Relationship between Cognitive Impairment and Depressive Symptoms

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Abstract

The purpose of the study was to assess association between depressive symptoms and different domains of the cognitive status in patients with acute ischemic stroke and to identify cognitive domains that significantly correlated with the presence of depressive symptoms. The study comprised 40 acute ischemic stroke patients (14 women and 26 men) aged 45-78 years (± SEM 55.6 yrs.), with 8-16 years of education (± SEM 13 years). Beck’s Depression Inventory (BDI) was used to assess depressive symptoms whereas the cognitive status was evaluated using a comprehensive neuropsychological testing battery which measures performance in different cognitive domains. The following domains were evaluated: visual-constructive performance in two dimensions and executive function, language, immediate recall, delayed recall, attention, divergent reasoning. The multiple regression analysis was applied. The results showed the overall regression model to be significant \[ R = 0.601; R^2 = 0.362; F(7.62) = 5.031; p < 0.001 \]. The language domain was found to be a significant partial predictor of depression, with poorer performance in this domain correlating with a higher prevalence of depressive symptoms.

Keywords: Ischemic stroke, cognition, depression.

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.¹⁻⁶ Patients suffering from post-stroke depression have been found to have more severe cognitive impairment compared to stroke patients who do not develop depression.⁷

Researchers have shown cognitive deficits to be significantly more frequent and severe in patients with left-sided stroke who develop major depression than in those with no depression.⁸ 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.⁹

Robinson (2006)⁶ reported that 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, non-verbal 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, he 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.6

In a one-year prospective study with 106 patients with first-ever stroke Kauhanen et al. (1999)10 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 strong association between the presence of dysphasia and a high risk of major depression in the same population.10

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.11 Aphasia represents a great problem for post-stroke depression investigators. Consequently, it is common for investigators to exclude from study patients with moderate or severe speech deficits, primarily those with speech comprehension disorders.12 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 poststroke depression.13

Gainotii (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; aphasia is a common sequela of damage to the dominant (left) cerebral hemisphere.14

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.6 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.10

Method
Subjects
The study comprised a group of 40 stroke patients (26 male, 14 female), aged 45-78 years (± SEM 55.6 yrs.) with 8 to 16 years of education (± SEM 13 years). The inclusion criterion for the acute (1-14 days) 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; 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**

**Setting**
The study was conducted at a private teaching hospital. As no invasive procedure was involved in the study, nor any additional drug was used for study purpose, only approval of Head of concerned department was obtained. Informed written consent was obtained either from the patient or from spouse/blood relative attendant after explaining the procedure and the purpose of the study. 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**
Symptoms of depression were assessed by using Beck Depression Inventory (BDI). 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. 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); the Verbal Fluency Tests (phonemic fluency and categorical fluency); the Rey Auditory Verbal Learning Test (RAVLT); the Rey-Osterrieth Complex Figure (ROCF); the Wisconsin Card Sorting Test (WCST); the Boston Diagnostic Aphasia Examination (BDAE) Repetition of Phrases, Complex Ideational Material and Instructions subtests; the Boston Naming Test (BNT); the Wechsler Memory Scale – Revised (WMS-R) Mental Control, Digit Repetition and Visual Memory Span subtests. This representation of results was done using a SPSS (version 12), multiple regression analysis, principal component analysis, and further analyses used factor scores on the first principal components of each of the cognitive domains selected. Scores of applied tests represented different domains of cognitive status and each domain was represented by the scores obtained on the tests assessing particular neuropsychological functions.

**Results**
The relationship between depression and different cognitive domains in the acute ischemic stroke patients group was tested using multiple regression analysis. Criterion variable were operationally defined as the total score on the BDI and 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). The results showed the overall regression model to be significant [$R=0.601; R^2=0.362; F(7.62)=5.031; p<0.001$]. 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 (Table 1).
Table 1. Partial Contributions of Predictors of BDI Performance

<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>Language</td>
<td>-3.822</td>
<td>0.018</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>

Discussion

Results 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.

Data on the relationship between depression and speech disorders are rather inconsistent. In previous studies the majority 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.

In this study we 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 them to respond 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 phrases and responses to instructions). 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.

Many explanations for the association between the poor performance in the language domain and depression in acute ischemic stroke have been proposed. One emphasizes 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 by Penfield and Roberts, back in 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.

Robinson (2003) stated 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 led 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. Given these findings, we can assume that depression and poorer performance in the domain of language...
actually represent two coexisting sequelae to the damage to the left cerebral hemisphere.

One possible explanation for the relationship is that depressive symptoms actually occur as a person’s reaction to his or her loss of certain language functions. This study 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 person and in this manner bring on a depressive reaction. One should not be forget that 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 is clear that depressive reaction may represent an expected response to the new circumstances.

The other 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 large number of neuropsychological tests measuring a particular mental function made one domain, and performance on these tests was represented by the first principal components. 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.

**Limitations**

In this study a limited small sample size was used. Also no public sector hospital was involved in the study. In this study we did not answer any gender discrimination as this is beyond the scope of this research paper. Keeping in mind all these factors further studies are required in this regard.

**References**


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