Depressive symptoms and cognitive impairment frequently occur already in the acute phase of ischemic stroke. The aim of the study was to determine whether there was an association between depressive symptoms and different domains of the cognitive status in acute ischemic stroke patients and to identify cognitive domains that significantly correlated with the presence of depressive symptoms. The study comprised 40 acute ischemic stroke patients (26 men and 14 women) aged 45-78 years, with 8-16 years of education. The presence of depressive symptoms was assessed using the self-reported Beck’s Depression Inventory (BDI), whereas the cognitive status was evaluated using a comprehensive neuropsychological testing battery measuring performance in different cognitive domains. The following domains were evaluated: executive function, language, immediate recall, delayed recall, attention, divergent reasoning, and visual-constructive performance in two dimensions. The multiple regression analysis was applied. The results showed a significant association between the presence of depressive symptoms and different cognitive domains. The domain of language was found to be a significant partial predictor of depression, with poorer performance in this domain correlating with a higher prevalence of depressive symptoms.

Key words: depressive symptoms, cognitive status, acute ischemic stroke

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INTRODUCTION

The nature of the relationship between cognitive impairment and depression following stroke involves a complex interaction between depression, localization of ischemic lesion, and cognitive impairment. The association between cognitive status and depressive symptoms has been well established in several studies (Berg, Palomaki, Lehtihalmes, Lonnqvist & Kaste, 2001; Carota, Berney, Aybek, Iaria, Staub, Ghika-Schmid, Annable, Guex & Bogousslavsky, 2005; Herrmann, Black, Lawrence, Szekely & Szalai, 1998; Kauhanen, Korpelainen, Hiltunen, Brusin, Mononen, Maatta, Nieminen, Sotaniemi & Myllyla, 1999; Nys, van Zandvoort, van der Worp, de Haan, de Kort & Kappelle, 2005; Robinson, 2006). Patients suffering from post-stroke depression have been found to have more severe cognitive impairment compared to stroke patients that do not develop depression (Sharpe, Hawton, Seagroatt, Bamford, House, Molyneux, Sandercock & Warlow, 1994). The cognitive deficits have been shown to be significantly more frequent and severe in patients with left-sided stroke who develop major depression than in those with no depression (Downhil & Robinson, 1994). This association between depression and impaired cognitive function is most striking in the acute phase of stroke, although it may persist for over one year following stroke. In addition, duration of depression is longer in patients with both depression and cognitive impairment compared to patients with depression and no cognitive impairment. On the other hand, recovery of cognitive function takes longer in depressed compared with non-depressed patients, suggesting that depression has a negative effect on recovery of cognitive function (Morris, Raphael & Robinson, 1992). Robinson (2006) reported that in one of the studies conducted by his group the neuropsychological assessment showed that patients with major depression had significant deficits in almost all domains of cognitive status, compared with non-depressed patients. Three and six months following stroke the patients showed deficits in the domains of verbal logical thinking, comprehension, nonverbal problem solving, verbal memory (primarily logical memory and serial learning), visual memory (primarily on measures of visual reproduction, visual recognition, and attention), executive functions (Trail Making Test Form A and verbal fluency) and visual-constructive functions. The latter study did not include subjects with aphasia. The neuropsychological assessment showed a significant association between major depression and cognitive impairment involving most of cognitive domains. Moreover, Robinson (2006) found that patients with major depression showed significantly more severe cognitive impairment, as assessed by the Mini mental state examination test, compared with subjects with minor depression or with no affective disorder. In a one-year prospective study with 106 patients with first-ever stroke Kauhanen et al. (1999) found a negative correlation between severity of depression and performance on neuropsychological tests assessing nonverbal problem solving, memory, attention, and psychomotor speed within a year following stroke. The same authors found a
strong association between the presence of dysphasia and a high risk of major
depression in the same population (Kauhanen, Korpelainen, Hiltunen, Maatta,
Mononen, Brusin, Sotaniemi & Myllyla, 2000). However, it is still unclear whether
it is depression leading to cognitive and functional impairments, or vice versa.

When discussing the relationship between post-stroke depression and cognitive
status, it is impossible not to mention a rather controversial association between
depression and aphasia. One of the studies that failed to demonstrate an association
between post-stroke depression and cognitive impairment did find a significant
association between aphasia and post-stroke depression (Astrom, Adolfsson, &
Asplund, 1993). Aphasia represents a great problem for post-stroke depression
investigators, primarily because diagnosing any psychiatric disorder following a
stroke requires that the patient should be able to answer the interviewer’s questions
(in a structured or semi-structured interview) in either a written or oral form. Even
moderate difficulties in patient’s comprehension can present an obstacle to making
diagnosis of a psychiatric disorder after stroke. Consequently, it is common for
investigators to exclude from study patients with moderate or severe speech deficits,
primarily those with speech comprehension disorders (Astrom et al., 1993;
Robinson, Starr, Kubos & Price, 1983). However, although patients with speech
comprehension disorders have generally been excluded from studies on post-stroke
depression, some authors have proposed that it is aphasia itself that causes post-
stroke depression (Gainotti, 1972). Gainoti (1972) suggests that depressive reaction
associated with left-sided lesions represents an expected response manifested in
depressive reactions and outbursts of anger for having lost speaking ability, speech
being one of the most important elements of every person’s life. Likewise, Benson
(1979) assumes that depression sometimes represents a secondary psychological
reaction to speech loss. Consequently, the practice of excluding patients with
aphasia (e.g. fluent and global aphasia) from research poses the question: What is
the real prevalence of depression among patients with aphasia? And also: Does the
exclusion of these patients change radically the prevalence estimates and the clinical
and pathological correlates of depression (Robinson, 2006)?

It is a fact that aphasia is a common sequela of damage to the dominant (left)
cerebral hemisphere. Although loss of the power of speech can predictably lead to
depression, available data indicate that non-fluent (Broca’s) aphasia is most likely
associated with a high prevalence/incidence of depression (Robinson, 2006). However, the true prevalence of depression among patients with aphasia and speech
comprehension disorders remains unclear. The relationship between non-fluent
(Broca’s) aphasia and depression may be affected by the fact that both depression
and non-fluent aphasia occur as a direct consequence of lesions of the left frontal
lobe (Robinson, 2006). Owing to the impossibility of assessing depression in
patients with language impairment, there have been attempts to construct alternative
diagnostic instruments based on information provided by patient’s relatives. Despite
the efforts, not even these instruments have been able to provide a valid assessment
of depression in patients with speech comprehension impairment (Kauhanen et al.,
2000). Previous research has shown that post-stroke depression can have a
significant effect on patient’s recovery from aphasia, and most authors agree that research should be directed toward studying the effects of antidepressive treatment on the clinical manifestations and longitudinal recovery in aphasic patients (Robinson, 2006).

METHOD

Sample

Our study comprised a group of 40 acute ischemic stroke patients (26 male, 14 female), aged 45-78 years, with 8 to 16 years of education. The inclusion criterion for the acute ischemic stroke group was the diagnosis of first-ever clinically verified acute ischemic stroke. The acute ischemic stroke diagnosis was established based on clinical symptoms and neuroradiological correlates obtained with brain computerized tomography. Only hospitalized patients were included. The exclusion criteria for the acute ischemic stroke group were: any previous (clinically verified) stroke; presence of sensory and/or motor aphasia or severe dysphasia; paralysis of the dominant arm; non-native speakers of Serbian (for better understanding of the verbal content of tests); visual and auditory impairments that made impossible performing test tasks; impaired consciousness; previous psychiatric disorders or history of depression; and Mini Mental Status Examination (MMSE) score under 15.

Procedure

The study was conducted at the Neurology Clinic of the Clinical Centre of Vojvodina in Novi Sad, Serbia, in the period from May 2007 to September 2008. The institutional ethics committee approved the study and each of the subjects included provided an informed consent to participation. In order to confirm the diagnosis of acute ischemic stroke each subject underwent neurological exam, brain computerized tomography and neuropsychological assessment. The neuropsychological assessment was performed during hospitalization, i.e., within two weeks following stroke onset.
Instruments

Presence of depressive symptoms was assessed using the Beck Depression Inventory (BDI) (Beck, Ward, Mendelson, Mock & Erbaugh, 1961). The inventory represents a one-dimensional scale for assessing depression, and is commonly used in research for its proven reliability and validity. It consists of 21 questions, each with four possible answers that are assigned a score ranging from 0 to 3, with higher scores indicating more severe symptoms. The total BDI score is obtained by simple addition of all the scores on 21 items, and the total score ranges from 0 to 63, with a higher score representing more severe depression. The intensity of depressive symptoms can be quantified by assigning one of the four possible degrees of the intensity of depressive symptoms. The cut off score for the presence of depressive symptoms is 9. It should be noted that the BDI serves primarily for detecting the presence of depressive symptoms and not for making a diagnosis of a depressive disorder, and should be used accordingly.

The neuropsychological assessment included an extensive neuropsychological battery comprising the following tests: the Trail Making Test Forms A and B (TMT A and B) (Reitan, 1958; Spreen & Strauss, 1991); the Verbal Fluency Tests (phonemic fluency and categorical fluency) (Goodglass & Kaplan, 1983; Lezak, 1995); the Rey Auditory Verbal Learning Test (RAVLT) (Rey, 1964); the Rey-Osterrieth Complex Figure (ROCF) (Osterrieth, 1944; Rey, 1941); the Wisconsin Card Sorting Test (WCST) (Heaton, 1981); the Boston Diagnostic Aphasia Examination (BDAE) Repetition of Phrases, Complex Ideational Material and Instructions subtests (Goodglass & Kaplan, 1983); the Boston Naming Test (BNT) (Kaplan, Goodglass & Weintraub, 1978); and the Wechsler Memory Scale - Revised (WMS-R) Mental Control, Digit Repetition and Visual Memory Span subtests (Wechsler, 1987).

Scores on the applied tests represented different domains of cognitive status. Each domain was represented by the scores obtained on the tests assessing particular neuropsychological functions. This representation of results was done using a principal component analysis, and further analyses used factor scores on the first principal components of each of the following cognitive domains:

The domain of executive function (comprising the TMT - B and several variables of the WCST: number of categories achieved, perseverative responses, perseverative errors, correct answers, wrong answers).

The domain of attention (comprising the TMT – A, the total score for attention and concentration on the WMS-R, and the WMS-R Digit Repetition subtest for verbal span forward and visual span forward).

The domain of language (comprising the BNT, and the short form BDAE subtests for repetitive speech, complex ideational material, and response to instructions).

The domain of delayed recall (comprising the variables: the ROCF delayed recall after 45 minutes, and the RAVLT - A7 list recall and the A list recognition.)
The domain of **divergent reasoning** (comprising phonemic fluency for the letters /S/, /K/, /L/ and categorical fluency (animals)).

The domain of **immediate recall** (comprising the WMS-R subtests: Digit Repetition – forward and backward and Visual Span – forward and backward).

The domain of **visual - constructive performance in two dimensions** (represented as the total score on the ROCF test).

**RESULTS**

The relationship between depression and different cognitive domains in the acute ischemic stroke patients group was tested using multiple regression analysis (Table 1). The criterion variable was operationally defined as the total score on the BDI. The predictor variables were operationally defined as the factor scores on the first principal components of the cognitive domains (**executive function, attention, language, memory, immediate recall, delayed recall, divergent reasoning**) and the total score on the ROCF (**domain of visual-constructive performance in two dimensions**).

<table>
<thead>
<tr>
<th>COGNITIVE DOMAINS</th>
<th>β</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Visual-constructive performance in two dimensions</td>
<td>-0.095</td>
<td>0.617</td>
</tr>
<tr>
<td>Executive function</td>
<td>0.789</td>
<td>0.580</td>
</tr>
<tr>
<td>Attention</td>
<td>-3.018</td>
<td>0.263</td>
</tr>
<tr>
<td><strong>Language</strong></td>
<td><strong>-3.822</strong></td>
<td><strong>0.018</strong></td>
</tr>
<tr>
<td>Delayed recall</td>
<td>-1.558</td>
<td>0.178</td>
</tr>
<tr>
<td>Divergent reasoning</td>
<td>2.394</td>
<td>0.072</td>
</tr>
<tr>
<td>Immediate recall</td>
<td>0.554</td>
<td>0.816</td>
</tr>
</tbody>
</table>

The analysis of the results showed the overall regression model to be significant [R=.601; R²=.362; F(7.62)=5.031; p<.001]. As regards individual predictors, only the domain of language showed statistical significance, i.e., poorer performance in the domain of language was associated with more severe depression.

**DISCUSSION**

Like the majority of previous similar studies, our results also have confirmed the association between depressive symptoms and cognitive status in the acute phase.
of ischemic stroke. The only significant partial predictor of depression found in our study was the domain of language. Poorer performance in this domain was associated with more frequent and severe depressive symptoms. This is consistent with the results of previous studies, primarily those focusing on the relationship between speech disorders, in particular aphasia, and development of depression.

However, data on the relationship between depression and speech disorders are rather inconsistent. A major problem of previous research in this field is that a large majority of studies have excluded patients with aphasia or severe dysphasia, due to the impossibility of assessing or the lack of adequate diagnostic methods for assessing the presence of depression in these patients. Depression is most difficult to diagnose in patients with language comprehension or production difficulties. Our study also excluded patients with aphasia and severe forms of dysphasia and included only patients with less intensive speech impairment. For our assessment, we considered whether the patient’s speech is sufficiently preserved to allow comprehension of verbal instructions and speech articulation sufficiently preserved to enable their responding to test requirements. It should be noted that the domain of speech in our study was represented by scores on the neuropsychological tests, such as Boston naming test and three Boston Diagnostic Aphasia Examination subtests (complex ideational material, repetition of phases and responses to instructions). These tests are used to assess abilities of naming, repeating phrases, comprehension of complex verbal material and comprehension and execution of simple and complex verbal instructions.

Several possible explanations for the association between the poor performance in the language domain and depression in acute ischemic stroke have been proposed. One concerns the attempts to explain the relationship through lesion location. Given the long-recognized domination of the left hemisphere in language lateralization, it is logical to expect that any left-sided brain damage, in our case left-sided stroke, leads to impairment of the language function. Clearly, the degree of speech impairment depends mainly on the precise location of ischemic stroke and the volume of the tissue affected by it. The assumption that the left cerebral hemisphere represents a leading anatomical structure for speech both in left-handed and right-handed individuals was first confirmed in the research by Penfield and Roberts, back in 1959 (Penfield & Roberts, 1959). More recently, a number of studies dealing with lesion location and depression have indicated that left-sided anterior lesions are associated with the development of depression (Gonzales-Torrecillas, Mendlewicz & Lobo, 1995; Robinson, 2003, 2006; Wade, Legh-Smith & Hewer, 1987). In a meta-analysis Robinson (2003) reported that in the first two months following acute ischemic stroke, left-sided frontal lesions and left-sided lesions of basal ganglia were the most frequent types of lesions in patients with major depression. A research group lead by the same author has recently confirmed the previous results, having found a significant association between the intensity of depression and left frontal lobe lesions in patients who suffered a stroke within previous 6 months (Narushima, Kosier & Robinson, 2003). Given these findings, we can assume that depression and
poorer performance in the domain of language actually represent two coexisting sequelae of the damage to the left cerebral hemisphere.

Another possible explanation for the relationship suggests that depressive symptoms actually occur as a person’s reaction to his or her loss of certain language functions. Considering that our sample excluded patients with aphasia and more severe forms of dysphasia, and included only relatively mild speech impairment, it is possible that even mild deficits in the language function, which can be manifested in various ways (e.g. difficulties in naming objects, articulation, repeating phrases, etc.), present a stress for a given person and in this very manner bring on a depressive reaction. It should not be forgotten that the speech ability plays a vital role in every person’s life, and any difficulty in this domain may be highly frustrating, and if occurring suddenly as part of the suffered stroke, accompanied with some physical deficits and a hospital environment, it becomes clear that depressive reaction may represent an expected response to the new circumstances. Another domain analyzed with the regression model that also contains considerable language function is the domain of divergent reasoning, comprising phonemic and categorical fluency tests. However, the divergent reasoning domain did not prove to be a significant partial predictor of performance on the BDI. The lack of significant contributions of the majority of partial predictors to predicting depression on the BDI can be interpreted as a high degree of inter-correlation, i.e. an overlap between the contents of the studied domains. It is possible that these domains, although representing different segments of cognitive status, might have been essentially “saturated“ by the same subject of measurement. Each domain was represented by the factor scores on the first principal components. A number of neuropsychological tests measuring a particular mental function made one domain, and performance on these tests was represented by the first principal components. Yet, although clinical neuropsychology tends to construct instruments that will be able to measure a „factorially clean“ psychic/mental function, this is frequently not possible, not due to any limitations of the very test applied, but rather because many psychic functions are overlapping with the content of another psychic function. Therefore, despite the careful selection of neuropsychological tests that will make a cognitive domain, there is overlapping between different domains, for the tests’ inability to measure a „factorially clean“ function. Consequently, this can result in some degree of the content overlap between cognitive domains and impossibility to single out more domains as significant partial predictors of performance on the BDI.
REFERENCES


Rezime

POVEZANOST DEPRESIVNIH SIMPTOMA I KOGNITIVNOG STATUSA KOD AKUTNOG ISHEMIČNOG MOŽDANOG UDARA

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Ključne reči: depresivna oboležja, kognitivni status, akutni ishemički moždani udar