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Depressive symptoms in patients admitted to a semi-intensive Stroke Unit

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Abstract

Aim of this study was to evaluate depressive symptoms in a semi-intensive Stroke Unit (SI-SU) by a scale specifically devised to assess depression in patients with stroke and to identify the symptoms better contributing to the early detection of post stroke depression (PSD). Fifty-four patients admitted to a SI-SU because of suffering from single, first-ever hemispheric stroke were enrolled. Depressive symptoms were assessed by the Post Stroke Depression Rating Scale (PSDRS). All patients were also evaluated by the National Institute of Health Stroke Scale (NIHSS), the modified Rankin scale, the Mini-Mental State Examination (MMSE) and the Frontal Assessment Battery (FAB). The PSDRS detected depressive symptoms in twenty-two patients (40%). The PSDRS scores were not influenced by severity of stroke, functional outcome, site of lesion and type of stroke. Three psychopathological factors were identified inside the PSDRS: "reactivity", "melancholic" and "apathetic", with significant inverse correlations with cognitive measures found only with the "apathetic" factor. Less than one-half items of the PSDRS were able to identify overt depressive symptoms. Depressive symptoms are a frequent and early complication in patients referred to a SI-SU with the PSDRS being a suitable tool to detect depressive symptoms in acute phases of stroke.

Key words: Cerebrovascular disease; depression; post-stroke depression; stroke.

Introduction

The post-stroke depression (PSD) is one of the main psychopathological consequences of stroke, but shows discrepancies in its prevalence depending on the criteria to select population, the setting (i.e., general population, hospital, rehabilitation ward) and the phase of stroke in which depression is evaluated. The prevalence of PSD is also related to the methods adopted for diagnosing depression; in general, low percentages are observed when DSM criteria are strictly applied. Conversely, depression scales (e.g., Hamilton Depression Scale, Montgomery and Aasberg Depression Rating Scale, Beck Depression Inventory, etc.) may detect a high number of subjects with PSD (1). In both cases, however, the evaluation of depressive symptoms is performed by means of criteria and/or tools not specifically devised to assess PSD. A systematic review of observational studies reports a 32% of subjects suffering from PSD in acute stroke (i.e., within one month from the onset), with the wider variation among patients from hospital settings (2).

Since PSD is a prominent negative factor of stroke recovery, many studies have investigated etiological mechanisms. A recent review has focused on two major hypotheses: a biological etiology including lesion location, neurotransmitters, inflammatory cytokines and gene polymorphism mechanisms, and a psychological hypothesis claiming to reactive factors and psychosocial stressors (3).

The aim of the study was to assess depressive symptoms by using a scale specifically devised to assess PSD, in patients consecutively admitted to a semi-intensive Stroke Unit (SI-SU), with a clinical diagnosis of stroke. We aimed to describe the main psychopathological dimensions of "acute" PSD and to identify the symptoms better contributing to an early detection of PSD. The study also intended to evaluate depressive symptoms in relationships with the type of stroke, measures of cognitive impairment and functional outcome.

Methods

Subjects

All subject enrolled in the present study were in-patients consecutively admitted to the SI-SU of the

CTO Hospital in Naples for acute ischemic stroke. Inclusion criteria were: a) education with at least three years of schooling; b) single, first-ever ischemic stroke; c) at least 72 hours allocation in the SI-SU with continuous monitoring of cardiac, respiratory, metabolic and neurological functions. Exclusion criteria were severe head trauma, prior neurological disorders (i.e., Parkinson's disease, multiple sclerosis, dementia and epilepsy), alcohol or drug abuse and previous significant psychiatric disturbances, with particular regard to major affective disorders. All patients underwent a complete clinical and instrumental evaluation including caregivers' interviews, medical, neurological, psychiatric, laboratory findings, and neuroimaging procedures (brain CT scan). All persons or their relatives gave informed consent to the study, which was carried on in agreement with the declaration of Helsinki and approved by the local ethics committee.

Sixty-nine consecutive patients fulfilling the inclusion/exclusion criteria were observed in the period January 2009 - June 2009. Fifteen of them (21.7%) were excluded from the evaluation for impaired consciousness or severe language disorder precluding psychiatric evaluation.

Stroke type was classified according to the Oxfordshire Community Stroke Project (OCPS) classification system (4), i.e., total anterior circulation infarcts (TACI), partial anterior circulation infarcts (PACI), posterior circulation infarcts (POCI) and lacunar infarcts (LACI). Patients with LACI, admitted to the SI-SU, due to their relatively benign course, were discharged from the semi-intensive ward within the first 72 hours and, therefore, were not included in the study.

The final sample consisted of 54 subjects (39 men and 15 women) including, according to OCSP criteria, 15 patients (27.8%) with TACI, 13 subjects (24.1%) with PACI and 26 (48.1%) with POCI. The site of the lesion was right in 34 patients (63%) and left in the remaining 20 subjects (37%). This discrepancy could arise from the exclusion of patients suffering from severe forms of aphasia.

Procedures

The assessment of stroke severity was performed, on admission, by means of the National Institute of Health Stroke Scale (NIHSS) (5). Approximately one week (6-10 days) from the admission all subjects underwent evaluation of functional outcome, cognitive impairment and depressive symptoms. Patients received the Mini-Mental State Examination (MMSE) (6, 7) and the Frontal Assessment Battery (FAB) (8, 9) in order to assess general cognition and executive functioning, respectively. The functional outcome was established with the modified Rankin scale (10).

Depressive symptoms were evaluated by means of the Post Stroke Depression Rating Scale (PSDRS) (11). The PSDRS is a psychiatric scale specifically devised to assess depressive symptoms in patients suffering from stroke. It is composed by 10 sections aimed to investigate (sections 1-9) different psychopathological aspects of PSD, namely, depressed mood, feelings of guilt, thoughts of death/and or suicide, vegetative disorders (sleep and appetite), apathy, anxiety, catastrophic reactions, hyperemotionalism, anhedonia. The tenth section, evaluating diurnal mood variation, is merely descriptive and does not contribute to the overall score. This score ranges from 0 to 45, given by the sum of the separate scores of each section (range 0-5); higher values correspond to more severe depressive symptoms.

The PSDRS was recently validated on a large series of patients at their first stroke episode, although in different settings (12). In this population a cut-off value ≥ 9 points was able to identify about 93% patients suffering from PSD. The same value was adopted in the present study to classify patients as affected by overt depressive symptoms. The PSDRS was administered by trained psychologists, which were blind to the neurological and cognitive evaluation.

Statistics

The effect of demographic variables on depressive symptoms was checked by means of multiple regression analysis assuming the overall PSDRS scores as the dependent variables and age, sex and education (years of schooling) as the independent one(s). The significance level has been fixed at p .0167 by considering an overall p .05 significance level divided by the number of independent variables on a Bonferroni basis. A similar procedure was adopted to evaluate the effect of clinical and functional measures (NIHSS and Rankin scores) on PSDRS scores; in this case the significance level was fixed, on a Bonferroni basis, at p. 025. The effect of the site and type of stroke on depressive symptoms was evaluated by two-way ANOVA, assuming PSDRS scores as dependent variable, with the site of the lesion (right versus left) and type of stroke (TACI, PACI and POCI) as main factors.

The characterization of psychopathological dimensions of PSD was attempted by means of a Factor Analysis. The scores of the nine sections of the PSDRS entered a Principal Component Analysis

with Varimax rotation (method of extraction: roots > 1). Then, the scores of the PSDRS sections loading on each of the main factors were used to obtain Factor scores. The relationships between depressive symptoms (PSDRS overall and Factor scores) with cognitive measures (MMSE and FAB) were evaluated by partial correlation analysis, with significance level (p .006) corrected by the number of comparisons. The differences between patients with and without overt depressive symptoms on each section of the PSDRS were evaluated by means of univariate non-parametric analysis (Mann-Whitney U test). Given the number of comparisons, only values at $p < 0.005$ were considered significant.

Results

The mean age of patients was 65.3 (± 10.5, SD) years and the mean years of schooling was 7.15 (± 3.8). Mean scores at NIHSS and Rankin scales were 7.23 (± 4.70) and 2.79 (± 1.19), respectively. Mean scores at the MMSE and FAB were 22.07 (± 6.83) and 9.50 (± 4.59), respectively. Mean score at PSDRS was 7.94 (± 5.00).

The multiple regression analysis on PSDRS scores versus demographic independent variables approached significance ($F(3, 53) = 3{,}428$; $p < .03$), with only gender exhibiting a significant effect (coefficient = 3.819; t = 2.62; p .011): women had higher scores at the PSDRS (Mean = 10.33 ± 4.89, SD) as compared with those in men (Mean = 7.03 ± 4.79, SD). Twenty-two patients (40%) were considered affected by overt depressive symptoms on the basis of a PSDRS score ≥ 9 (cut-off level). The percentage of depressed women (10/15; 67%) was more than two folds higher than that in men (12/39; 31%), chi square = 4.391, $p < .05$.

The PSDRS scores were not influenced by the severity of the stroke (NIHSS) or short-term functional outcome (Rankin) (multiple regression analysis ($F(2, 53) = .507$; p NS)). The two-way ANOVA showed that neither the site of the lesion ($F(1, 48) = .013$; p NS), nor the type of stroke ($F(2, 48) = .929$; p NS) affected PSDRS scores, with no interaction.

The Principal Component Analysis had a Bartlett's chi-square = 122.59 ($p < .0001$) and generated three Factors which explained 61.5% of the variance. The structure matrix after rotation (Table 1) showed that the first Factor (magnitude = 2.996, variance = .333) loaded on items assessing anxiety, catastrophic reactions and hyperemotionalism. This Factor was called "reactivity". The second Factor (magnitude = 1.338, variance = .149) was related to items evaluating thoughts of death/and or suicide and vegetative disorders; it has been labeled "melancholic". The third Factor had a magnitude = 1.193 (variance = .133) and loaded on items assessing apathy and anhedonia; this was called "apathetic".

The partial correlation analysis (Table 2) showed a trend toward a negative significant correlation of PSDRS scores with both MMSE and FAB scores. Strong significant inverse correlations were observed only between the "apathetic" Factor and MMSE and FAB. No correlation approached significance between "reactivity" and "melancholic" Factors and cognitive measures. The items better discriminating subjects with and without overt depression were depressed mood, anxiety, catastrophic reactions, hyperemotionalism and anhedonia (Table 3).

Discussion

The present study confirms that depressive symptoms are part of the early clinical presentation of a

Table 1

Principal Component Analysis of the Post-Stroke Depression Rating Scale (PSDRS) sections: reference structure matrix after rotation (Varimax procedure). Values > .50 are underlined

	Reactivity	Melancholic	Apathetic
Depressed mood	.457	.281	.212
Feelings of guilt	.346	-.362	.381
Thoughts of death/and or suicide	-.072	<u>.808</u>	-.008
Vegetative disorders	.162	<u>.624</u>	-.036
Apathy	.090	-.123	<u>.726</u>
Anxiety	<u>.592</u>	.126	.092
Catastrophic reactions	<u>.849</u>	-.055	.022
Hyperemotionalism	<u>.865</u>	.004	-.197
Anhedonia	-.215	.246	<u>.785</u>

Table 2

Partial correlation analysis: Post-Stroke Depression Rating Scale (PSDRS) overall and PSDRS Factors versus cognitive and executive measures, Mini Mental State Examination (MMSE) and Frontal Assessment Battery (FAB)

	MMSE	FAB
PSDRS overall	-.354 (trend)	-.289 (trend)
PSDRS "reactivity"	-.225 (NS)	-.124 (NS)
PSDRS "melancholic"	-.056 (NS)	-.121 (NS)
PSDRS "apathetic"	-.512 (< .0001)	-.438 (< .001)

Table 3

Differences between patients with and without depression on single sections of the Post-Stroke Depression Rating Scale (PSDRS) (Mann-Whitney U test)

	U	tied p-value
Depressed mood	171.0	< .001
Feelings of guilt	297.5	NS
Thoughts of death/and or suicide	318.0	NS
Vegetative disorders	226.0	NS
Apathy	270.0	NS
Anxiety	131.5	< .0001
Catastrophic reactions	80.0	< .0001
Hyperemotionalism	80.5	< .0001
Anhedonia	197.5	< .005

first ever acute stroke in patients referred to a SI-SU. Overt depression affects, at different levels, about 40% of patients without history of previous mood disorders and this percentage is not different from that observed in other studies of patients with acute stroke. In a systematic review PSD was shown in about 32% of patients within one month the stroke onset, exhibiting the higher percentage in hospital-based studies (2). Our data underline that PSD is mainly an early complication of stroke. This would alert clinicians to pay attention in evaluating depressive symptoms in patients admitted to a Stroke Unit, in particular when considering that PSD can negatively influence the adherence to rehabilitative programs and survival (13, 14). Our results confirm that PSDRS is a suitable tool to detect depressive symptoms in acute phases of stroke and to describe the main psychopathological dimensions underlying PSD. In this perspective, the study confirms the PSDRS' validity already shown in previous studies evaluating PSD in different multiple settings, although without reference to single mood items (11, 12). The PSDRS avoids limitations given by the rigid application of clinical diagnostic criteria (e.g., DSM), which can led to underestimate depressive symptoms in patients with stroke (1) and, similarly, it avoids the use of scales assessing "functional" depression not specifically devised to evaluate PSD.

In our sample women showed a particular vulnerability to PSD (67% versus 31% in men). However, female susceptibility is controversial (15-19) and frequently associated with a history of depressive disorder prior to stroke (19) and to left hemispheric lesions (17). The present study is unable to address this question (which remains unanswered for functional depression as well), but the higher prevalence of PSD in women in our sample seems not been influenced by a previous depressive disorder, since this was considered in the exclusion criteria.

Depressive symptoms were not related to the severity of stroke or short-term functional outcome. This result was somewhat unexpected because many studies report relationships between these factors and PSD; however, it has been also reported that association between stroke severity, functional outcome and depressive symptoms becomes clear some months from stroke onset (18, 20-22). Furthermore, most of these studies enroll or pool patients in different phases of the disease and preclude a direct comparison with our sample, where all patients were investigated 6-10 days after stroke in a SI-SU. Moreover, the exclusion of those with severe neurological symptoms or with a benign course might have contributed to the lack of this possible association. Our results are consistent with the view that the risk of developing PSD in the acute phase of stroke cannot be predicted on the basis of stroke severity and short-term outcome.

In our study, the hemispheric site of the lesion and the type (OCSP) of stroke did not affect PSDRS scores. The hypothesis of a possible association of depressive symptoms with hemispheric site has not always been confirmed (23, 24). A recent Italian study showed, in a large population of patients with first-ever ischemic stroke, an association of TACI with higher depression severity scores at the Montgomery-Aasberg Depression Rating Scale (MADRS) (25). Data from PSDRS in our sample did not replicate these results. Several factors may account for this discrepancy, namely, the size of the sample, the time after onset and the tools adopted to assess depression. The acute phase of stroke, in particular, could have played a role in our patients in determining functional effects in brain regions remote from the site of the lesion but connected with it (diaschisis concept).

The Principal Component Analysis on PSDRS sections identified three distinct factors characterizing the psychopathological profile of PSD. The

Factor "reactivity" mainly reflects the subjects' tendency to respond to the illness condition with angry or exaggerated sense of frustration. The Factor "melancholic" includes some of the core features of melancholic depression, in particular those regarding vegetative symptoms and "nihilistic" features of depression. Finally, the factor "apathetic" characterizes a dimension in which the emotional withdrawal and the loss of interest and pleasure are the main symptoms. Only the apathetic factor was related to measures of general cognitive (MMSE) and executive impairment (FAB). Similar findings were recently reported in a study on PSD in a geriatric population investigated by the MADRS (26). The authors identified three factors (anhedonia, sadness and agitation), with only the first factor correlating with cognitive impairment. The relationship between apathy and cognitive dysfunction in PSD is also supported by data from clinical and neuroimaging studies. Starkstein *et al.* report an association between post-stroke apathy and both PSD and cognitive disturbances (27). Okada *et al.* found apathy in one-half of patients with stroke. Although no relationships was observed between the apathy score and specific regional distribution of lesions on MRI, subjects with apathy were more depressed, showed lower scores at tests investigating frontal lobe functions, and reduced r-cerebral blood flow in the right dorsolateral frontal and left fronto-temporal regions (28). Our results support the view that PSD, also in its early appearance after stroke onset, may be looked as a heterogeneous clinical entity. In fact, the phenomenological dimensions "reactivity" and "melancholic" are mainly related the psychological features of PSD, whereas the apathetic dimension is better explained by neurological mechanisms (29).

Our study finally showed that some PSDRS sections are able to better differentiate patients with or without depression: in fact, depressive mood, anxiety, catastrophic reactions, hyperemotionalism and anhedonia seem to be early symptoms of depression in stroke patients. This result is similar to that reported in patients referred to a Stroke Unit: crying and related behaviors (i.e., emotionalism, catastrophic reactions), as well as overt sadness, were the most reliable indicators of depressed mood (30).

The present study is not free from some criticism. The relatively low number of our patients represents a possible limitation. However, the size of the sample is not different from that in many studies reported by Hackett et al's review (2); on the other hand, our group is characterized by very homogeneous conditions, such as similar setting, similar time from stroke onset and exclusion of prior depression. Another limitation is the lacking of a control group (depressed patients without stroke). However, PSDRS is a validated tool for stroke patients (12) and contributed to identify these features also in our selected sample.

In conclusion, the high prevalence of depressive symptoms in acute stroke suggests a careful psychiatric evaluation, supported by scales specifically devised to assess PSD, as part of management protocols in patients referred to a Stroke Unit. This because, probably, there is no need to wait until a few weeks have elapsed before evaluating stroke patients for PSD.

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