Cognition and Functional Capacity After Thrombolysis: Preliminary Results in a Brazilian Sample

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Evidences support that thrombolysis is associated to a better functional outcome but not to intact cognition after subacute stroke. The purpose of this study is to compare cognition and functional capacity, 6–10 months after stroke, in patients treated with thrombolysis with rt-PA (tissular plasminogen activator) and those who were not. From October 2008 to March 2010, 15 patients treated with thrombolysis with rt-PA and 30 patients who did not receive this treatment, underwent an extensive neuropsychological assessment and answered questionnaire about functionality. General cognitive performance, measured through the mean score of each cognitive domain, showed impairment with \( z \) score \( \geq -1.50 \). Functional capacity was verified using PFAQ (Pfeffer Functional Activities Questionnaire) relative to instrumental activities of daily living. Five or more points in PFAQ demonstrated functional impairment. Continuous variables were analyzed by students’ \( t \)-test and categorical ones by Chi-square. Cognitive deficits were present in 20% of all subjects. In the group who received treatment with thrombolysis with rt-PA, 46.7% had language impairment, 33.3% had visuospatial impairment, and 26.7% had visual memory impairment. This group presented 20% of patients with functional impairment. General cognitive performance \( (p = 0.624) \) and functional capacity \( (p = 0.664) \) showed no difference between groups. There was a statistically significant difference between groups concerning neglect \( (p = 0.004) \) and sustained visual attention \( (p = 0.028) \). Findings suggest that patients who received thrombolysis presented less neglect and less visual attention deficits but did not show better general cognitive functioning or functional capacity.

**Keywords:** stroke, thrombolysis, cognition, neuropsychology, functional outcome

**Introduction**

The occlusion or rupture of the central nervous system arteries causing an interruption in cerebral blood flow is defined as a cerebrovascular accident or stroke (Chandra et al., 2006; Lotufo, 2005). Ischaemic stroke is the most common among adults (Chandra et al., 2006), causing loss of blood circulation in the affected region, depriving cerebral tissue from oxygen and necessary nutrients (Barker-Collo & Feigin, 2006; Lezak, Howieson, & Loring, 2004).

After stroke, many patients may present functional and cognitive impairment. Beyond these sequelae, stroke can harm the patients’ financial life and familial relationships and may cause an impact on the health
Cognition and functional capacity after thrombolysis

It is known that the brain can reorganize itself, resulting in cognitive improvement in the first month after stroke. However, some patients do not show any cognitive improvement and can deteriorate cognition in long term (Nys et al., 2005). Cognition may be stable during two years after stroke. Cognitive worsening is seen when dementia starts. Dementia may be reversed to mild cognitive impairment, but the frequency and circumstances are not clarified (Nys, van Zandvoort, de Kort, Jansen, de Haan, & Kapelle, 2007; Nys et al., 2005). Aging and feminine gender are identified as risk factors for cognitive impairment. Lesion volume is associated with adverse cognitive outcome after stroke. Cognitive impairment is associated to adverse functional outcome (Nys et al., 2005).

Treatment with thrombolysis with recombinant rt-PA (tissular plasminogen activator) has proven reduction of absolute risk and relative risk in morbidity (NINDS (The National Institute of Neurological Disorders and Stroke) rt-PA Stroke Study Group, 1995, as cited in Moro, Longo, & Massaro, 2009). It is associated to favorable clinical outcome in three months (Hacke et al., 1995; NINDS, 1995; as cited in Nys, van Zandvoort, Algra, Kappelle, & de Haan, 2006), in six months, and in one year (Kwiatkowski et al., 1999; as cited in Nys et al., 2006) after stroke. Thrombolysis allows the recanalization of occluded arteries, resulting in increase of cerebral reperfusion and reduction of lesion volume. Shorter is the time between stroke occurrence and its treatment, greater are the chances of success (ATLANTIS (Alteplase Thrombolysis for Acute Noninterventional Therapy in Ischemic Stroke), ECASS (The European Cooperative Acute Stroke Study), and NINDS rt-PA Study Group Investigators, 2004, as cited in Moro et al., 2009).

Thrombolysis is associated to a better functional outcome but not to an improved cognition after subacute stroke (Nys et al., 2006). Studies on neuropsychological outcomes and predictive studies of this pathology give useful information about cost-effectiveness of intervention programs aiming at social re-insertion of patients after a stroke episode (Barker-Collo & Feigin, 2006; Nys et al., 2005). In this context, the purpose of this study is to compare cognition and functional capacity, 6–10 months after stroke, in patients treated with thrombolysis with rt-PA and those who were not.

Method

Participants

From October 2008 to March 2010, 15 patients treated with thrombolysis with rt-PA (group T—“thrombolysis”) and 30 patients who did not receive it (group NT—“no thrombolysis”), previously admitted in a stroke unit of a public hospital and followed after discharge in an outpatient facility, underwent an extensive neuropsychological assessment and were questioned about their functional status.

Clinical variables were: stroke type, etiological diagnosis of ischemic stroke following TOAST (Trial of Org 10172 in Acute Stroke Treatment) criteria, subtype of ischemic stroke according to Bamford (1991) criteria (TACI (Total Anterior Circulation Infarct), PACI (Partial Anterior Circulation Infarct), POCI (Posterior Circulation Infarct) and LACI (Lacunar Infarct)), lesion location in brain CT (computerized tomography), stroke severity in admission measured by NIH-SS (National Institute of Health Stroke Scale), and pre-existing vascular risk factors. The vascular risk factors considered were: hypertension, diabetes mellitus, dyslipidemia, previous TIA (transient ischemic attack), migraine, alcohol consumption, congestive heart failure, angina, acute
myocardial infarction, tobacco use, intermittent claudication, endarterectomy, and contraceptive use. Tobacco use was considered as a vascular risk factor if the patient was a current smoker and alcohol consumption was registered if there was a consumption of 500 ml per day or an intoxication once a week at least (Cabral et al., 2009). An experienced stroke neurologist determined stroke type and location from CT or MRI (magnetic resonance image), following the established guidelines (Brazilian Society of Cerebrovascular Diseases, 2001). Socio-demographic variables used were age, gender, education, socioeconomic status (ABIPEME (Brazilian Association of Market Research Institutes), 2007), and labor status.

Subjects included in the sample fulfilled the following inclusion criteria: patients who had suffered first ischaemic stroke 6–10 months previously, those who received treatment with thrombolysis with rt-PA, those who did not present hemorrhagic transformation after treatment with thrombolysis with rt-PA, those who did not receive treatment with thrombolysis with rt-PA but had suffered first ischaemic stroke and were matched as a control group, and those who agreed in participate of this study. The exclusion criteria were: patients who had not suffered ischaemic stroke, those who had suffered previous stroke; patients who had not received treatment with thrombolysis with rt-PA and were not considered as a control group, those who were less than six months after stroke or more than 10 months after stroke, those who presented hemorrhagic transformation after thrombolysis, those who presented psychiatric illness and/or dementia, and those who presented comprehension deficits or expressive language deficits (aphasia).

Instrumentation

Concerning neuropsychological examination, raw scores found in the neuropsychological tests were grouped in the following cognitive domains:

(1) Reasoning: Similarities (WAIS-III) (Wechsler, 2004);

(2) Verbal memory: Rey Auditory Verbal Learning Test (Malloy-Diniz, Lasmar, Gazinelli, Fuentes, & Salgado, 2007; Rey, 1964; as cited in Lezak, Howieson, & Loring, 2004);

(3) Visuospatial memory: Rey-Osterrieth Complex Figure Test (Rey, 1941; as cited in Lezak et al., 2004; Rey, 1998, 1999);

(4) Attention: Mental Control (WMS-III) (Wechsler, 1997), Trail Making Test (Army Individual Test Battery, 1944; as cited in Lezak et al., 2004; Oliveira-Souza et al., 2000); Digit Span (WAIS-III) (Wechsler, 2004);

(5) Neglect: Cancellation task—unstructured letters (Weintraub, 2000);

(6) Language: COWA (Controlled Word Association) Test (Benton & Hamsher, 1989; as cited in Lezak et al., 2004; Machado, Fichman, Santos, Carvalho, Fialho, Koenig, & Caramelli, 2009), Category Fluency Test (Fichman et al., 2009; Lezak et al., 2004), Boston Naming Test (Kaplan, Goodglass, & Weintraub, 1983; Mansur, Radanovic, Araújo, Taquemori, & Greco, 2006), and Token Test—Chalfont version (De Renzi & Vognolo, 1962, as cited in Lezak et al., 2004; M. J. Mäder, personal communication, May 5, 2000);

(7) Visuospatial organization: Clock Drawing Test (Atalaia-Silva & Lourenço, 2009; Spren & Strauss, 1998), ROCFT (Rey-Osterrieth Complex Figure Test—copy trial) (Rey, 1941, as cited in Lezak et al., 2004);

(8) Executive functions: Weigl Test (Weigl, 1941; as cited in Lezak et al., 2004), Modified Wisconsin Sorting Cards Test (Lezak et al., 2004; M. J. Mäder, personal communication, May 5, 2000; Nelson, 1976), Stroop Test (Stroop, 1935; as cited in Lezak et al., 2004), and Verbal Fluency Test (COWA Test) (Benton & Hamsher, 1989; as cited in Lezak et al., 2004; Machado et al., 2009);
(9) Motor function: Luria’s Fist-Edge-Palm Test (Luria, 1966; as cited in Lezak et al., 2004; Nitrini, Caramelli, Herrera, Charchat-Fichman, & Porto, 2005);

(10) Functional capacity: PFAQ (Pfeffer Functional Activities Questionnaire) (Pfeffer, Kurosaki, Harrah, Chance, & Filos, 1982).

Research Design and Analysis

This was an observational longitudinal case-control study.

The raw scores obtained in neuropsychological tests were categorized in the groups “with cognitive impairment” and “no cognitive impairment”. In order to establish mean and SD (standard deviation) of neuropsychological assessment was administered to a control group composed by 54 community-dwellers. General cognitive performance was measured through the overall mean score of each cognitive domain. Cognitive impairment was considered present with a z score $\geq$ -1.50. Functional capacity was relative to instrumental activities of daily living, and in the questionnaire (PFAQ), a score of five or more points demonstrates functional impairment. Therefore, the raw scores found in PFAQ were categorized in “with functional impairment” and “no functional impairment”. Continuous variables were analyzed by students’ $t$-test and categorical ones by Chi-square.

Ethics

This study was approved by the ethics committee of the University of the Region of Joinville under the protocol 110/09.

Results

Compared to the general group of patients (subjects), control group did not differ in age, education, and socioeconomic status, but there was a statistically significant difference concerning gender ($p < 0.001$) (see Table 1).

| Variable          | Subject (T + NT) n = 45 (100%) | Control n = 54 (100%) | $p$-value |
|-------------------|---------------------------------|-----------------------|----------|
| Age (years)       | Mean (SD) 59.96 (13.17)         | 60.06 (12.15)         | 0.964    |
| Educational level | Mean (SD) 5.02 (3.56)           | 6.261 (3.08)          | 0.067    |
| Gender            | Male 33 (73.3) Female 12 (26.7) | 18 (33.3) Female 36 (66.7) | < 0.001 |
| Socioeconomic status | C 25 (55.6) B 10 (22.2) A 0 (0.0) | D 7 (15.6) E 3 (6.7) | 0.314 |

The comparison of the neuropsychological characteristics of the sample and the control group shows a statistically significant difference in measures of declarative memory (verbal and visual), visuospatial functions, verbal functions, reasoning, neglect, and motor functions (see Table 2). However, there was no difference in three aspects concerning measures of executive functions (errors, perseverative errors, and perseverative errors percentage of Modified Wisconsin Cards Sorting Test) and in one aspect of attention measure (time elapsed in Trail Making Test part B) among the three groups. Those results, therefore, showed that there was difference in neuropsychological performance in the majority of the tests used.
### Table 2

**Neuropsychological Characteristics of the Sample, the Participants Treated With Thrombolysis With rt-PA, the Participants Not Treated With Thrombolysis With rt-PA and the Control Group (Numerical Variables)**

| Variable | Subject (T + NT) n = 45 (100%) Mean (SD) | No thrombolysis (NT) n = 30 (66.7%) Mean (SD) | Thrombolysis (T) n = 15 (33.3%) Mean (SD) | Control (C) n = 54 Mean (SD) | p-value |
|----------|------------------------------------------|-----------------------------------------------|-------------------------------------------|-------------------------------|--------|
| RAVLT<sup>1</sup> | | | | | |
| Total | 29.38 (9.71) | 28.57 (10.25) | 31.00 (8.61) | 40.28 (10.61) | <0.0001 |
| A6 | 5.00 (3.10) | 4.90 (3.14) | 5.20 (3.12) | 7.63 (3.19) | <0.0001 |
| A7 (Recognition) | 4.67 (3.49) | 4.20 (3.53) | 5.60 (3.31) | 7.65 (3.02) | <0.0001 |
| ROCFT<sup>2</sup> | | | | | |
| Copy | 17.88 (10.26) | 16.58 (9.37) | 20.47 (11.76) | 27.84 (5.46) | <0.0001 |
| ROCFT<sup>2</sup> Mean (SD) | | | | | |
| Immediate memory | 8.11 (7.12) | 6.78 (6.44) | 10.77 (7.88) | 12.07 (6.05) | 0.002 |
| Delayed memory | 8.69 (7.62) | 7.42 (6.44) | 11.23 (9.30) | 12.75 (5.33) | 0.002 |
| Mental Control<sup>3</sup> | | | | | |
| Mean (SD) | 11.73 (4.36) | 11.43 (3.64) | 12.33 (5.64) | 16.26 (4.01) | <0.0001 |
| Verbal Fluency—Semantic<sup>4</sup> | | | | | |
| Mean (SD) | 6.18 (3.84) | 6.27 (3.16) | 6.00 (5.07) | 10.39 (3.38) | <0.0001 |
| Clock Drawing Test<sup>5</sup> | | | | | |
| Mean (SD) | 111.29 (85.78) | 130.93 (94.16) | 72.00 (47.78) | 61.72 (24.85) | <0.0001 |
| Trail Making Test<sup>7</sup> | | | | | |
| Mean (SD) | 191.11 (8.52) | 20.30 (6.95) | 16.33 (10.91) | 23.96 (0.19) | <0.0001 |
| Token Test<sup>8</sup> | | | | | |
| Mean (SD) | 8.76 (4.04) | 8.90 (3.47) | 8.47 (5.12) | 11.87 (9.19) | <0.0001 |
| Digit Span<sup>9</sup> | | | | | |
| Mean (SD) | 1.60 (0.91) | 1.67 (0.84) | 1.47 (1.06) | 2.19 (0.70) | 0.002 |
| Digit Span<sup>9</sup> Mean (SD) | | | | | |
| Categories | 8.11 (4.51) | 8.23 (4.15) | 7.87 (5.30) | 6.69 (4.17) | 0.263 |
| Preservative errors | 4.20 (3.69) | 4.50 (3.20) | 3.60 (4.58) | 3.41 (2.62) | 0.311 |
| % Preservative errors | 50.99 (33.31) | 48.73 (40.58) | 52.12 (29.75) | 49.68 (31.96) | 0.928 |
| Cancellation Task<sup>11</sup> | | | | | |
| Mean (SD) | 269.73 (162.39) | 307.33 (163.64) | 194.27 (165.45) | 164.69 (72.53) | 0.446 |
| Similarities<sup>12</sup> | | | | | |
| Mean (SD) | 10.33 (6.68) | 9.60 (5.80) | 11.80 (8.10) | 14.35 (7.13) | 0.012 |

**Notes.**<sup>1</sup> Rey Auditory Verbal Learning Test;<sup>2</sup> Rey-Osterrieth Complex Figure Test;<sup>3</sup> Mental Control (WMS-III);<sup>4</sup> Verbal Fluency—phonological;<sup>5</sup> Verbal Fluency—semantic;<sup>6</sup> Clock Drawing Test;<sup>7</sup> Trail Making Test;<sup>8</sup> Token Test;<sup>9</sup> Modified Wisconsin Card Sorting Test;<sup>10</sup> Digit Span (WAIS-III);<sup>11</sup> Cancellation task—Mesulam;<sup>12</sup> Similarities (WAIS-III);<sup>13</sup> Stroop Test; and<sup>14</sup> Boston Naming Test.
Table 3
Socio-demographic Characteristics of the Sample, the Participants Treated With rt-PA and the Participants Not Treated With Thrombolysis With rt-PA

| Variable         | Subject (T + NT) | No thrombolysis (NT) | Thrombolysis (T) | p-value |
|------------------|------------------|----------------------|------------------|---------|
| Gender           |                  |                      |                  |         |
| Female           | 13 (28.9)        | 8 (26.7)             | 5 (33.3)         | 0.646   |
| Male             | 32 (71.1)        | 22 (73.3)            | 10 (66.7)        |         |
| Mean (SD)        | 59.96 (13.17)    | 61.57 (12.38)        | 56.73 (14.53)    |         |
| Age (years)      |                  |                      |                  |         |
| ≥ 60             | 24 (53.3)        | 18 (60.0)            | 6 (42.9)         | 0.230   |
| 46–59            | 14 (31.1)        | 8 (26.7)             | 6 (42.9)         | 0.250   |
| ≤ 45             | 7 (15.6)         | 4 (13.3)             | 2 (14.2)         |         |
| Mean (SD)        | 5.02 (3.56)      | 4.80 (2.99)          | 5.47 (4.60)      |         |
| Educational level| +8               | 7 (15.6)             | 3 (20.0)         | 0.560   |
|                  | 5–8              | 11 (24.4)            | 8 (31.1)         |         |
|                  | ≤ 4              | 27 (60)              | 19 (63.3)        |         |
| Retirement       | Yes              | 26 (57.8)            | 20 (66.7)        | 0.091   |
|                  | No               | 19 (42.2)            | 10 (33.3)        |         |

Stroke survivors treated with thrombolysis with rt-PA did not differ from those who did not receive this treatment in relation to age, sex, education (in years), and stroke severity in admission (see Table 3).

Most patients had suffered supratentorial (88.9%), atherothrombotic strokes (64.4%), with PACI (partial anterior circulation syndrome) as seen in Table 4. Groups did not differ in age (p = 0.250), gender (p = 0.646), educational level (p = 0.560), stroke severity measured by NIH-SS (p = 0.080), Bamford (1991) criteria (p = 0.768), TOAST classification (p = 0.097), and side of lesion (p = 0.190). The mean age in group T was of 56.73 years (SD = 14.53). The mean educational level was 5.5 years of schooling (SD = 4.60), 57.1% were working and 46.7% had left hemisphere lesions. Group NT had a mean age of 61.57 (SD = 12.38), 4.8 years of education (SD = 2.99) in average, 66.7% were retired and 60% had right hemisphere lesions.

The comparison between raw scores found in the two groups (T and NT) showed statistically significant difference in the following tests: Cancellation task—unstructured letters (p = 0.026), Trail Making Test—form A, time elapsed (p = 0.028), and Stroop Test II—errors (p = 0.007). The Stroop Effect (III/I) showed bordering results (p = 0.050) as seen in Table 5.
### Table 4 continued

| Variable       | Subject (T + NT) n = 45 (100%) | No thrombolysis (NT) n = 30 (66.67%) | Thrombolysis (T) n = 15 (33.33%) | p-value |
|----------------|---------------------------------|--------------------------------------|----------------------------------|---------|
| Hemisphere     |                                 |                                      |                                  |         |
| Right          | 24 (53.4)                       | 18 (60.0)                            | 6 (40.0)                         |         |
| Left           | 17 (37.8)                       | 10 (33.3)                            | 7 (46.7)                         |         |
| Bilateral      | 2 (4.4)                         | 1 (3.3)                              | 1 (6.7)                          | 0.190   |
| Brain stem     | 1 (2.2)                         | 1 (3.3)                              | 0                                |         |
| Bilateral + brain stem | 1 (2.2) | 0                                      | 1 (6.7)                          |         |
| Hypertension   |                                 |                                      |                                  |         |
| Yes            | 31 (68.9)                       | 21 (70.0)                            | 10 (66.7)                        | 0.822   |
| No             | 14 (31.1)                       | 9 (30.0)                             | 5 (33.3)                         |         |
| Diabetes mellitus |                                 |                                      |                                  |         |
| Yes            | 9 (20)                          | 7 (23.3)                             | 2 (13.3)                         | 0.434   |
| No             | 36 (80)                         | 23 (76.7)                            | 13 (86.7)                        |         |
| Dyslipidemia   |                                 |                                      |                                  |         |
| Yes            | 6 (13.3)                        | 4 (13.3)                             | 2 (13.3)                         | 0.143   |
| No             | 39 (86.7)                       | 26 (86.7)                            | 13 (86.7)                        |         |
| Previous TIA   |                                 |                                      |                                  |         |
| Yes            | 3 (6.7)                         | 2 (6.7)                              | 1 (6.7)                          | 1.000   |
| No             | 41 (91.1)                       | 26 (86.7)                            | 0                                |         |
| Migraine       |                                 |                                      |                                  |         |
| Yes            | 6 (13.3)                        | 4 (13.3)                             | 2 (13.3)                         | 0.143   |
| No             | 39 (86.7)                       | 26 (86.7)                            | 13 (86.7)                        |         |
| Alcohol consumption |                                 |                                      |                                  |         |
| Yes            | 9 (20)                          | 8 (26.7)                             | 1 (6.7)                          | 1.000   |
| No             | 36 (80)                         | 22 (73.3)                            | 14 (93.3)                        |         |
| Congestive heart failure |                                 |                                      |                                  |         |
| Yes            | 2 (4.4)                         | 2 (6.7)                              | 0                                | 0.312   |
| No             | 43 (95.6)                       | 28 (93.3)                            | 0                                |         |
| Angina         |                                 |                                      |                                  |         |
| Yes            | 2 (4.4)                         | 2 (6.7)                              | 0                                | 0.312   |
| No             | 43 (95.6)                       | 28 (93.3)                            | 0                                |         |
| Acute myocardial infarction |                                 |                                      |                                  |         |
| Yes            | 4 (8.9)                         | 4 (13.3)                             | 0                                | 0.143   |
| No             | 41 (91.1)                       | 26 (86.7)                            | 0                                |         |
| Tobacco use    |                                 |                                      |                                  |         |
| Yes            | 22 (48.9)                       | 17 (56.7)                            | 5 (33.3)                         | 0.144   |
| No             | 23 (51.1)                       | 13 (43.3)                            | 10 (66.7)                        |         |
| Intermittent claudication |                                 |                                      |                                  |         |
| Yes            | 1 (2.2)                         | 1 (3.3)                              | 0                                | 0.480   |
| No             | 44 (97.8)                       | 29 (96.7)                            | 0                                |         |
| Endarterectomy |                                 |                                      |                                  |         |
| Yes            | 1 (2.2)                         | 0                                    | 1 (6.7)                          | 0.157   |
| No             | 44 (97.8)                       | 0                                    | 14 (93.3)                        |         |
| Contraceptive use |                                 |                                      |                                  |         |
| Yes            | 2 (4.4)                         | 1 (3.3)                              | 1 (6.7)                          | 0.613   |
| No             | 43 (95.6)                       | 29 (96.7)                            | 14 (93.3)                        |         |

**Notes.** 1LACI: Lacunar Infarct; 2TACI: Total Anterior Circulation Infarct; 3PACI: Partial Anterior Circulation Infarct; and 4POCI: Posterior Circulation Infarct.

### Table 5

**Neuropsychological Characteristics (Numerical Variables) of Participants Treated and Not Treated With Thrombolysis With rt-PA**

| Variable       | Subject (T + NT) n = 45 (100%) | No thrombolysis (NT) n = 30 (66.67%) | Thrombolysis (T) n = 15 (33.33%) | p-value |
|----------------|---------------------------------|--------------------------------------|----------------------------------|---------|
| RAVLT<sup>1</sup> |                                 |                                      |                                  |         |
| A1             | 3.42 (1.63)                     | 3.43 (1.45)                          | 3.40 (1.99)                      | 0.949   |
| A5             | 7.62 (2.88)                     | 7.23 (2.94)                          | 8.40 (2.67)                      | 0.407   |
| Total          | 29.38 (9.71)                    | 28.57 (10.25)                        | 31.00 (8.61)                     | 0.434   |
| Mean (SD)      | 5.00 (3.10)                     | 4.90 (3.14)                          | 5.20 (3.12)                      | 0.764   |
| A7             | 4.67 (3.49)                     | 4.20 (3.53)                          | 5.60 (3.31)                      | 0.208   |
| Recognition    | 10.96 (3.11)                    | 10.67 (3.26)                         | 11.53 (2.80)                     | 0.385   |
| ROCFT<sup>2</sup> |                                 |                                      |                                  |         |
| Copy           | 17.88 (10.26)                   | 16.58 (9.37)                         | 20.47 (11.76)                    | 0.236   |
| Mean (SD)      | 8.11 (7.12)                     | 6.78 (6.44)                          | 10.77 (7.88)                     | 0.077   |
| Immeante memory |                                 |                                      |                                  |         |
| Delayed memory | 8.69 (7.62)                     | 7.42 (6.44)                          | 11.23 (9.30)                     | 0.114   |
| Mental Control<sup>3</sup> Mean (SD) | 11.73 (4.36) | 11.43 (3.64) | 12.33 (5.64) | 0.520   |
| Verbal Fluency—FAR<sup>4</sup> TOTAL (F + A + R) Mean (SD) | 16.80 (9.88) | 17.03 (8.64) | 16.33 (12.31) | 0.826   |
### Table 5 Continued

| Variable                  | Subject (T + NT) n = 45 (100%) | No thrombolysis (NT) n = 30 (66.7%) | Thrombolysis (T) n = 15 (33.3%) | p-value |
|---------------------------|---------------------------------|-------------------------------------|--------------------------------|---------|
| **Verbal**                |                                 |                                     |                                |         |
| Fluency—Semantic<sup>5</sup> | Animals 9.31 (3.98)          | 9.47 (3.33)                        | 9.00 (5.17)                    | 0.715   |
| Mean (SD)                 | 6.62 (3.07)                     | 6.97 (2.71)                        | 5.93 (3.69)                    | 0.292   |
| **Clock Drawing Test<sup>6</sup>** | Time—part A 111.29 (85.78)     | 130.93 (94.16)                     | 72.00 (47.78)                  | 0.028   |
|                          | Connections—part A 19.11 (8.52) | 20.30 (6.95)                       | 16.33 (10.91)                  | 0.189   |
|                          | Time—part B 180.93 (155.27)    | 194.27 (165.45)                    | 154.27 (133.86)                | 0.422   |
|                          | Connections—part B 8.87 (9.19)  | 8.40 (8.86)                        | 9.80 (10.06)                   | 0.635   |
| **Token Test<sup>8</sup>** | Mean (SD) 8.76 (4.04)          | 8.90 (3.47)                        | 8.47 (5.12)                    | 0.739   |
| **DIGIT SPAN<sup>9</sup>** | Forward 6.22 (2.25)            | 5.80 (1.85)                        | 7.07 (2.79)                    | 0.075   |
|                          | Backward 2.89 (1.67)           | 2.80 (1.54)                        | 3.07 (1.94)                    | 0.619   |
|                          | Total 9.11 (3.46)              | 8.60 (2.79)                        | 10.13 (4.45)                   | 0.163   |
| **Cancellation Task<sup>10</sup>** | Time 269.73 (162.39)         | 307.33 (163.64)                    | 194.53 (135.38)                | 0.026   |
|                          | Omissions left 2.82 (5.71)     | 3.90 (6.74)                        | 0.67 (0.90)                    | 0.073   |
|                          | Omissions right 2.33 (4.12)    | 3.07 (4.84)                        | 0.87 (1.19)                    | 0.092   |
| **Similarities<sup>11</sup>** | Mean (SD) 10.33 (6.68)         | 9.60 (5.80)                        | 11.80 (8.10)                   | 0.303   |
| I                        | Time 36.09 (19.50)             | 36.47 (19.89)                      | 35.33 (19.34)                  | 0.857   |
|                          | Errors 1.16 (2.01)             | 1.10 (2.23)                        | 1.27 (1.53)                    | 0.797   |
| II                       | Time 39.78 (23.54)             | 41.17 (24.84)                      | 37.00 (21.24)                  | 0.122   |
|                          | Errors 1.53 (2.24)             | 1.73 (2.57)                        | 1.13 (1.36)                    | 0.007   |
| III                      | Time 53.09 (30.68)             | 58.10 (31.71)                      | 43.07 (26.71)                  | 0.582   |
|                          | Errors 3.89 (4.48)             | 5.13 (4.95)                        | 1.40 (1.55)                    | 0.404   |
|                          | Stroop Effect (II/I) 1.50 (0.73)| 1.65 (0.76)                        | 1.20 (0.55)                    | 0.050   |
| **Boston Naming Test<sup>13</sup>** | Mean (SD) 32.27 (13.91)    | 30.87 (11.79)                      | 35.07 (17.54)                  | 0.346   |

**Notes.** 1 Rey Auditory Verbal Learning Test; 2 Rey-Osterrieth Complex Figure Test; 3 Mental Control (WMS-III); 4 Verbal Fluency—phonological; 5 Verbal Fluency—semantic; 6 Clock Drawing Test; 7 Trail Making Test; 8 Token Test; 9 Digit Span (WAIS-III); 10 Cancellation task—Mesulam; 11 Similarities (WAIS-III); 12 Stroop Test; and 13 Boston Naming Test.

In Table 6, the neuropsychological characteristics are shown in specific cognitive domains. Considering all subjects, the most prominent impairments were: language (37.8%), visuospatial organization (33.3%), and visual memory (31.1%). Group T presented the same pattern of deficits as the whole group. Forty-six point seven percent of the patients who received thrombolysis had language impairment. Thirty-three point three percent had visuospatial impairment and 26.7% had visual memory impairment. The subjects from group NT showed neglect (40%). Language, visuospatial organization, verbal memory, and visual memory impairments were present, each one in 33.3% of the subjects. There was a statistically significant difference between groups concerning neglect ($p = 0.004$).

Functional impairment was seen in 37.8% of all subjects and cognitive impairment in 24.4% of them. Functional with cognitive impairment was seen in 20% of the subjects in group T while 26.7% of the subjects in group NT presented those deficits. Finally, Table 7 shows that general cognitive performance ($p = 0.624$) and functional capacity ($p = 0.664$) showed no difference between groups.
Table 6
Neuropsychological Characteristics in Cognitive Domains of Participants Treated and Not Treated With Thrombolysis With rt-PA

| Variable         | Subject (T + NT)  | No thrombolysis (NT) | Thrombolysis (T) | p-value |
|------------------|-------------------|----------------------|------------------|---------|
| Reasoning¹       | With impairment   | 3 (6.7)              | 2 (6.7)          | 1 (6.7) | 1.000 |
|                  | No impairment     | 42 (93.3)            | 28 (93.3)        | 14 (93.3) | 0.153 |
| Verbal           | With impairment   | 12 (26.7)            | 10 (33.3)        | 2 (13.3) | 0.649 |
|                  | No impairment     | 33 (73.3)            | 20 (66.7)        | 13 (86.7) | 0.624 |
| Memory²          | With impairment   | 14 (31.1)            | 10 (33.3)        | 4 (26.7) | 0.004 |
|                  | No impairment     | 31 (68.9)            | 20 (66.7)        | 11 (73.3) | 0.384 |
| Visual           | With impairment   | 11 (24.4)            | 8 (26.7)         | 2 (13.3) | 0.100 |
|                  | No impairment     | 34 (75.6)            | 22 (73.3)        | 13 (86.7) | 0.664 |
| Attention²       | With impairment   | 12 (26.7)            | 12 (40.0)        | 0 (0.0) | 0.097 |
|                  | No impairment     | 33 (73.3)            | 18 (60.0)        | 15 (100.0) | 0.000 |
| Language³        | With impairment   | 17 (37.8)            | 10 (33.3)        | 7 (46.7) | 0.384 |
|                  | No impairment     | 28 (62.2)            | 20 (66.7)        | 8 (53.3) | 0.682 |
| Visualspatial    | With impairment   | 15 (33.3)            | 10 (33.3)        | 5 (33.3) | 0.000 |
|                  | No impairment     | 30 (66.7)            | 20 (66.7)        | 10 (66.7) | 0.153 |
| Organization⁴    | With impairment   | 2 (4.4)              | 1 (3.3)          | 1 (6.7) | 0.153 |
|                  | No impairment     | 43 (95.6)            | 29 (96.7)        | 14 (93.3) | 0.624 |
| Executive        | With impairment   | 4 (8.9)              | 4 (13.3)         | 0 (0.0) | 0.978 |
|                  | No impairment     | 41 (91.1)            | 26 (86.7)        | 15 (100.0) | 0.664 |

Notes.
1 Reasoning: Similarities (WAIS-III); 2 Verbal Memory: delayed recall—Rey Auditory Verbal Learning Test (A7—RAVLT); 3 Visual Memory: delayed recall—Rey-Osterrieth Complex Figure Test; 4 Attention: Mental Control (WMS-III), Digit Span (WAIS-III), Trail Making Test—part A, Trail Making Test—part B, Stroop Effect (III/I); 5 Neglect: Cancellation task time elapsed, Cancellation task left omissions, Cancellation task right omissions; 6 Language: Verbal Fluency—phonological (FAR), Verbal Fluency Semantic (Animals), Token Test, Boston Naming Test, Similarities; 7 Visuospatial Organization: Clock Drawing Test, Rey-Osterrieth Complex Figure Test (copy); 8 Executive Functions: Modified Wisconsin Cards Sorting Test (number of categories), Modified Wisconsin Cards Sorting Test (number of errors), Modified Wisconsin Cards Sorting Test (number of perseverative errors), Trail Making Test—part B; 9 Motor Functions: Luria task (Fist—Edge—Palm); 10 General Cognitive Performance: cognitive domain’s mean: verbal memory, visual memory, attention, neglect, language, visuospatial organization, executive functions and motor functions; and 11 Functionality: Functional Activities Questionnaire (Pfeffer et al., 1982).

Table 7
Cognitive Performance and Functional Capacity of the Participants Treated With Thrombolysis With rt-PA and the Participants Not Treated With Thrombolysis With rt-PA

| Variable         | Subject (T + NT)  | No thrombolysis (NT) | Thrombolysis (T) | p-value |
|------------------|-------------------|----------------------|------------------|---------|
| General cognition performance¹ | z-score | -0.94 (0.96) | -1.08 (0.93) | -0.65 (0.25) | 0.153 |
|                  | With cognitive impairment | 11 (24.4) | 8 (26.7) | 3 (20.0) | 0.624 |
|                  | No cognitive impairment | 34 (75.6) | 22 (73.3) | 12 (80.0) | 0.978 |
| Functional status² | With functional impairment | 17 (37.8) | 8 (26.7) | 3 (20.0) | 0.664 |
|                  | No functional impairment | 28 (62.2) | 22 (73.3) | 12 (80.0) | 0.978 |

Notes.
1 General cognitive performance obtained through cognitive domain’s mean: verbal memory, visual memory, attention, neglect, language, visuospatial organization, executive functions, motor functions; and 2 Functional status measured by Functional Activities Questionnaire (Pfeffer et al., 1982).

Discussion and Conclusions

The present study showed that patients who received thrombolysis presented less neglect but did not show better cognitive functioning or functional capacity. Kettunen, Nurmi, Koivisto, Dastidar, and Jehkonen (2012) observed that thrombolysis was an independent predictor of the absence of neglect in right hemisphere stroke...
patients. According to literature, the study of Nys et al. (2006) did not show any difference in cognitive performance when comparing patients who had received thrombolysis to those who did not. In the present study, 80% of the patients who received thrombolysis showed intact cognitive and functional status seven months after stroke, in average. Nys et al. (2006) verified 52% of subjects with intact cognitive functioning and 83% without functional impairment, after thrombolysis, six months after stroke. This group found that only basic functional outcome was associated with thrombolysis. They assumed that this treatment might have a short-term influence on cognitive function but not in long term (Nys et al., 2006).

In our study, patients who received thrombolytic treatment showed less sustained visual attentional deficits. Barker-Collo, Feigin, Lawes, Senior, and Paraq (2010) observed the presence of attentional deficits six months after stroke that improved with time. They also verified that sustained visual attention, measured by Trail Making Test—form A, as in this study, emerged as a predictor of cognitive ability and that attentional deficits were associated with functional impairment. Hyndman, Pickering, and Ashburn (2008) reported the association between attention and functional status after stroke. In another study, Nys et al. (2005) found that perceptual and attentional dysfunction emerged as functional impairment predictors in follow-up.

This study intends to demonstrate how neuropsychological assessment can play an important role in stroke recovery, even if it is not possible to assess patients in the acute phase, it is feasible and necessary during outpatient follow-up. So, if one can gather accurate information about the patients’ cognitive functioning and his functional capacity, it might help in decision-making. After stroke, important decisions concerning patients’ return to work or independent life must be taken. In some cases, changes in daily life can improve quality of life. Therefore, cognitive deficits and functional impairment after stroke may influence the return to previous occupation or to an independent life despite physical recovery (Gottesmann & Hillis, 2010).

Finally, the findings suggest that patients who received thrombolysis presented less neglect but did not show better cognitive functioning or functional capacity. These patients also showed less visual attention deficits. We hypothesize that thrombolysis might have some influence on long-term cognition, however, other studies did not verified it. Future studies are needed to clarify this assumption.

**Limitations**

We consider as weaknesses of this study the small sample used; the neglect assessment that used only one cancellation task; the fact that functional capacity was not verified through FIM (functional independence measure); and due to logistic reasons, the impossibility to have BI (Barthel index) in discharge. As strength of our work, we see the fact that in the context of outpatient follow-up, neuropsychological assessment can bring useful information and help professionals, families, and patients to make important decisions and changes in their life. To our knowledge, this study is the first to happen in Brazil.

**References**

ABIPEME (Brazilian Association of Market Research Institutes). (2007). *Critério de classificação socioeconômico do Brasil (CCSEB)*. São Paulo: ABA, ANEP, ABIPEME. Retrieved from http://www.abep.org/codigosguias/CCEB2008-Base2006e2007.pdf

Atalaia-Silva, K. C., & Lourenço, R. A. (2008). Translation, adaptation and construct validation of the clock test among elderly in Brazil. *Public Health Journal, 42*(5), 930-937. doi: 10.1590/S0034-89102008000500020

Bamford, J., Sandercock, P., Dennis, M., Burn, J., & Warlow, C. (1991). Classification and natural history of clinically identifiable subtypes of cerebral infarction. *Lancet, 337*(8756), 1521-1526. doi: 10.1016/0140-6736(91)93206-O
Barker-Collo, S., & Feigin, V. (2006). The impact of neuropsychological deficits on functional stroke outcomes. *Neuropsychology Review, 16*, 53-64. doi:10.1007/s11065-006-9007-5

Barker-Collo, S., Feigin, S., Lawes, C., Senior, H., & Paraq, V. (2010). Natural history of attention deficits and their influence on functional recovery from acute stages to 6 months after stroke. *Neuropedemiology, 35*, 255-262. doi: 10.1159/000319894

Brazilian Society of Cerebrovascular Diseases. (2001). First Brazilian consensus of the acute phase of stroke. *Archives of Neuropsychiatry, 59*(4), 972-980. doi: 10.1590/S0004-282X2001000600026

Cabral, N. L., Gonçalves, A. R. R., Longo, A. L. L., & Eluf-Neto, J. (2009). Incidence of stroke subtypes, prognosis and prevalence of risk factors in Joinville, Brazil: A two-year, community-based study. *Journal of Neurology, Neurosurgery and Psychiatry, 80*(7), 755-761. doi: 10.1136/jnp.2009.172098

Chandra, R., Pandav, R., Laxminarayan, R., Zang, Z. X. (2006). Neurological disorders. In D. T. Jamison, J. G. Breman, A. R. Measham, G. Alleyne, M. Claeson, D. B. Evans, P. Jha, A. Mills, & P. Musgrove (Eds.), *Disease control priorities in developing countries* (pp. 627-643). Washington D. C.: World Bank. Retrieved from http://www.ncbi.nlm.nih.gov/books/NBK11793

Fichman, H. C., Fernandes, C. S., Nitrini, R., Lourenço, R. A., Paradela, E. M. P., Carthey-Goulart, M. T., & Caramelli, P. (2009). Category fluency task: Influence of age and education. *Dementia & Neuropsychologia, 3*(1), 49-54.

Gottesmann, R. F., & Hillis, A. E. (2010). Predictors and assessment of cognitive dysfunction resulting from ischemic stroke. *Lancet Neurology, 9*(9), 895-905. Retrieved from http://dx.doi.org/10.1016/S1474-4422(10)70164-2

Hyndman, D., Pickering, R. M., & Ashburn, A. J. (2008). The influence of attention deficits on functional recovery post stroke during the first 12 months after discharge from hospital. *Journal of Neurology, Neurosurgery and Psychiatry, 79*, 656-663. doi:10.1136/jnnp.2007.125609

Kaplan, E., Goodglass, H., & Weintraub, S. (1983). *Boston naming test*. Austin, T. X.: Pro-Ed Inc.

Kettunen, J. E., Nurmi, M., Koivistoinen, A. M., Dastidar, P., & Jehkonen, M. (2012). The presence of visual neglect after thrombolytic treatment in patients with right hemisphere stroke. *The Scientific World Journal, 2012*, 1-5. doi: 10.1100/2012/434120

Lezak, M. D., Howieson, D. B., & Loring, D. W. (2004). *Neuropsychological assessment*. New York: Oxford University Press.

Lotufo, P. A. (2005). Stroke in Brazil: A neglected disease. *São Paulo Medical Journal, 123*(1), 3-4. Retrieved from http://www.scielo.br/scielo.php?script=sci_arttext&pid=S1516-3180200500100001&lng=en&tlng=en.http://dx.doi.org/10.1590/S1516-31802005000100001

Machado, T. H., Fichman, H. C., Santos, E. L., Carvalho, V. A., Fialho, P. P., Koenig, A. M., & Caramelli, P. (2009). Normative data for healthy elderly on the phonemic verbal fluency task—FAS. *Dementia & Neuropsychologia, 3*(1), 55-60. Retrieved from http://demneuropsy.com.br/imageBank/PDF/dnv03n01a10.pdf

Malloy-Diniz, L. F., Lasmar, V. A. P., Gazinelli, L. S. R., Fuentes, D., & Salgado, J. V. (2007). The Rey auditory verbal learning test: Applicability for the Brazilian elderly population. *Brazilian Psychiatry Journal, 29*(4), 324-329. Retrieved from http://dx.doi.org/10.1590/S1516-44462006000500053

Mansur, L. L., Radanovic, M., Araújo, G. C., Taquemori, L. Y., & Greco, L. L. (2006). Boston naming test: Performance of Brazilian population from São Paulo. *Pro-Fono Cientific Update Journal, 18*(1), 13-20. Retrieved from http://www.scielo.br/scielo.php?script=sci_arttext&pid=S0104-56872006000100003&lng=en&nrm=iso

Moro, C. H. C., Longo, A. L. L., & Massaro, A. R. (2009). Intravenous thrombolysis. In C. H. C. Moro, & S. R. C. Fábio (Eds.), *Continued improvement program in stroke treatment* (pp. 32-47). São Paulo: Sociedade Brasileira de Doenças Cerebrovasculares.

Nelson, H. E. (1976). A modified card sorting test sensitive to frontal lobe defects. *Cortex: A Journal Devoted to the Study of the Nervous System and Behavior, 12*(4), 313-324.

Nitrini, R., Caramelli, P., Herrera Jr., E., Charchat-Fichman, H., & Porto, C. S. (2005). Performance in Luria’s Fist-Edge Palm Test according to educational level. *Cognitive and Behavioral Neurology, 18*(4), 211-214. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/16340394

Nys, G. M. S., van Zandvoort, M. J. E., Algra, A., Kappelle, L. J., & de Haan, E. H. F. (2006). Cognitive and functional outcome after intravenous recombinant tissue plasminogen activator treatment in patients with a first symptomatic brain infarct. *Journal of Neurology, 253*, 237-241. doi: 10.1007/s00415-005-0966-x

Nys, G. M. S., van Zandvoort, M. J. E., de Kort, P. L. M., Jansen, B. P. W., de Haan, E. H. F., & Kapelle, L. J. (2007). Cognitive disorders in acute stroke: Prevalence and clinical determinants. *Cerebrovascular Diseases, 23*, 408-416. doi: 10.1159/000101464
Nys, G. M. S., van Zandvoort, M. J. E., de Kort, P. L. M., … Kapelle, L. J. (2005). The prognostic value of domain-specific cognitive abilities in acute first-ever stroke. *Neurology, 64,* 821-827. doi: 10.1212/01.WNL.0000152984.28420.5

Oliveira-Souza, R., Moll, J., Passman, L. J., Cunha, F. C., ... Marrocos, R. P. (2000). Trail making and cognitive set-shifting. *Archives of Neuropsychiatry, 58*(3B), 826-829. doi: 10.1599+-+0/S0004-282X2000000500006

Pfeffer, R. I., Kurosaki, T. T., Harrah Jr., C. H., Chance, J. M., & Filos, S. (1982). Measurement of functional activities in older adults in the community. *Journal of Gerontology, 37*(3), 323-329.

Rey, A. (1999). *Copy and memory recall complex figures test: Manual (Teste de copie d’une figure complexe).* São Paulo: Casa do Psicólogo.

Spreen, O., & Strauss, E. (1988). Clock drawing. In O. Spreen, & E. Strauss (Eds.), *A compendium of neuropsychological tests* (pp. 483-488). New York: Oxford University Press.

Wechsler, D. (1997). *WMS-III: Weschler memory scale.* San Antonio: The Psychological Corporation.

Wechsler, D. (2004). *WAIS-III: Wechsler adult intelligence scale.* São Paulo: Casa do Psicólogo.

Weintraub, S. (2000). Neuropsychological assessment of mental state. In M. M. Mesulam (Ed.), *Principles of behavioral and cognitive neurology* (pp. 121-173). New York: Oxford University Press.