Importance of retardation and fatigue/interest domains for the diagnosis of major depressive episode after stroke: a four months prospective study

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Importance of retardation and fatigue/interest domains for the diagnosis of major depressive episode after stroke: a four months prospective study

Lentificação e fadiga/interesse no diagnóstico do episódio depressivo maior após o acidente vascular cerebral: um estudo prospectivo de quatro meses

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Objective: Post-stroke major depressive episode is very frequent, but underdiagnosed. Researchers have investigated major depressive episode symptomatology, which may increase its detection. This study was developed to identify the depressive symptoms that better differentiate post-stroke patients with major depressive episode from those without major depressive episode. Method: We screened 260 consecutive ischemic stroke patients admitted to the neurology clinic of a university hospital. Seventy-three patients were eligible and prospectively evaluated. We assessed the diagnosis of major depressive episode using the Structured Clinical Interview for DSM-IV and the profile of depressive symptoms using the 31-item version of the Hamilton Depression Rating Scale. For data analysis we used cluster analyses and logistic regression equations. Results: Twenty-one (28.8%) patients had a major depressive episode. The odds ratio of being diagnosed with major depressive episode was 3.86; (95% CI, 1.23-12.04) for an increase of one unit in the cluster composed by the domains of fatigue/interest and retardation, and 2.39 (95% CI, 1.21-4.71) for an increase of one unit in the cluster composed by the domains of cognitive, accessory and anxiety symptoms. The domains of eating/weight and insomnia did not contribute for the major depressive episode diagnosis. Conclusion: The domains of retardation and interest/fatigue are the most relevant for the diagnosis of major depressive episode after stroke.

Descriptors: Stroke; Depression; Depressive disorder, major; Signs and symptoms; Clustering

Resumo

Objetivo: O episódio depressivo maior após acidente vascular cerebral é muito frequente, mas é subdiagnosticado. Pesquisas têm investigado a sintomatologia do episódio depressivo maior pós-acidente vascular cerebral, o que pode facilitar sua identificação. Este estudo foi desenvolvido para identificar os sintomas depressivos que melhor diferenciam pacientes com episódio depressivo maior daqueles sem episódio depressivo maior após o acidente vascular cerebral. Método: Foram triados consecutivamente 260 pacientes com acidente vascular cerebral admitidos à enfermaria de neurologia de um hospital universitário, dos quais 73 pacientes foram acompanhados. Para investigar o diagnóstico de episódio depressivo maior foi utilizada a Entrevista Clínica Estruturada para DSM-IV e para a sintomatologia depressiva a Escala de Avaliação para Depressão de Hamilton, versão 31 itens. Para a análise dos dados foi utilizada a análise de clusters e regressão logística. Resultados: Vinte e um (28,8%) pacientes tiveram episódio depressivo maior. O odds ratio para o diagnóstico de episódio depressivo maior foi 3,86; (95% IC, 1,23-12,04) para um aumento de uma unidade no cluster dos domínios interesse/fadiga e lentificação, e 2,39 (95% IC, 1,21-4,71) para um aumento de uma unidade no cluster dos domínios cognitivos, acessórios e ansiedade. Os domínios apetite/peso e insônia não contribuíram para o diagnóstico de episódio depressivo maior. Conclusão: Os domínios de lentificação e interesse/fadiga são os mais relevantes para o diagnóstico do episódio depressivo maior após acidente vascular cerebral.

Descritores: Acidente cerebral vascular; Depressão; Transtorno depressivo maior; Sinais e sintomas; Análise por conglomerados

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Introduction

Major depressive episode (MDE) is a common complication of stroke, with a reported prevalence ranging from 10 to 34%. Depression after stroke is associated with increased mortality, impairment in physical activities and language functioning, and reduced quality of life. Diagnosis and treatment of post-stroke depression (PSD) have been associated with improvement in functional recovery and reduction in cognitive impairment. Thus, early recognition and management of depression have been considered as critical for functional improvement after stroke. However, detection of depression after stroke is bellow 20-50%. Although several factors may contribute to such under-detection, the first step to improve the diagnosis of depression is to recognize the most specific symptoms. In particular, symptoms relevant for diagnosing primary depression may not be as relevant for diagnosing depression in special populations such as elders, and depression associated with medical conditions including stroke. For instance, somatic symptoms such as fatigue, psychomotor retardation, reduced concentration, insomnia, and reduced appetite may be directly related to the cerebrovascular event and are not as useful in diagnosing depression after stroke. Of note, somatic symptoms of depression have been reported to compromise the response to treatment and to be associated with refractoriness and chronicity.

Some studies have investigated the profile of depressive symptomatology in stroke patients by verifying the frequencies of neuropsychiatric symptoms or studying psychological and autonomic symptoms and signs associated with depressive mood. Several studies have suggested that depression after stroke has distinct psychopathological characteristics compared to primary depression and to depression associated with other medical conditions. Gainotti et al. found that PSD after stroke had a predominance of anxiety, catastrophic reactions, hyperemotionalism and reactive diurnal mood variations, whereas primary major depression had a predominance of depressed mood, guilt feelings, suicidal thoughts and an increase in early morning unexplained insomnia. In addition, Beblo and Driessen found that patients with PSD suffered from more serious physical signs of depression (appetite loss, weight loss, lack of energy) and fewer cyclic (diurnal variation, difficulty falling asleep, multiple awakenings during sleep, early morning awakening) and ideational disturbances (ideas of suicide, self-deprecation, pessimism, mood-congruent delusions) than those with primary major depression. Consistent with Gainotti et al., Fedoroff et al. also found that anxiety symptoms were more frequent in acute stroke patients with major depression than in patients with major depression who had had either acute myocardial infarctions or acute spinal cord injury. In contrast, Caeiro et al. reported that apathy/loss of interest was the only symptom with increased frequency in depressed acute stroke patients compared with depressed acute coronary patients within the first 4 days after the medical event. Taken together these studies support the notion that specific symptoms characterize post stroke depression, but inconsistencies among these reports may warrant additional research on this topic.

Given the psychopathological specificity of PSD, several studies have investigated the symptoms that best explain the PSD diagnosis. Coster et al. using the 17-item Hamilton Depression Rating Scale (HAM-D-17) found that depressed mood followed by reduced appetite, thoughts of suicide, psychomotor retardation, psychic anxiety, and fatigue significantly distinguished post-stroke patients with MDE from non-depressed patients. In their study most psychological symptoms had relatively low discriminative properties.

However, some methodological aspects should be taken into account to ensure that the results are representative of a post-stroke depression (i.e., a depressive episode etiologically related to the stroke). For instance, the inclusion of patients with previous personal history of major depressive disorder (MDD) or previous stroke, patients with different types of stroke (intracerebral hemorrhage, intraventricular hemorrhage, subarachnoid hemorrhage and ischemic), and patients with stroke in the cerebellum and brainstem may have limited or dilurred the conclusions about the psychopathology of PSD. The aim of this study was to identify the domains of depressive symptomatology that best explain diagnosis of MDE within 4 months after stroke. In an effort to accomplish this objective, we included only patients after their first-ever supratentorial ischemic stroke and without previous history of MDD. In addition, we used the 31-item version of the Hamilton Depression Rating Scale (HAM-D-31) to explore a more comprehensive psychopathological profile.

Method

1. Patients

We screened 260 consecutive male and female inpatients, 18 years or older, admitted to the neurological unit of the Clinical Hospital of the Universidade de São Paulo School of Medicine (HC-FMUSP) with diagnosis of ischemic stroke from August 2002 to May 2007. The clinical diagnosis of stroke was performed by a neurologist according to the World Health Organization criteria and confirmed by magnetic resonance imaging (MRI). Patients were excluded from the study if they had history of stroke or other central nervous system diseases (amyotrophic lateral sclerosis, subarachnoid hemorrhage, Binswanger’s disease, brain tumors, and multiple sclerosis), no supratentorial stroke, Cushings syndrome, alcohol and drug dependence in the last 12 months, history of MDE, current MDE with onset before the stroke, bipolar disorder, psychotic disorder, and aphasia that would restrict the interview. It was not possible to obtain information about history of MDE before stroke in 23 patients (patients with aphasia = 15, low level of consciousness = 2, severe physical condition = 3, and other reasons = 3). Of the 237 patients with complete previous history data, 77 met the inclusion and exclusion criteria and 73 of them were enrolled in the prospective phase of the study (four patients that met the inclusion and exclusion criteria refused to participate in the study). The institutional review board of the HC-FMUSP approved the study protocol and informed written consent was obtained from all included subjects.

2. Assessment

The 73 enrolled patients were evaluated at three different intervals after stroke. The first evaluation occurred between 6 and 23 days (mean ± SD; 12 ± 3.8), the second between 30 and 51 days (36 ± 6), and the third between 83 and 108 days (92.3 ± 54) after the stroke. A psychiatrist performed the diagnosis of MDE, using the Structured Clinical Interview for DSM-IV (SCID) according to the Diagnostic and Statistical Manual of Mental Disorder, 4th edition (DSM-IV) and assessed the severity of depressive symptoms using the HAM-D-31 in all three intervals.

3. Statistics

In this study with 73 post-stroke patients, 21 with MDE and 52 without MDE, we investigated the domains of depressive
symptoms from the HAM-D-31 that best predicted diagnosis of MDE performed with the SCID. We used the seven domains of depressive symptoms of the HAM-D-31 described by Jarmeson et al.21: 1) cognitive symptoms (worthlessness, hopelessness, helplessness, depressed mood, guilt feelings); 2) accessory symptoms (loss of insight, paranoid symptoms, obsessive and compulsive symptoms, hypochondriasis, depersonalization and derealization, diurnal variation, agitation); 3) retardation (retardation, psychic retardation, motoric retardation, loss of libido); 4) fatigue/interest (oversleeping, hypersomnia, napping, work and interest, anergy); 5) eating/weight symptoms (increased appetite, decreased appetite, weight gain, weight loss); 6) insomnia (middle insomnia, late insomnia, early insomnia); 7) anxiety (anxiety-psychic, anxiety-somatic). The suicidal item of the HAM-D-31 (item 3) was analyzed separately. For patients who met MDE criteria the domains were rated at evaluation in which they had the highest score in the HAM-D-31 (before starting antidepressant treatment). For patients who did not meet criteria for MDE in any of the three post-stroke evaluations we first calculated the means of each HAM-D-31 symptom and then established the domains based on these means. We excluded the symptom of depressed mood from the cluster analysis since it was present in all depressed patients. The suicidal item of the HAM-D-31 was analyzed separately due to its relevance and because it was not included in Jarmeson’s study.21 We performed a cluster analysis with the seven domains of the HAM-D-31 symptoms to select the best model to predict the diagnosis of depression in our sample. With this model we first investigated symptomatology divided into three domains. A logistic regression analysis was performed. The stepwise method for selected variables was used for the final model.

Statistical analyses were performed using the Special Package for Social Sciences, version 14. Analyses of sociodemographic data were performed to verify whether the two groups of patients with and without MDE were comparable. The chi-square test or Fisher’s exact test were used for categorical variables. Continuous variables presented normal distribution according to the Kolmogorov-Smirnov test and the t-test was then used to compare the two groups. Depressed and non-depressed patients presented equality of variances for age but not for the HAM-D-31, consequently we used the t-test for the former analysis and Welch’s test for the latter. Significance levels were set at alpha = 0.05.

Results
Seventy-three ischemic stroke patients were followed-up for four months (mean ± SD age, 48.7 ± 14.6; range 19 to 79 years; 57.5% male). The incidence of MDE was 28.8% (21 patients). There were no statistically significant differences between patients with and without MDE in terms of gender, marital status, occupation, educational level, and mean age (Table 1). The average HAM-D-31 score was 23.1 ± 5.2 in the group of patients with MDE and 5.7 ± 3.6 in non-depressed patients (p < 0.001).

The best model of the cluster analysis resulted in the inclusion of three domains of symptoms: domain 1, composed of the domains of cognitive symptoms, accessory symptoms and anxiety; domain 2, composed of the domains of retardation and fatigue/interest; domain 3, composed of the domains of eating/weight and insomnia.

Logistic regression analysis was performed using the MDE as the dependent variable and symptoms domains, gender and age as independent variables. The symptom domain including eating/weight and insomnia (domain 3), gender and age did not show significant association with diagnosis of MDE and was withdrawn from the final model. Retardation and fatigue/interest domains (domain 2), and cognitive symptoms, domain of accessory symptoms and anxiety domains (domain 1) were each independently associated with the presence of MDE within 4 months after stroke in regression analyses. Table 2 shows that patients with an increase in one unit in the symptoms domains of domain 2 (retardation, fatigue/interest domains) were associated with an almost four times greater risk of being diagnosed with MDE within 4 months after the stroke (odds ratio [OR], 3.86; 95% CI, 1.23-12.04). An increase of one unit in the score of domain 1 (cognitive symptoms, accessory symptoms and anxiety domains) had more than a two-fold risk of being diagnosed with MDE within 4 months after the stroke (OR, 2.39; 95% CI, 1.21-4.71). Eight patients (11%) scored in the suicidal ideation item of HAM-D-31, six (28.6%) of the 21 patients with MDE and two (3.9%) of the 52 patients without MDE (p = 0.006). In the logistic regression analysis with MDE within 4 months after stroke as the dependent variable, an increase in one unit in the suicidal ideation symptom was associated with a seven-fold risk of being diagnosed with MDE (OR, 7.85; 95% CI, 1.29-47.96) independently of age and gender.

Table 1 - Sociodemographic characteristics and severity of depressive symptoms within 4 months after stroke by present or absent MDE

<table>
<thead>
<tr>
<th>Nominal variables</th>
<th>Present</th>
<th>Absent</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender*</td>
<td>N (%)</td>
<td>N (%)</td>
<td>0.792</td>
</tr>
<tr>
<td>Men</td>
<td>11 (27.5)</td>
<td>26 (72.5)</td>
<td></td>
</tr>
<tr>
<td>Women</td>
<td>10 (30.3)</td>
<td>23 (69.7)</td>
<td></td>
</tr>
<tr>
<td>Marital status*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Married</td>
<td>15 (31.3)</td>
<td>33 (68.7)</td>
<td>0.516</td>
</tr>
<tr>
<td>Occupation*</td>
<td>13 (26.5)</td>
<td>36 (73.5)</td>
<td>0.546</td>
</tr>
<tr>
<td>Educational level*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ 8 years of study</td>
<td>14 (30.4)</td>
<td>32 (69.6)</td>
<td>0.681</td>
</tr>
<tr>
<td>≥ 9 years of study</td>
<td>7 (25.9)</td>
<td>20 (74.1)</td>
<td></td>
</tr>
<tr>
<td>Numerical variables</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HAM-D-31**</td>
<td>23.1 (6.2)</td>
<td>5.7 (2.6)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Age**</td>
<td>50 (16.4)</td>
<td>48.3 (14)</td>
<td>0.054</td>
</tr>
</tbody>
</table>

N = 73. MDE = major depressive episode. * chi-square test. ** t-test

Table 2 - Final model of the logistic regression analysis of patients with and without MDE after stroke by domains of symptoms of HAM-D-31

<table>
<thead>
<tr>
<th>β</th>
<th>SE</th>
<th>p-value</th>
<th>OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Constant</td>
<td>-11.103</td>
<td>4.392</td>
<td>0.011</td>
<td>0.000</td>
</tr>
<tr>
<td>Domain 1: Cognitive*, accessory and anxiety domains</td>
<td>0.871</td>
<td>0.347</td>
<td>0.012</td>
<td>2.388</td>
</tr>
<tr>
<td>Domain 2: Retardation and fatigue/interest domains</td>
<td>1.351</td>
<td>0.580</td>
<td>0.020</td>
<td>3.862</td>
</tr>
</tbody>
</table>

N = 73
* The item 1 (depressive mood) of HAM-D-31 was not included in this analysis because it was present in all individuals with major depression episode.
Gender, age and domain 3 were not included in final model because they were not significantly associated with MDE.
Discussion

We investigated the psychopathology of incident MDE in 73 first ever supratentorial ischemic stroke patients. The cohort was prospectively followed-up for 4 months. The cluster analysis revealed that the retardation and fatigue/interest domains were the best in explaining the diagnosis of MDE. These domains were composed of HAM-D-31 items: retardation; psychic retardation, motor retardation, loss of libido, oversleeping, hypersomnia, napping, work and interest, and anergia. These findings reinforce the relevance of retardation for the diagnosis of depression after stroke suggested by previous studies. Lipsey et al. compared groups of patients with MDE after stroke and patients with functional major depression using the Present State Examination (PSE) syndrome profile, and also reported that the cluster of slowness (slowness and underactivity, slow speech, muteness, and restriction of quantity of speech) was more frequent in the group of patients with MDE after stroke. Coster et al. used the 17-item version of the HAM-D and found that psychomotor retardation and fatigue were among the symptoms with the strongest sensitivity for the diagnosis of MDE after stroke. It is important to stress that, in contrast to Coster et al., our sample, decreased interest and energy were also good discriminators between depressed and non-depressed patients. To our knowledge this is the first report of the relevance of decreased interest in diagnosing PSD patients, although this symptom has been previously highlighted as a good discriminator to diagnosing depression in medically ill subjects in a general hospital.

The domains of cognitive, anxiety, and accessory symptoms (domain 1) also explained the diagnoses of MDE after stroke although the odds ratio was lower compared to domain 2. The items of HAM-D-31 considered in domain 1 were worthlessness, hopelessness, guilt feelings, loss of insight, paranoid symptoms, obsessive and compulsive symptoms, hypochondriasis, depersonalization and derealization, diurnal variation, agitation, anxiety psychic and anxiety somatic. Finally, the domains of insomnia and eating/weight did not explain the diagnosis of MDE after stroke. The symptoms comprised in these domains were increased or decreased appetite; weight gain or weight loss; middle insomnia; delayed insomnia and initial insomnia. This finding is in accordance with data reported by Coster et al. showing that early and middle insomnia, early morning awakening, and loss of weight had minor discriminative properties and most psychological symptoms, such as ‘hypochondriasis’, ‘lack of insight’ and ‘feelings of guilt’ had even lower discriminative power for the diagnosis of MDE after stroke. Corroborating these findings, Beblo and Driessen reported that patients with PSD suffered from fewer cyclic disturbances (diurnal variation, difficulty in falling asleep, multiple awakenings during sleep, early morning awakening) than those with primary depression.

Depressed mood (not included in the cluster analysis) was present in all patients with MDE, suggesting that patients with loss of interest or pleasure as the only core symptom (‘A’ criterion) of MDE, or depressed patients denying the depressed mood, are not common after stroke. On this matter, Fedoroff et al. investigated the existence of post-stroke patients unable or unwilling to acknowledge their depressed mood. They reported that 46 of 205 patients met all the criteria for diagnosis of MDE according to DSM-III and only 10 of 205 failed to meet the criteria only because they did not have depressed mood. These patients without depressed mood had a mean of one autonomic symptom, compared with a mean of almost four autonomic symptoms in the depressed group. The authors concluded that if there is “masked” depression (i.e. depression without depressed mood) after stroke, it occurs in a minority of patients. According to Paradiso et al. only 2% to 3% of post-stroke patients with depressive symptoms do not have depressed mood (i.e. “masked” depression).

Suicidal ideation, as assessed by the HAM-D-31, was present in eight (11%) patients in this 4-month follow-up after stroke, a rate similar to those previously reported. Kishi et al. found that 6.6% of their patients had suicidal plans during the acute period after stroke in an in-hospital psychiatric evaluation. Pohjasvaara et al. in a prospective study, found that suicidal ideas were present in 9.8% of their patients at 3 months, and in 14% at 15 months of follow-up after stroke. In our sample, suicidal ideation was present in six (28.6%) of the 21 patients with MDE, and a one-point increase in the item suicidal ideation was associated with an OR of 7.8 of being diagnosed with MDE. The rate of suicidal ideation in MDE patients in our sample is relatively higher than in previous reports, where it ranged between 14% and 18%.

One strength of our results is that our sample was composed of patients without previous history of MDD at their first-ever, ischemic, supratentorial stroke. Secondly, we prospectively followed a cohort of stroke survivors, while others performed a cross-sectional evaluation or used a case-control design. Among those who developed a prospective study, the use of a two-step procedure to diagnose depression including a psychiatric evaluation only for those with suspicion of depression or including patients with previous stroke and previous history of depression limits the specificity of the conclusions.

Another relevant point of our investigation is the use of the HAM-D-31, a more comprehensive scale, to evaluate depressive symptomatology. The advantage of the HAM-D-31 is that it includes some symptoms of the DSM-IV criteria for MDE not contemplated in other scales, such as the reverse vegetative symptoms (items 22 to 28) including hypersomnia, oversleeping, napping, increased appetite, weight gain, psychic and motor retardation, and also cognitive symptoms (items 29 to 31) including helplessness, hopelessness and worthlessness.

The prospective nature of our study and the exclusion of patients with previous history of MDE allowed us to obtain data regarding incidence (and not prevalence) of MDE within the first 4 months after stroke. The four-month incidence of MDE of 28.8% found in our sample is similar to the 27% found between the second and fourth months after stroke and the 25% found between 3 weeks and 3 months after stroke in studies that also excluded patients with previous history of depression, though both studies have performed cross-sectional evaluations. The prospective design of our study provides data about MDE incidence along various intervals after the stroke. For example, the incidence was 8.2% in the first month, 14.9% in the second month and 22.9% in the third month. An earlier prospective study developed by Robinson et al. found a 15% prevalence of MDE at 2 weeks and 22% at 3 months after stroke in a sample of 40 patients. However, the authors included ischemic and hemorrhagic strokes, patients with stroke involving the brainstem and cerebellum, and patients with previous personal history of depression. Another prospective study, developed by Kauhanem et al. reported a 9% incidence of MDE at 3 months and 16% at 12 months after the first ischemic stroke. Although they excluded patients with previous history of depression, they also included patients with stroke in the brainstem and cerebellum. Aben et al., also in a prospective study, reported an incidence of joint major and minor depression of 21.6% at one month after stroke, 5.1% at three months, 6% at six months, 5.6%
at nine months and 7.1% at one year after stroke.\textsuperscript{30} The one-year cumulative incidence of depression was 38.7% with 23.3% being major depressive disorder and 15.4% minor depressive disorder. Although they excluded patients (4.1%) with current depressive episode at the time of the stroke, 21.8% of their patients had previous personal history of depression. In summary, our study is the first to use the prospective approach to investigate the incidence of MDE in patients with first ever supratentorial ischemic stroke without previous history of depression.

A final contribution of our study regards the gender distribution of the incident post-stroke MDE. Although our sample was not specifically powered to evaluate gender distribution of depression, we did not find any association between gender and the 4-month cumulative incidence of MDE after stroke. On the other hand, a post-hoc analysis of baseline data including patients with previous history of depression revealed a trend of higher rate of previous history of depression in women (22.1%) compared to men (12.8%) (p = 0.057). This previous gender distribution of MDE is in line with the literature consensus that the prevalence of MDD in women is two-fold that found for men in the general population.\textsuperscript{31} This absence of difference in gender distribution of MDE after stroke signals that post-stroke depression has distinct biological and/or psychological etiological factors. Although several studies have found similar results\textsuperscript{29,32-35} or even a positive association of male sex with MDE\textsuperscript{36} or with higher depressive symptomatology after stroke,\textsuperscript{37} some have reported an increased prevalence of MDE among females.\textsuperscript{16,28,30} The only study designed to verify the influence of sex on PSD reported a 12.3% prevalence of MDE for males and 23.6% for females at 2 weeks after stroke. Methodological issues may have contributed to this discrepancy. Past personal history of depression and history of previous stroke have been reported to be risk factors for MDE after stroke.\textsuperscript{30,33-37} The inclusion of patients with such risk factors may have biased the gender ratio of depression after stroke. For example, including patients with previous history of depression will probably inflate the occurrence of MDE in females, because of the 2:1 (female/male) ratio of depression in the general population, as mentioned above. Paradiso and Robinson's finding may support this hypothesis since they found that the risk factor for depression in women was personal history of psychiatric disorder. On the contrary, men tend to have more stroke recurrence than women. Consequently, the inclusion of patients with recurrent stroke will probably inflate the occurrence of depression in males.

Several limitations of this study have to be considered. First, our sample is composed of patients in a teaching general hospital, restricting the generalization of results for patients from other settings. Second, we followed the patients for 4 months after stroke and incident depressive episodes after this period may have different psychopathological presentation. Third, in the infirmary evaluation we used the criteria of 1 week of depressive symptomatology instead of 2 weeks, as required by the DSM-IV. This may have overestimated the diagnosis of MDE in the first evaluation after stroke. Fourth, the use of stepwise selection procedures in our model may lead to results which only describe our current sample; independent studies will be needed to fully validate our results. Fifth, we did not investigate the influence of the lesion location and severity of neurologic impairment in the relationship between the domains of depressive symptoms and the diagnosis of the MDE. Although this was not the objective of our study, and others have also focused exclusively on the psychopathology,\textsuperscript{2} the inclusion of such data could further contribute to the understanding of the pathophysiology of the depressive symptoms and post-stroke MDE. Finally, cluster analysis does not define the contribution of any individual symptom for the diagnosis of MDE. However, this analysis allows physicians to identify the domain (cluster) of depressive symptoms with major weight when considering diagnosing MDE in stroke patients.

### Conclusion

Despite these limitations, our study suggests that the cluster retardation and the cluster fatigue/interest including several somatic symptoms (i.e., retardation, psychic retardation, motoric retardation, loss of libido, oversleeping, hypersonnia, napping, and anergia) were the best to differentiate patients with MDE after stroke from those non-depressed ones, independent of age and gender. Moreover, depressed mood proved to be an excellent marker of MDE and should be used as a target for clinicians screening for depression after stroke. These results support previous opinions for an inclusive approach to the diagnosis of depression in stroke patients\textsuperscript{2} and that the distinction between symptoms due to depression and those due to medical illness is not crucial for MDE diagnosis.\textsuperscript{12}
References
