

A NEUROPSYCHIATRIC AND NEUROIMAGING STUDY OF UNILATERAL AND BILATERAL STRIATAL ISCHEMIC LESIONS

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1- Supplementary Materials and Methods

(a) Definition of cognitive functions

Global mental functioning. Global mental functioning includes orientation, attention, memory, language and visual-spatial skills. The Mini-Mental State Examination (MMSE) was used to assess global mental state.¹ MMSE adjusted cut-off score of 21 or below was considered as pathological.

Orientation. Orientation refers not only to one's spatial relationships, but also to recognition of temporal and personal relationships. Evaluating a patient's orientation in space, time, and person is the bedrock of our mental status examination. We considered the patient having disorientation or confusion when one lacks one or more of these capacities.¹

Attention deficit. Attention deficit means a person wanders off task, lacks persistence, has difficulty sustaining focus, and is disorganized; and these problems are not due to defiance or lack of comprehension. Attention was assessed by Stroop test with name color print of non-color words and name color print of color words.²

Executive function. Executive functions (or cognitive control) are a set of cognitive operations that are necessary for the cognitive control of behavior for achievement of chosen goals. The executive functions have been seen as regulated by the prefrontal regions of the frontal lobes and associated areas. To assess different aspects of executive functioning, we used the Trail Making Test -Part A [mean±SD, 35.5±10.5 sec] and Part B [mean±SD, 75.5±21.5 sec],³ and the Stroop test (name color print of non-color words [mean reading time±SD, 16.10±3.5 sec] and name color print of color words [mean reading time±SD, 30.15±8.20]).²

Frontal functioning. The frontal lobe is the same part of the brain that is responsible for cognitive functions such as planning for the future, judgment, decision-making skills, attention span, and inhibition. The Wisconsin Card Sorting Test (WCST) was used to measure frontal lobe dysfunctions.^{4,5} Categories achieved [mean score±SD, 4.9±1.5], correct responses [65.5±11.5], errors [46.5±20.5], perseverative responses [20.5±8.5], failure to maintain [0.8±0.6] were calculated to assess strategic planning, organized searching, the ability to use environmental feedback to shift cognitive sets, goal orientated behavior, and the ability to modulate impulsive responding.

Mnemonic functioning

Autobiographical memory. Autobiographical memory refers to our memory for specific episodes, episodic memory, and to our conceptual, generic, and schematic knowledge of our lives, autobiographical knowledge. They are the content of the self and define who we are, who we have been, and, importantly, who we can yet become.^{7,8} To examine autobiographical memory, we simply asked the patients to report the 5 most important personal events of their life.

Episodic memory. Episodic memory is a past-oriented memory system that allows reexperiencing of one's own previous experiences (such as times, location geography, associated emotions, and other contextual who, what, when, where, why knowledge) that can be explicitly stated or conjured up.⁹ Episodic memory was assessed by the *Rey Auditory Verbal*

Learning Test (RAVLT), including measures of immediate free recall/new learning (List A Trials 1–3/ List B) [mean±SD, 6.3±2.1/ 6.2±2.5] and delayed free recall (short- and long-delay) [mean±SD, 10.2±2.5].¹⁰

Semantic Memory. Semantic memory refers to the capacity for recollecting general knowledge and facts (ideas, meaning and concepts) about the world. Controlled Oral Word Association test (COWA)¹¹ [mean ± SD of animals named, 18±4.5] was used to measure the subject's capacity to generate words belonging to the *category of animals*.

Short-term memory. Primary memory is the capacity for holding, a small amount of information in mind in an active, readily available state for a short period of time. This memory was assessed by the Rey Auditory Verbal Learning Test (RAVLT)¹⁰ with five presentations of a 15-word list are given, each followed by attempted recall [mean+SD, 6.3±2.1].

Long-term memory. Long-term memory is a multi-storage memory system in which knowledge and skills are stored for a long time. We assessed delayed recall and recognition by RAVLT [List A, mean±SD, 11.3±2.3]

Visuospatial memory. This memory is a form of memory responsible for the recording of visual information about one's environment and identify, integrate, and analyze space and visual form, details, structure and spatial relations. This functioning was assessed by Rey-Osterrieth Complex Figure test¹² [30 min recall, 15±6.5] as described before.

Visuospatial functions

Visuospatial disorientation. Patients have been evaluated with specific tasks to identify possible spatial orientation disorders, also called topographic orientation disorders, that is, inability to judge the spatial orientation of objects or lines in space. The type of visuospatial deficit typically involves deficits in distinguishing familiar or unfamiliar places. *Benton's Judgment of Line Orientation test (BJLO)*¹³ [mean±SD, 11.5±2.1] was given to measure spatial thinking. Subjects were asked to match two angled lines to a set of 11 lines that are

arranged in a semicircle and separated 18 degrees from each other. The patient was also asked about if his/her location and surroundings are familiar or unfamiliar.

Visuospatial neglect. Spatial neglect is primarily a disorder of attention whereby patients characteristically fail to orientate, to report or to respond to stimuli located on the contralesional side.¹⁴ *Line bisection task*, (patients were required to bisect 10 horizontal lines measuring 18 cm with their dominant hand [mean±SD, 6±1.5 mm];¹⁵ and the bells test, consisting in encircling the bells (n=35) among distractors (n=280) [mean±SD, 6±1]¹⁶ were used for quantitative and qualitative assessment of visual neglect in the near extrapersonal space.

Motor neglect. Motor neglect is defined as underutilisation of one side, without defects of strength, reflexes or sensibility.¹⁷ When the patient demonstrated *underutilisation of the upper extremity* for tasks that could be performed with the "healthy side" even when this was inconvenient, we accepted this neurological manifestation as a sign of motor neglect [when they required a change in position of the body for 5 times].

Visual extinction. In the same way, visual stimulations (finger movements) were applied either in a particular visual hemi-field (left or right) or in both visual hemi-fields at the same time. Visual extinction was diagnosed when bilateral stimulations were repeatedly judged as unilateral stimulation [5 tests in both visual hemi-fields].

Language functions.

Ege Aphasia Test was used to assess aspect of language functioning, including *naming* [maximum score is 60 points], *verbal fluency task* [maximum score is 10 points] and comprehension [maximum score is 10 points].¹⁸ Reading [maximum score is 20 points], writing [maximum score is 10 points], counting [maximum score is 24 points] were also assessed by the same battery.

Semantic processing

We used the *Pyramids and Palm Trees test (PPTT)*¹⁹ to examine the verbal (word comprehension) [mean±SD, 49.9±1.8] and non-verbal (picture comprehension) [mean±SD, 48.9±2.1] aspects of semantic processing. PPTT was administered to all subjects. Each page in the test booklet depicted the stimulus centered at the top of the page. There were two additional images, the target and a distracter. Subjects were asked to decide which of the additional items could best be matched to the stimulus. The maximum possible score was 52.

(b) Definition of motor disorders

Ataxia. Patient with ataxia experience a failure of muscle control in their arms and legs, resulting in a lack of balance and coordination or a disturbance of gait

Chorea. Chorea is an abnormal involuntary movement disorder which is characterized by brief, irregular contractions that are not repetitive or rhythmic, but appear to flow from one muscle to the next.

Dystonia. The dystonias are movement disorders in which sustained muscle contractions cause twisting and repetitive movements or abnormal postures. The movements could be involuntary and sometimes painful, may affect a single muscle; a group of muscles such as those in the arms, legs, or neck; or the entire body.

Hemiballismus. Hemiballismus is a movement disorder characterized with the appearance of flailing, ballistic, undesired movements of the limbs

Parkinsonism. Parkinsonism is any condition that causes a combination of the movement abnormalities characterized by tremor, bradykinesia, rigidity, and postural instability.

Tremor. Tremor is an unintentional, rhythmic, muscle movement involving to-and-fro movements of one or more parts of the body. Parkinsonian tremor is caused by damage to structures within the brain that control movement. The tremor is classically seen as a "pill-rolling" action of the hands but may also affect the chin, face, lips, and legs. Dystonic tremor occurs in individuals of all ages who are affected by dystonia, a movement disorder which

causes muscles to be over-active, resulting in abnormal postures or sustained, unwanted movements.

(c) Definition of behavioural disorders

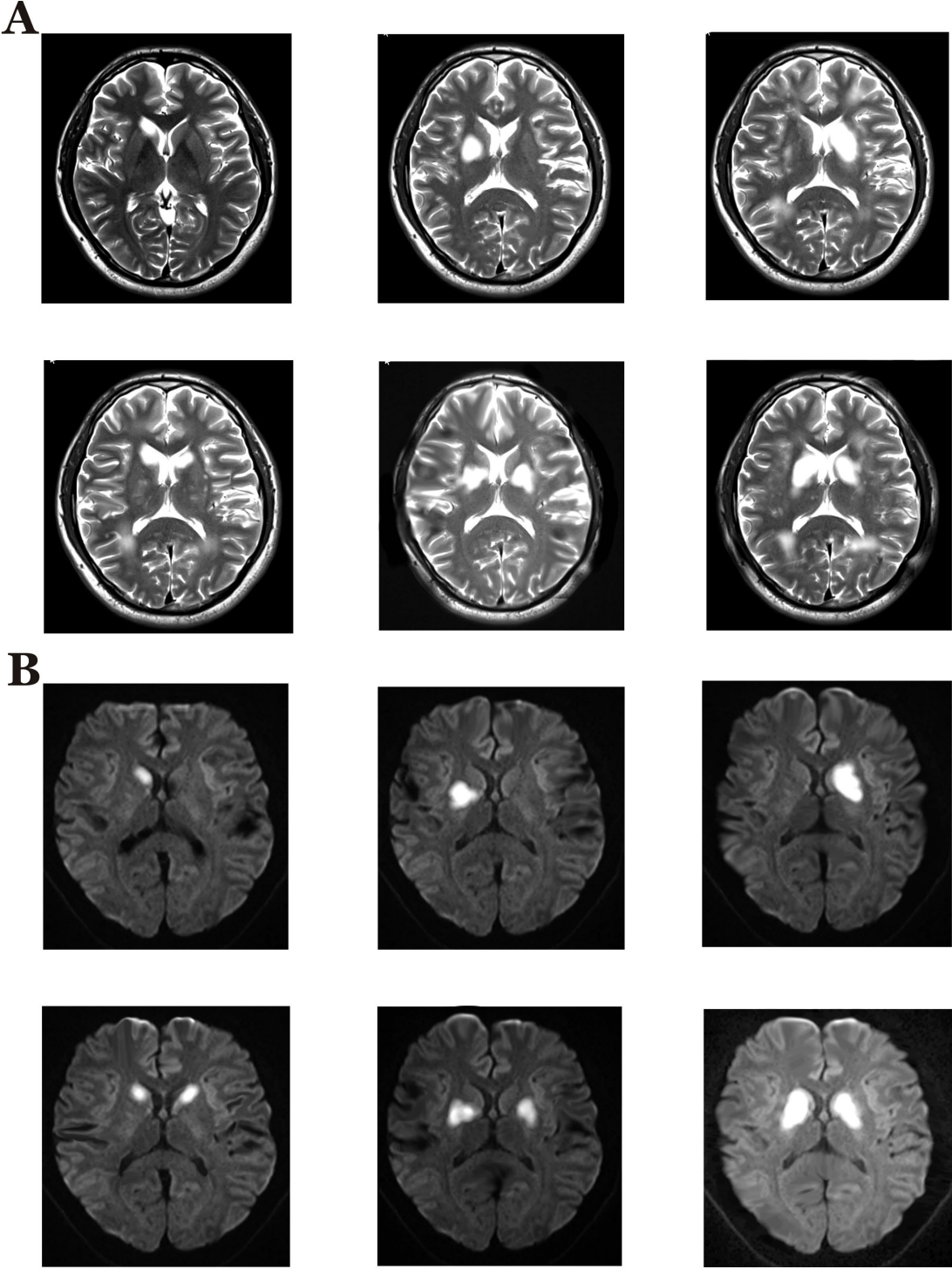
Abulia. Abulia is loss of drive, expression, loss of behavior and speech output, slowing and prolonged speech latency, and reduction of spontaneous thought content and initiative.

Apathy. Apathy refers to a reduction in self-initiated cognitive, emotional, and behavioural activity. Symptoms of apathy overlap with features of depression, but the two conditions are unique and can be reliably differentiated in patient samples.

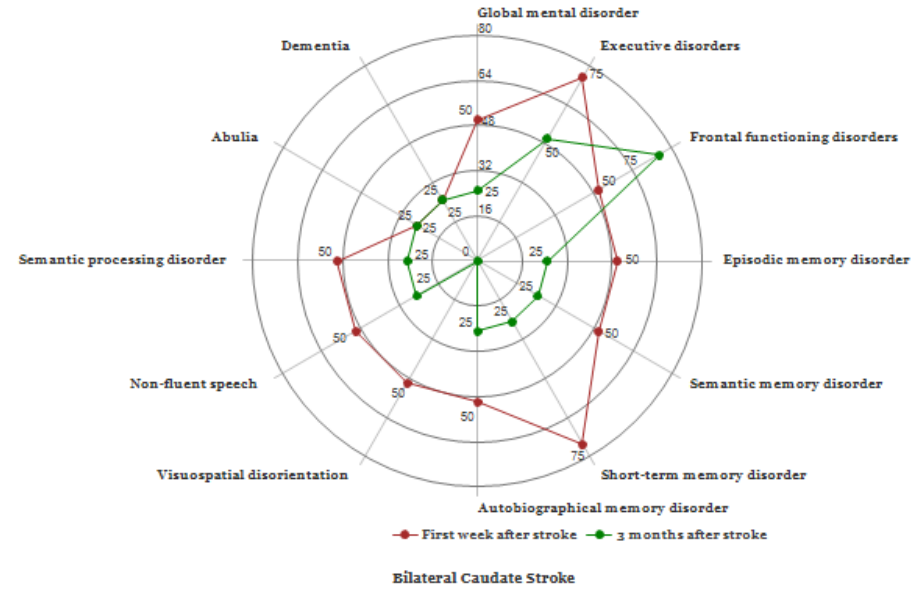
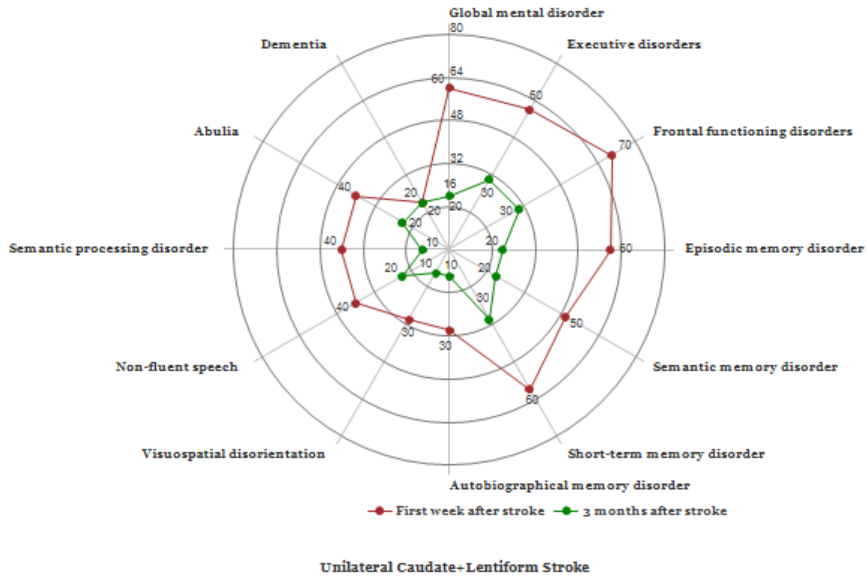
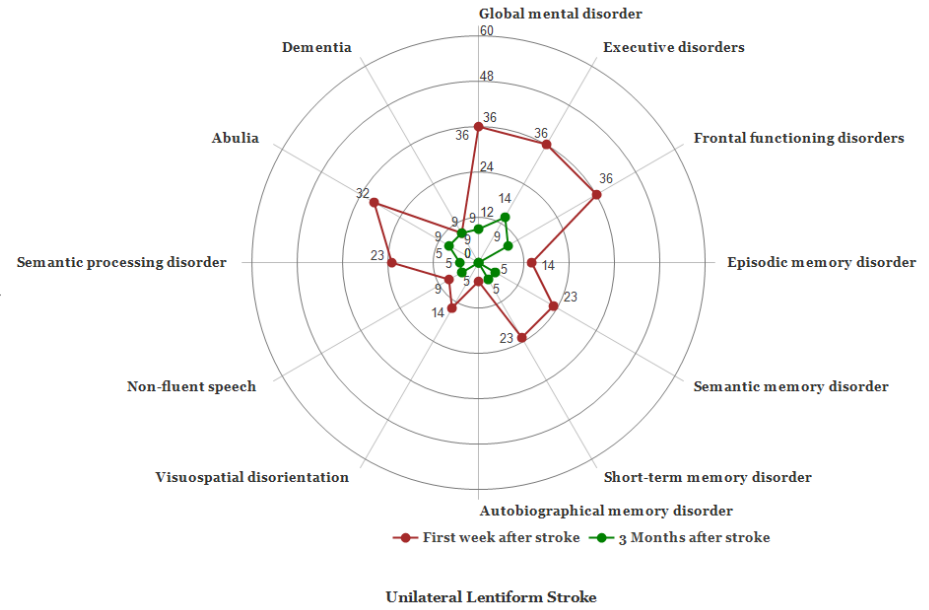
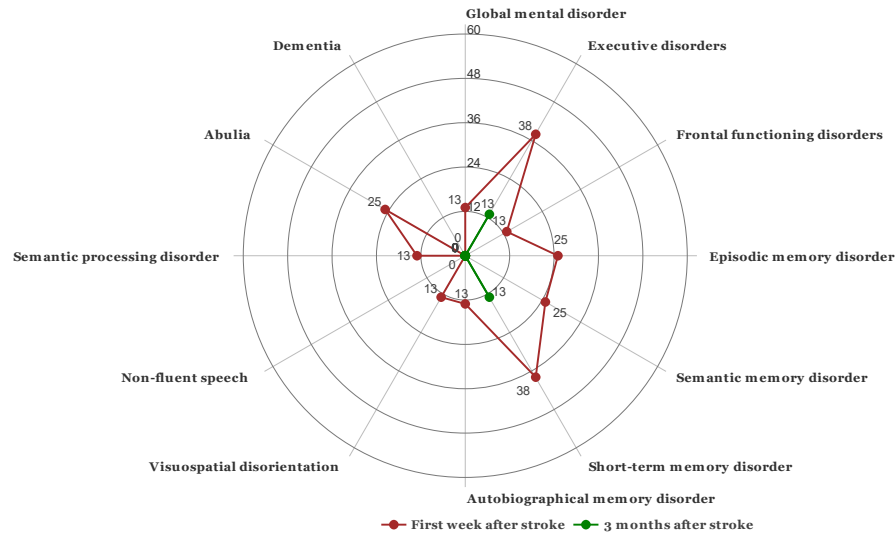
Dementia. Diagnosis of dementia (major neurocognitive disorder) neurocognitive disorder) was based on history, examination, and appropriate objective assessments, using standard criteria such as DSM-5.²⁰ For diagnosis of dementia, requires substantial impairment to be present in one or (usually) more cognitive domains. The impairment must be sufficient to interfere with independence in everyday activities.

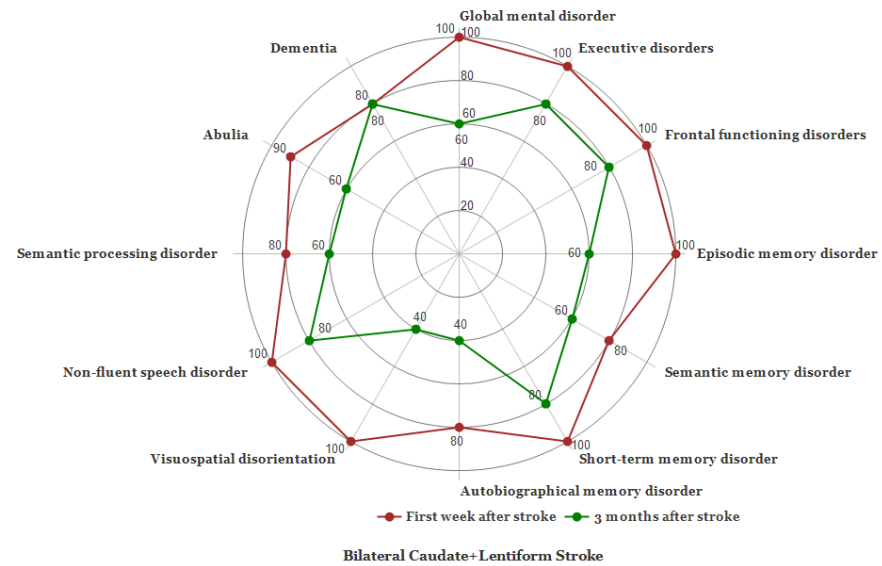
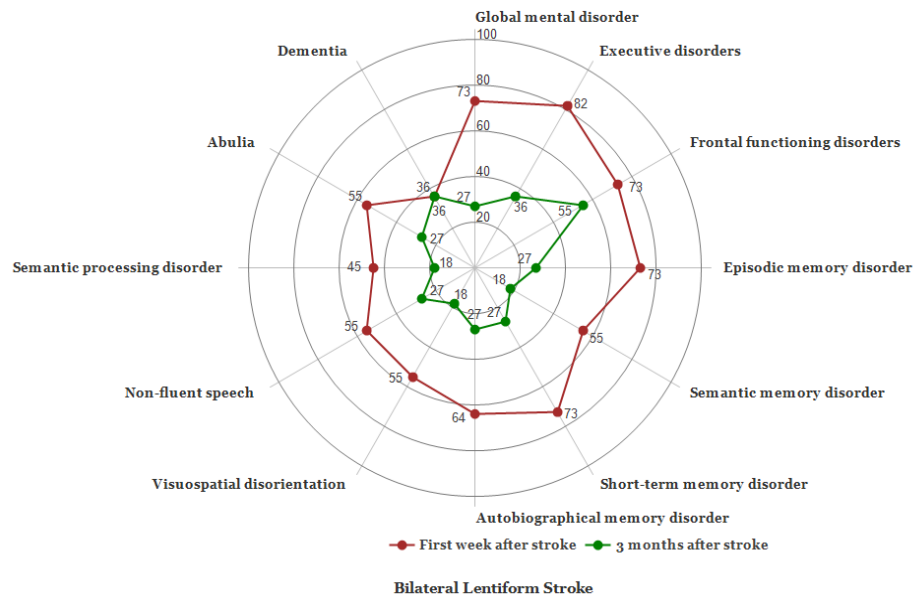
Perseveration. Perseveration is repetitive and continuous behaviour, speech or thought that occurs due to changes in cognitive skills such as memory, attention, and mental flexibility.

(2) Supplementary Figures



Supplementary Figure S1. (A) T₂-weighted MR images T₂-weighted MRI discloses unilateral and bilateral striatal infarcts ; (B) Diffusion-weighted MRI shows hyperintense signal in unilateral and bilateral striatum. These are brain MRI lesions observed in different types of striatal infarcts.





Supplementary Figure S2. Frequency (%) of broad categories of neuropsychological impairments in patients with unilateral and bilateral lesions. FS: first week after stroke; 3M: 3 months after stroke. See also *Table 1 and 2*.

(3) Supplementary Results

To assess whether patients with cognitive deficits (CDs) and patients without CDs were not different in terms of stroke volume in six distinct cognitive groups, we used the non-parametric Mann-Whitney test. We found that patients with executive disorders, memory disorders, visuospatial disorders, body awareness disorders, semantic processing disorders had larger stroke volume than patients without ($Z = -2.11, P = 0.035$).

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