed and coordination. Deficits in rapid naming may reflect longstanding developmental issues given his history of learning disability and improvement on other processing/response speed tasks. Performance on tasks of spatial perception and rapid visual scanning did not improve at follow-up despite resolution of supranuclear gaze palsy, suggesting that this injury complication did not account for these findings. Rather, these visuo-spatial deficits are consistent with outcome of medial thalamic stroke in adults (Kraft et al., 2015). Additionally, past studies suggest visual processing speed is associated with thalamic volume (Van der Werf et al., 2000) and adult thalamic stroke commonly results in mildly impaired visual processing speed (Kraft et al., 2015). Therefore, our findings suggest pediatric thalamic stroke may lead to an increased risk for persistent cognitive deficits, particularly tasks requiring visuospatial analysis and processing speed, despite initial cognitive improvements.

Furthermore, TC's pattern of recovery of learning and memory processes was variable across modalities. Specifically, although visual memory was less affected at baseline, specifically face memory, and improved across recovery, he demonstrated persisting and striking deficits in his ability to encode verbal information, especially list-learning at both Times 1 and 2. At follow-up, he displayed relatively better retention of narrative information, despite weak encoding.

The pattern of TC's cognitive recovery may certainly be associated with TC's age at injury, and the fact that he had no pre-existing or complicating health issues, other than developmental language and learning concerns following a premature birth. Past research indicates significantly greater impairment in numerous cognitive domains when stroke occurs during the first year of life, in comparison to childhood years (Avila et al., 2010; Lansing et al., 2004; Max et al., 2010). Despite this general developmental "rule," impairments in visuospatial skills, verbal abilities, memory, and executive functioning skills are greater when stroke occurs during older adolescence in comparison to early childhood (i.e. ages 1–6 years old; Allman & Scott, 2013; Everts et al., 2008). This developmental pattern is consistent with TC's persisting deficits on visuo-spatial tasks, processing speed tasks, and memory tasks, although the *location* of his injury creates more clear expectations for a specific pattern of cognitive deficits, especially given sparing of the cortex in this case.

Regarding our second aim specifically considering memory deficits following pediatric thalamic stroke, our results provide evidence that verbal memory deficits result from thalamic stroke even in young, otherwise healthy, patients. TC demonstrated persisting challenges in tasks assessing verbal learning and memory, which seemed to be accounted for by poor encoding, minimal benefit from repetition, and impaired cued recall and forced-choice recognition. Memory deficits are associated with stroke in general during childhood (Lansing et al., 2004), although pediatric stroke more likely affects cortical structures. The fact that TC's injury was limited to subcortical structures allows for further consideration of the specific effects of these injuries. The verbal learning deficit is consistent with those described in adult patients with thalamic stroke (Hampstead & Koffler, 2009; Kuljic-Obradovic et al., 2007; Rusconi et al., 2014; Zoppelt et al., 2003), particularly following anterior and medial thalamic nuclei infarcts,

which were implicated in TC's case (Hampstead & Koffler, 2009; Kuljic-Obradovic et al., 2007, Van der Werf et al., 2003). The anterior thalamic nuclei, connected to the mammillo-thalamic tract, are thought to be an extension of the hippocampal system (Aggleton & Brown, 1999; for review see Carlesimo, Lombardi, Caltagirone, & Barban 2015) and damage to these nuclei are associated with retrieval deficits (Aggleton, Dumont, & Warburton, 2011). Although the role of the medial thalamic nuclei in memory has been highly debated (Aggleton et al., 2011; Edelstyn et al., 2002; Kishiyama et al., 2005), research suggests damage to the medial thalamic nuclei can impact encoding, due to the connection between this region and the prefrontal cortex, which contributes to encoding (Pergola, Ranft, Mathias, & Suchan, 2013; for review see Carlesimo et al., 2015). Although the pattern of performance on memory measures described in TC is more consistent with an encoding than a retrieval deficit, Aggleton et al. (2011) suggest the medial thalamic nuclei may contribute to both "familiarity-based recognition" (i.e. forced-choice recognition tasks) and "recollective-based recognition" (i.e. cued-recall tasks). Conversely, other studies have suggested the medial thalamic nuclei primarily contribute to executive functioning, which indirectly influences memory, such as attending to information and using organizational strategies during encoding (Van der Werf et al., 2000; for review see Mitchell & Chakraborty, 2013). This latter executive function theory could provide further explanation for TC's specific memory deficits, as this theory suggests that while he can encode "big picture" information, his lack of self-monitoring and organizational skills result in an inability to recall specific details or benefit as expected from repetition. Although TC's performance was adequate on standardized assessment of executive functioning skills (e.g., working memory, shifting, and problem-solving), subtle executive dysfunction may not be easily identified on these kinds of assessments. In sum, TC's verbal memory impairment is consistent with that described following adult thalamic stroke affecting anterior and medial thalamic nuclei and resulting in impaired encoding, recall, and recognition (Aggleton et al., 2011), with potential contributions of executive dysfunction.

Moreover, TC made numerous intrusive errors on the verbal list learning task. Thalamic stroke in adulthood has been commonly associated with language production disorders, including focus on unrelated information (Carrera & Bogousslavsky, 2006) or "strange paraphasia" (i.e. providing meaningless descriptions rather than the accurate label; Demonet, 1997). In contrast, TC's intrusive errors, although inaccurate, were associated with the word-list categories and reflected semantic errors. These errors are more consistent with confabulation errors, which are not consistently associated with adult thalamic stroke (Kopelman, 2015), but have been shown to result from bilateral paramedian infarcts in some cases (Schmahmann, 2003) and may be due to damaged connections between the medial thalamic nuclei and the prefrontal cortex.

Our findings suggest longstanding anterograde memory deficits associated with pediatric paramedian thalamic stroke may be exclusive to verbal information. At 2 months post-injury, face memory was within normal limits, and TC's performance on a design memory task was better than that of CC by 7 months post-injury. Research with adult patients has provided inconsistent findings regarding visual memory skills following thalamic stroke, with some studies highlighting impaired visual memory

(Chen et al., 2005; Pergola et al., 2013; Sagnier et al., 2015), while other studies reveal comparable performance to control participants (Rusconi et al., 2014; Zoppelt et al., 2003).

The final aim of our study sought to identify whether adolescents with thalamic stroke experience longstanding cognitive deficits beyond memory deficits. TC demonstrated weaknesses in fine motor speed/coordination, spatial perception, and rapid naming. Adults with thalamic stroke do not consistently present with longstanding deficits in motor speed, spatial abilities, and language abilities (Rusconi et al., 2014; Van der Werf et al., 2003). Although these weaknesses in TC may be a result of thalamic stroke, they could also be explained by a longstanding developmental pattern given history of prematurity, developmental language delay, and learning disabilities, or by potential cerebellar involvement. For example, motor dysfunction is associated with damage to the medial thalamus (Amici, 2012; Schmahmann, 2003) as well as to cerebellar damage (Koziol et al., 2014). Visual scanning deficits and poor verbal fluency are also associated with cerebellum impairment (Koziol et al., 2014). Future studies of pediatric thalamic stroke should further examine these specific cognitive domains to provide a better understanding of potential etiology.

Furthermore, existing research of adults with medial thalamic stroke has suggested the presence of long-term executive dysfunction including attention, maintenance, set-shifting, planning, and problem-solving (Chen et al., 2005; Liebermann et al., 2013; Van der Werf et al., 2003), as well as disinhibition, impulsivity, and impaired verbal generation (Van der Werf et al., 2003), although these findings have not been consistently upheld (Liebermann et al., 2013; Van der Werf et al., 2003; Zoppelt et al., 2003). Research has also suggested that flexibility and goal-directed behavior are often compromised following thalamic stroke, particularly when the medial thalamic nuclei are affected (Hunt & Aggleton, 1998; Parnaudeau et al., 2015). However, research of executive dysfunction following thalamic stroke has primarily focused on adults and some findings are based on animal models (Corbit, Muir, & Balleine, 2003; Parnaudeau et al., 2015). In the case of TC, brief and sustained attention, phonemic fluency, planning, and set-shifting abilities were either spared or had recovered by 7 months post-injury. Poor performance on a cognitive inhibition task could be explained by underlying problems with rapid naming (Protopapas, Archonti, & Skaloumbakas, 2007). That is, in contrast to the typical profile associated with adult thalamic stroke, there was little evidence of persisting, significant deficits in executive dysfunction in this case, although the presence of poor insight, poor encoding, and errors on verbal recall suggests at least some mild executive dysfunction. Specifically, on memory assessments, TC's semantically related errors indicated weaknesses associated with the prefrontal cortex, suggesting possible executive dysfunction. Nonetheless, this case result suggests that pediatric thalamic stroke may not be associated with significant and widespread impacts on executive functioning sometimes described in adult patients with similar injuries. But additional research is needed to further examine executive function following pediatric thalamic stroke.

Consistent with our findings, younger age at stroke has been associated with better executive functioning outcomes (Max et al., 2010; O'Keefe et al., 2014). Additionally, studies have shown greater cognitive impairment associated with age when

comparing long-term outcomes of adolescent to adult stroke survivors (Knoflach et al., 2012). This may be due to increased prevalence of risk factors such as cardiac diseases, hypertension, hyperlipidemia, and diabetes, associated with adult stroke in comparison to adolescents and young adults (Deng et al., 2012; Goeggel Simonetti et al., 2015). Thus, greater long-term cognitive deficits observed in adulthood versus adolescence may be due, in part, to the additional risk factors associated with aging.

Moreover, anterior and medial thalamic stroke in adulthood is associated with personality changes and executive dysfunction, such as apathy (Carrera & Bogousslavsky, 2006). Seven months following his stroke, TC's behavioral presentation indicated some lack of awareness and insight, as well as flat affect, although he and his mother indicated that his behavioral function was back to baseline. In addition, standardized parent and self-report questionnaires suggested that TC's behavioral or emotional functioning was within expectations for a boy his age. Thus, based on these standardized assessments, TC did not demonstrate significant, long-standing emotional and behavioral changes, suggesting these symptoms may not be present in pediatric thalamic stroke patients.

In regard to TC's adaptive functioning, his cognitive weaknesses at 7 months following his stroke, including verbal learning and memory impairments, are likely to persist, at least to some degree (Rasquin et al., 2004; Wagle et al., 2011), and may impact his academic and vocational outcomes given demands for new learning. In fact, cognitive impairment following pediatric stroke is significantly associated with reduced adaptive functioning skills and quality of life (O'Keefe et al., 2017). Yet information provided via clinical interviews suggested that TC quickly returned to his pre-injury level of independence in daily life. Over time, TC achieved his goal of earning a bachelor's degree at a university away from home following completion of a prerequisite program. This likely demonstrated the benefits of environmental supports and comprehensive rehabilitation, as cognitive outcomes are greater for individuals who immediately begin cognitive rehabilitation after stroke (Prokopenko et al., 2013; Zucchella et al., 2014). His success also highlights his strong adaptive functioning skills and, possibly, the absence of significant executive dysfunction, which is often observed following adult thalamic stroke and is predictive of impaired adaptive behavior skills following brain injury (Perna, Loughan, & Talka, 2012). Additionally, past studies examining stroke in childhood have indicated that older age at the time of stroke predicts fewer adaptive functioning deficits, possibly due to the maturation of these skills in older adolescence (Hurwitz et al., 2004; O'Keefe et al., 2017). Therefore, relatively spared adaptive functioning skills following thalamic stroke may be particularly unique to older adolescence. In the case of TC, the persistent cognitive deficits associated with paramedian thalamic stroke did not prevent him from achieving his post-high school goals, highlighting the potential disassociation between cognitive and adaptive functioning in older adolescence.

TC's largely successful recovery was supported by his comprehensive rehabilitation immediately following his thalamic stroke. Research shows children with memory deficits due to stroke have found success through cognitive rehabilitation using organizational strategies and external cues, such as planners, lists, or timers as reminders (Franzen et al., 1996; Wilson et al., 2001; Yerys et al., 2003). Consequently, clinicians

and caregivers of children with thalamic stroke should address core memory deficits through cognitive rehabilitation and incorporation of external cues to compensate for memory difficulties. Participation in cognitive rehabilitation focused on attention and executive functioning skills is also linked to a higher likelihood of executive functioning recovery (Bogdanova, Yee, Ho, & Cicerone, 2016). In addition, outcomes are greater for youth who immediately begin rehabilitation after stroke, as was the case for TC, indicating that treatment for children should be urgent (Prokopenko et al., 2013; Zucchella et al., 2014). Research examining the most efficacious cognitive rehabilitation for children, however, remains limited. Additionally, there are few research-based guidelines for cognitive rehabilitation for this population (Bogdanova et al., 2016). Moreover, these findings are not specific to thalamic-mediated memory or executive problems. Nonetheless, TC's case suggests that timely and appropriate treatment may improve adolescents' ability to compensate for cognitive deficits, and thus improve functional, real-world success. Future research should focus on examining cognitive rehabilitation for this population, to ultimately provide treatment guidelines and effective clinical treatment for childhood stroke survivors, and those with thalamic stroke more specifically.

#### **4.2. Limitations & future directions**

Although the current study provided a novel examination of the long-term outcomes of thalamic stroke in adolescence, it is not without its limitations. First, although a wide variety of assessments were administered, some cognitive and behavioral domains were not evaluated, which could have provided further explanation of the specific nature of TC's deficits. Specifically, a detailed assessment of language abilities was not conducted as part of our neuropsychological evaluation. Although TC demonstrated adequate formulation of verbal responses and comprehension of task instructions, as well as repetition, we did not formally evaluate comprehension or higher order language or examine for subtle linguistic difficulties associated with cerebellar dysfunction (Koziol et al., 2014). Furthermore, standardized adaptive behavior and quality of life questionnaires were not administered, and we relied on parent and patient report for this information.

In addition, RICIs could not be calculated for every measure, due to insufficient technical information required to calculate RICIs, which limited our ability to determine the significance of some score differences during the recovery phase. Moreover, not all neuropsychological assessments used at Time 1 were administered at Time 2, resulting in inconclusive evidence for long-term changes on particular assessments. However, performances on the majority of the assessments which were not administered at Time 2 were not impaired at Time 1. Thus, these tests were not administered at Time 2 to prioritize administration of assessments on which TC's performance had initially been impaired. Although our data suggest spared visual memory abilities, future research should verify this finding by assessing visual memory in larger pediatric samples.

Furthermore, TC's twin brother, CC, was used as a case control, given similarities in their prenatal and postnatal experiences, as well as genetic comparability. It is

important to note that prior to his stroke, TC had pre-existing learning difficulties and was academically supported through special education, although he no longer qualified for these services at the time of his stroke. TC's history of learning difficulties may have influenced his trajectory of recovery such that these results may not be easily generalizable to developmentally typical youth with thalamic injury. Moreover, despite their similar histories and shared genetic profile, CC may have a unique cognitive profile discrepant from TC's pre-injury performance which is highlighted by his relatively poorer performance on some tasks when compared to TC. We have attempted to address this limitation by using a conservative threshold of 1.5 standard deviations when comparing scores between participants. Nevertheless, because we do not have data on TC's actual baseline abilities, caution is necessary when comparing the profiles of these two subjects.

Further research is warranted to investigate the unique aspects of recovery from thalamic stroke in youth. Given TC's functional success following his injury and our evaluations, future studies should investigate the persistence of verbal learning and memory deficits and its effects on functional outcomes. In addition, direct assessment of TC's executive functions indicated these skills were spared or had recovered by the seven-month evaluation, although qualitative examination and performance on memory measures suggests the possibility of mild executive dysfunction. Future research is needed to further consider recovery of executive functions following thalamic stroke in youth. Moreover, future case studies are needed to determine whether the presence of persisting weaknesses in spatial perception, aspects of processing speed, semantic fluency, and bilateral fine motor/speed coordination are a result of thalamic stroke, or whether these findings reflect our patient's unique pre-injury profile or the potential involvement of the cerebellum. Considering the prevalence and impact of stroke on children and adolescence, this research is necessary to inform clinicians of long-term cognitive outcomes to consider when planning treatment and rehabilitation for children with thalamic stroke.

#### **4.3. Conclusion**

The current case report provides a unique observation of the cognitive deficits associated with bilateral paramedian thalamic stroke in adolescence. This novel examination of the long-term outcomes of pediatric anterior and medial thalamic stroke revealed that the majority of cognitive deficits observed during the acute recovery phase improve across time and that functional outcome may be very good. The current case highlights significant improvement in cognitive abilities over time, with little evidence of persistent executive or adaptive dysfunction, following pediatric thalamic stroke. However, anterograde memory deficits, particularly verbal encoding, persisted seven months following the stroke. Therefore, although children and adolescents may significantly recover in many cognitive domains, longstanding impairments in verbal memory should not be overlooked. Tailored rehabilitation intervention and planning for pediatric stroke survivors should consider their age and focus on their developmentally specific needs.

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