Poststroke depression and its multifactorial nature : results from a prospective longitudinal study

POSTSTROKE DEPRESSION AND ITS MULTIFACTORIAL NATURE: RESULTS FROM A PROSPECTIVE LONGITUDINAL STUDY

Running head: The multifactorial nature of poststroke depression

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ABSTRACT

Objective

Poststroke depression (PSD) is commonly observed in stroke patients and has a negative impact on functional outcome and quality of life. Therefore, a prospective, longitudinal epidemiological study was conducted aiming to determine prevalence and risk factors for PSD at 1,3,6,12 and 18 months poststroke.

Methods

A total of 222 patients were included in the study and 201 patients entered data analysis. Demographic data, vascular risk factors, stroke characteristics, functional and neurocognitive outcome measures and psychosocial factors were considered as potential risk factors for PSD. Clinically significant signs and symptoms of PSD were quantified by means of the Cornell Scale for Depression (CSD) and the Montgomery and Åsberg Depression Rating Scale (MADRS).

Results

PSD was present at 1,3,6,12 and 18 months poststroke in 24.5%, 27.1%, 28.3%, 19.8% and 26.3% of the patients respectively. Univariate regression analyses revealed that PSD was significantly associated with stroke severity, physical disability, cognitive impairment and stroke outcome during the 18 months time frame of the study. Reduced social activities and the presence of apraxia were consistently associated with PSD whereas aphasia was only significantly associated in the first 6 months after stroke. Patients with relational problems had a 3 times greater risk of becoming depressed at 18 months poststroke than patients without relational problems (OR=3.09; 95%CI=1.31-7.26).

Conclusions

Risk factors for PSD seem variable indicating the need for clinicians to consider the dynamic and multifactorial nature of PSD emphasizing the importance of a rigorous and long-term monitoring and support of stroke patients and their caregivers.

Background

Stroke is a major health problem worldwide and imposes a significant health and economic burden [1,2]. It has a sudden and often dramatic impact on the person and his/her family [3]. Stroke is also responsible for secondary problems such as dementia, epilepsy, fractures and depression [4-6]. The prevalence of poststroke depression (PSD) varies between 20% and 65%, depending on the population studied, the definition of depression as well as assessment measures used and the assessment time interval [7,8]. Although PSD leads to increased mortality [9], poor functional outcome [10], decreased quality of life [11] and social isolation [12,13], a consensus on the course and associated factors of depression has not been reached. The most frequently cited risk factors for PSD in literature are stroke severity, physical disability or functional impairment [14,15], as well as age, gender, history of depression and lack of family and social support [16]. Other possible risk factors include unilateral neglect, apraxia and aphasia. Few studies examine and report a link between neglect and depression or depressive symptoms [16,17] but little research is done concerning apraxia and its risk to PSD [18]. Aphasia is a common language disorder and neuropsychological consequence of stroke, with a prevalence of one-third of all stroke patients in acute phase [19]. As PSD may be common in aphasic stroke patients [20], exclusion of these patients in an epidemiological study about PSD has to be avoided. However, communication difficulties may complicate the assessment of depression in patients with stroke. This emphasizes the importance of administering observational methods in stroke patients with communication difficulties.

The aim of this study was to examine a much broader range of variables than most studies did, as the aetiology of PSD is likely to be multifactorial. Accordingly, this epidemiological study was designed to determine prevalence of PSD and to assess which neuropsychological, clinical or functional factors are associated with depression during 18 months follow-up after stroke.

Material and methods

This study is part of the Middelheim Interdisciplinary Stroke Study (MISS) on clinical, biochemical, neuroimaging, neuropsychological and electrophysiological evaluation of patients with ischemic stroke or transient ischemic attack (TIA) [21-24]. In order to study risk factors for PSD, a prospective, longitudinal epidemiological study was conducted between 2005-2012 aiming to determine prevalence and risk factors for PSD at 1,3,6, 12 and 18 months poststroke. Patients admitted to the stroke unit with first or recurrent stroke were eligible for inclusion if acute stroke symptoms matched the WHO diagnostic criteria for ischemic or haemorrhagic stroke. Lesion location was confirmed on neuroimaging (CT and/or MRI) and grouped as left or right hemispherical or both and was further subdivided according to the arterial territory involved: anterior cerebral artery (ACA), middle cerebral artery (MCA), posterior cerebral artery (PCA) or vertebrobasilar artery. TIA was defined as symptoms lasting less than one hour in the absence of acute cerebral ischemia on imaging [25].

Information on previous depressive symptoms, vascular risk factors, education, employment, marital status, family composition (number of children) and use of psychotropic medication was obtained by means of an interview of patients and their relatives and from the clinical records, using structured case report forms. Recorded vascular risk factors comprised previously diagnosed and treated conditions. History of depression was defined as the occurrence of at least one depressive episode that had required treatment with antidepressant medication or attention of a general practitioner, psychologist or psychiatrist.

The Functional Independent Measure Scale (FIM) and the Barthel Index (BI) were used at 24 hours poststroke and all follow-up assessments to evaluate disability [26] and to gage the level of independence in activities of daily living (ADL) [27]. The National Institute of Health Stroke Scale (NIHSS) [28] measured stroke severity and outcome was assessed by

the modified Rankin Scale (mRS) [29]. Stroke Impact and quality of life before stroke was measured with the Belgian-Dutch version of the Stroke Impact Scale (SIS) (v3.0) [30] as previously described [24]. Cognitive functioning was assessed with the Mini Mental State Examination (MMSE) [31] and the cognitive domain of the FIM and SIS.

A neuropsychological screening was performed to assess presence or absence of confusion, agnosia, aphasia, dysarthria, apraxia and unilateral neglect.

Relational problems since stroke onset and other psychosocial factors possibly affecting the onset of depression were assessed at 18 months poststroke by means of a questionnaire using informant-based questions (Table 1).

Patients were classified as depressed if they scored 8 or more on the Cornell Scale for Depression (CDS). Indeed, a score of 8 or more suggests significant depressive symptoms [32]. The questionnaire contains 19 items that focus on visible behaviour to make it possible for caregivers or proxies to estimate the severity of patient symptoms. The CSD was used at baseline to detect significant depressive symptoms before stroke onset. Depressive symptoms were quantified during follow-up visits using the CSD and the Montgomery and Åsberg depression rating scale (MADRS) an interview based and observer-rated scale putting little emphasis on somatic symptoms [33].

All patients were assessed by trained interviewers within seven days of stroke onset and re-evaluated at 1,3,6,12 and 18 months poststroke. The study protocol was approved by the Ethics Committee of ZNA (ZiekenhuisNetwerk Antwerpen) and the University of Antwerp. Informed consent was obtained from each participant or proxy in case of aphasia, confusion or reduced consciousness.

Statistical analysis

Data were analysed with SPSS 20.0 for windows and using R, version 13.1 (www.r-project.org). For group comparisons of descriptive sample characteristics (demographic, neuropsychological, clinical data) the Student's t-test was used for continuous, normally distributed data. Non-parametric statistical tests (Mann-Whitney U Rank Sum or Wilcoxon Signed-Rank test) were used for non-normal distributed data or small numbers. The Chi-square or Fisher's exact test (with expected counts <5) was used for dichotomous variables. Correlations were estimated using the Spearman rank correlation coefficient and univariate linear regression was performed using both CSD and MADRS as outcome variable. Univariate logistic regression was performed, and Odds ratio's (OR) with 95% Confidence Intervals (CI) calculated, using the dichotomized CDS as outcome, whereby a score of 8 or more suggests significant depressive symptoms [32]. A value of $P<0.05$ was considered significant. Where appropriate, results were given as mean values ± standard deviation (SD).

Results

Study population (Table 2)

A total of 222 patients met entry criteria and were prospectively included in the study. Sixteen patients died before the first follow-up visit, four patients refused further participation for no apparent reason and one patient returned abroad. The study population that entered data analysis consisted of 201 patients. The composition of the study population groups at 1,3,6,12 and 18 months poststroke was different as some patients died before their next follow-up visit while others were not available at time of assessment. The characteristics of the study population as a whole and of the different groups at the follow-up visits are presented in Table 2.

Dropouts

Those who died (*n*=16) or refused to participate (*n*=5) before their first follow-up visit did not differ from those investigated regarding to age, gender, previous depressive symptoms, vascular risk factors, education, employment, marital status and use of medication before stroke. However, dropouts were more likely to be divorced (23.8% vs. 7.0%; *P=0.022*) and had more right MCA involvement (45% vs. 23.4%; *P=0.034)*. Dropouts were less mobile before stroke as measured by SIS mobility (85.2 ± 12.7 vs. 95.9 ± 8.8; *P=0.004*) and suffered a more severe stroke (NIHSS=14.2 ± 10.1 vs. 6.8 ± 7.1; *P=<0.001*). Furthermore, dropouts experienced more neglect (47.4% vs. 22.6%; *P=0.026*), had higher dependency for care according to the BI (34.3 ± 40.0 vs. 65.2 ± 37.1; *P=<0.001*) and were more functionally (38.0 ± 29.8 vs. 62.0 ± 28.0; *P=<0,001*) and cognitively impaired (19.6 ± 12.4 vs. 27.6 ± 9.4; *P=<0,001*) due to stroke as measured by FIM. There was no difference in the mean CSD total score at baseline between the two latter groups.

Prevalence of significant PSD symptoms and use of antidepressants

Transforming the continuous variable CSD to a categorical variable, being depressed (≥ 8 on CSD) or not clinically depressed (< 8 on CSD), showed that prevalence rates of the depressed groups ranged between 19.8% and 28.3% during the 18 months time frame of the study. Cross-sectionally the prevalence rates were 24.5% (23/94) at 1 month, 27.1% (46/170) at 3 months, 28.3% (28/99) at 6 months, 19.8% (23/116) at 12 months and 26.3% (41/156) at 18 months poststroke.

The use of antidepressants at follow-up was significantly more frequent than at baseline as shown in Figure 1.

PSD symptoms in relation to demographic data, medical history and stroke characteristics

Comparing depressed and non-depressed patients at 1,3,6,12 and 18 months poststroke, there were no significant differences with regard to gender, education, employment, marital status, family composition, vascular risk factors, history of depression, use of psychotropic medication and stroke localization.

Although no statistically significant difference was found with regard to gender, women were more represented in the depressed group at all times except at 18 months poststroke (Figure 2). At 18 months after stroke the depressed group consisted of 65.9% men and 34.1% women. Considering the possibility of more social and family support, number of children was included in the data analysis. In general, depressed patients had fewer children but no statistical significant difference could be demonstrated.

Mean age of the study population group as a whole and the groups at month 1,3,6,12 and 18 is shown in table 2 and ranges between 68 and 70.1 years old. When comparing the depressed and non-depressed groups at different follow-up visits, depressed patients were younger than non-depressed patients at 6 months poststroke (62.4 ± 15.7 vs. 70.2 ± 13.7; *P=0.016*). No other significant differences were found.

PSD symptoms in relation to physical and cognitive deficits (Figure 3, Table 3)

At 1 month after stroke, the mean scores of all functional scales of the depressed group were lower than the non-depressed group but no statistically significant difference could be demonstrated. Only stroke severity at 1 month poststroke showed statistically significant lower scores in depressed patients as compared to non-depressive patients (NIHSS=5.3 ± 5.7 vs. 2.0 ± 3.1; *P=0.038*). In contrast to this latter group, patients with PSD at 3 months poststroke were significantly more dependent with regard to ADL functions (BI=77.6 ± 32.6 vs. 92.9 ± 17.0 *P=<0.001*), had more functional impairment (FIM motoric=70.4 ± 24.0 vs.

83.2 ± 13.9 *P=<0.001*, mRS=2.8 ± 1.3 vs. 1.8 ± 1.1 *P=<0.001*, SIS mobility=71.5 ± 25.2 vs. 88.1 ± 15.8 *P=<0.001*), were participating significantly less in daily social activities (SIS activity=65.7 ± 24.4 vs. 83.1 ± 17.5; *P=<0.001*) and were more cognitively impaired as measured by the MMSE (25.8 ± 4.4 vs. 27.1 ± 4.1; *P=0.001*) and cognitive domains of FIM (28.5 ± 8.8 vs. 32.4 ± 5.1; *P=0.002*) and SIS (76.3 ± 26.6 vs. 92.4 ± 13.5; *P=<0.001*). At 3 months poststroke, stroke severity (NIHSS) was on average worse for depressed patients than non-depressed patients but no statistically significant difference was found. At 6 months poststroke depressed patients had a more severe stroke (NIHSS), worse outcome (MSR), were less mobile (SIS mobility), more cognitively impaired (SIS memory, FIM cognition) and experienced more difficulties with communication (SIS communication) but none of these scales representing the functional capacity of the patient was significantly different from the none depressed patients except for FIM cognition and SIS activity.

At 6 months poststroke depressed patients were significantly more cognitively impaired (FIM cognition=31.8 ± 3.8 vs. 32.5 ± 5.3; *P=0.020*) and participated significantly less in daily social activities than none depressed patients (SIS activity=73.2 ± 18.7 vs. 83.7 ± 16.1; *P=0.006*). Mean scores of BI and motoric FIM revealed to be even higher in the depressed group at 6 months poststroke reflecting more independency in daily activities (ADL) and less functional impairment then non-depressed patients. Furthermore, there was no difference between the two groups with regard to mean MMSE total scores.

Just like previous findings, mean scores of the functional scales at 12 months poststroke were different between depressed and non-depressed patients. Although no significant difference was found, there was a general tendency of worse mean scores of all functional scales comparing depressed and non-depressed patients. However, only a statistically significant difference was found between the two latter groups for stroke outcome (mRS=2.4 ± 1.3 vs. 1.6 ± 1.3; *P=0.009*), daily social activities (SIS activity=70.7 ± 20.2 vs. 86.6 ± 14.8

P=0.001) and cognitive impairment (SIS cognition=84.1 ± 21.4 vs. 93.4 ± 13.5; *P=0.012*, MMSE=25.1 ± 6.0 vs. 27.7 ± 3.9; *P=0.010*).

At 18 months poststroke all functional scales representing the functional capacity of the patients were significantly different comparing both groups (Table 3) except for care dependency (BI) and the MMSE.

PSD symptoms in relation to relational problems since stroke onset and other psychosocial factors (Table 1)

None of the potential psychosocial problems taken into account were significantly different between depressed and non-depressed patients except for relational problems and the absence of caregivers. A higher prevalence of persistent relationship problems present at time of questioning, emerged in the last 18 months and related to the effects of stroke, was observed in patients with PSD compared to non-depressed stroke patients (24.4% vs. 2.6%; *P=<0.001*). At 18 months poststroke, 62.7% of the patients who received any form of active care, by proxies or professionals, were not depressed (*P=0.030*).

Risk factors for PSD: univariate linear and logistic regression analysis (Table 4,5 & 6)

Potential risk factors for developing PSD were analysed by correlation and univariate linear and logistic regression analysis at 1,3,6,12 and 18 months poststroke using CSD, MADRS and dichotomized CSD as dependent variables. Spearman rank correlation coefficients and p-values for linear regression analysis (MADRS) are shown in Table 4.

Univariate linear regression analyses revealed that PSD was significantly associated with most functional scales at 1,3,6,12 and 18 months poststroke except for month 6 and some at month 12. No significant association could be found between PSD and patient's mobility (SIS mobility), physical (FIM motoric) and cognitive (FIM cognition, MMSE) impairment or

dependency for care at 6 months poststroke. At 12 months poststroke there was no association between PSD and patient's ability to communicate (SIS communication), cognitive impairment (FIM cognition) and the level of independence in activities of daily living (BI).

Univariate logistic regression analysis using the dichotomized CSD as outcome variable showed similar significant associations between PSD and functional scales at the different measure points except at 1 and 6 months poststroke. At 1 month poststroke merely stroke severity (NIH) was significantly associated with PSD. The risk to become depressed increased with 18% when stroke severity increased with one unit on the NIHSS (OR=1.18; 95%CI=1.061-1.33). SIS activity was the only functional variable significantly associated with PSD at 6 months poststroke. The risk to become depressed decreased with 4% when the patient's activities increased with one unit on the SIS (OR=0.96; 95%CI=0.94-0.99). Logistic regression analysis of potential functional risk factors for developing PSD is shown in Table 5. Age was significantly associated with PSD at 6 months poststroke. The risk to become depressed at 6 months poststroke decreased with 4% when the patient's age increased with 1 year (OR=0.96; 95%CI=0.93-0.99).

The presence of neglect was mainly associated with PSD a 1 month poststroke. According to the dichotomized CSD, patients with the presence of neglect at 1 month poststroke had an approximately six times greater risk of becoming depressed than patients without neglect (OR= 5.82; 95%CI=1.47-22.98).

For apraxia, consistent associations were found at all different measure times whereas aphasia was only significantly associated with CSD and MADRS at 1,3 and 6 months poststroke. Neurocognitive outcome measures and their significant associations with CSD and MADRS at any time during 18 months follow-up are shown in Table 6.

Patients with relational problems since stroke onset, emerged in the last 18 months and related to the effects of stroke had a 3 times greater risk of becoming depressed at 18 months

poststroke than patients without relational problems (OR=3.09; 95%CI=1.31-7.26). Furthermore, those with persistent relationship problems present at time of questioning had even more risk for PSD (OR=12.04; 95%CI=3.12-46.46).

Discussion

This study was designed to determine prevalence of PSD and to examine which neuropsychological, clinical or functional factors are associated with depression during 18 months follow-up after stroke.

Prevalence and use of antidepressants

We found depressive symptoms to be frequent with little change in prevalence during 18 months follow-up after stroke. Between the different groups, depressive symptoms range between 20 to 28%. These prevalence rates are similar to some studies [34] but lower than others [35]. The use of antidepressants at 1,3,6,12 and 18 months poststroke (21.3%, 25.3%, 38.4%, 35.3% and 30.8% respectively) was significantly more frequent than at baseline (Figure 1) and might have led to an improvement of depressive symptoms and consequently to a lower prevalence of PSD at all times in our study. The use of antidepressant medication is presumably a confounding factor that might have lead to less significant associations between PSD and the different variables.

Demographic data

In our study no statistically significant difference was found with regard to gender. However, in accordance to existing literature [36], women were more represented in the depressed groups up to 12 months poststroke. At 18 months poststroke a shift in gender occurred in our sample and men became more (65.9%) depressed as compared to woman, which is in

accordance with results of Berg et al. [37]. According to Paradiso et al. [38] PSD may be of a different nature in men and women. Physical disability can be of greater importance in men over time, or men may have different coping abilities concerning health problems than women [37]. At 6 months poststroke depressed patients were younger than non-depressed patients. This finding is in accordance with Carota et al. who defined age <68 years as an independent predictor of PSD within the first year after stroke [35].

Physical and cognitive deficits

The correlation between physical disability and the development of PSD and depressive symptoms is the most robust correlation found in literature during the last 2 decades [16,35]. Although statistical significance was not always reached in our study, a clear and important trend was noticed at all different measure points between the depressed and non-depressed patient groups with regard to functional disability (Figure 3). Patients with PSD were more physically and cognitively impaired, had higher stroke severity and outcome mean scores, were more care dependent and had less quality of life as measured by SIS than non-depressed patients except at month 6. At 6 months poststroke the mean MMSE total score was almost identical and the BI and FIM motoric mean scores were even marginally higher indicating a lower dependency in care and less functional impairment for depressed compared to non-depressed patients. This unexpected result is probably induced by the different composition of the study population and the much younger age of the depressed group at 6 months poststroke assuming an overall better physical and cognitive condition of these patients before stroke. The higher levels of PSD in the younger patients may well reflect the greater significance of, and reaction to, the effects and implications of a stroke at 6 months poststroke. Additionally, the loss of self-esteem, familial and professional achievement probably is important for development of PSD [12].

Despite available evidence on the association between aphasia and PSD [35,39,40], it is important to note that only few studies investigated the prevalence of depressive symptoms in aphasic stroke patients. Therefore, the inclusion of patients with aphasia offers an added value to our study. Aphasia was only significantly associated with PSD in the first 6 months after stroke which is consistent with other findings [41]. Regardless of the fact that a significant number of patients with aphasia spontaneously improve, it is necessary to start treatment as soon as possible and to observe patients for the potentially occurrence of depressive symptoms.

Apraxia is an important sequel of stroke and is usually investigated in relation to lesion location [18,43] and functional outcome [44]. However, little is known concerning apraxia and its risk to PSD. In our study apraxia was consistently associated with PSD up to 18 months poststroke and should be more considered as a possible risk factor for PSD in further research.

Relational problems

This same assumption applies for relational problems emerged since stroke onset and related to the effects of stroke. Patients with relational problems at 18 months poststroke had a 3 times greater risk of becoming depressed and is therefore an additional risk factor to be considered for PSD.

Limitations

Similar to other studies, our study has limitations. The main limitation of this study is the variable composition of the study population at the different measure points. Some patients died before their next follow-up visit while others were not available for assessment. As the different assessment scales did not take spasticity into account, the possible relationship

between spasticity and PSD could not be studied. Another possible limitation is that some associations with PSD were not revealed as such due to the use of antidepressants. Consequently, the findings of our study may underestimate the prevalence and risk factors of PSD.

Future perspectives

Despite its high prevalence, PSD remains poorly recognized and under-treated, whilst there is ample evidence of treatment efficacy [45]. PSD is considered a treatable complication of stroke therefore early detection of depressive symptoms and identification of risk factors or patients at risk for depression is most helpful to promote early diagnosis, to implement early and adequate treatment and to improve quality of life, both for stroke patients and for their caregivers. The structural use of a screening instrument [46,47] and prediction rule [48] in daily care of stoke patients will promote early recognition of depression and enables clinicians to estimate the risk of PSD. Further knowledge and understanding of PSD and its risk factors may contribute to further development of these screening and prediction tools.

Conclusions

In conclusion, stroke severity, physical and cognitive impairment, a greater dependency with regard to ADL functions, reduced social activities and psychosocial factors are associated with significant poststroke depressive symptoms during the 18 months time frame of the study. Comparable to other studies physical impairment remains an imperative risk factor for PSD. In contrast to physical disability, cognitive impairment including aphasia, apraxia, neglect etc. are mostly not considered but prove to be significantly associated with PSD. Additionally, relationship problems present at 18 months poststroke and related to the effects of stroke were observed in patients with PSD compared to non-depressed stroke patients and

become herewith a significant and not to be underestimated risk factor for PSD. These variable results indicate the need for clinicians to consider the dynamic and multifactorial nature of PSD and emphasize the importance of a rigorous and long-term monitoring and support of stroke patients and their caregivers.

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Table legend

Table 1: Questionnaire of psychosocial events in the last 18 months.

Table 2: Patient's Characteristics.

Data given as mean ± SD or as percentage.

Table 3: Comparing depressive and non-depressive stroke patients 18 months poststroke.

Student t-test (independent) for continuous variables or the Mann Whitney U Rank Sum test in case of a non-normal distribution or small numbers. Data given as mean ± SD.

NIHSS: National Institute of Health Stroke Scale, mRS: Modified Rankin Scale, BI: Barthel Index, FIM: Functional Independent Measure scale, MMSE: Minimental State examination, SIS: Stroke Impact Scale.

Table 4: Correlations and univariate linear regression analysis of potential risk factors.

ρ = Spearman rank correlation coefficient, P= p value Linear regression. Only significant *P*-values are shown.

NIHSS: National Institute of Health Stroke Scale, mRS: Modified Rankin Scale, BI: Barthel Index, FIM: Functional Independent Measure scale, MMSE: Minimental State examination, SIS: Stroke Impact Scale, CSD: Cornell Scale for Depression.

Table 5: Univariate Logistic regression analysis of potential functional risk factors for developing PSD.

Data given as odds ratios and confidence interval, only significant associations are shown.

NIHSS: National Institute of Health Stroke Scale, mRS: Modified Rankin Scale, BI: Barthel Index, FIM: Functional Independent Measure scale, MMSE: Minimental State examination, SIS: Stroke Impact Scale.

Table 6: One-way Anova of potential risk factors for developing PSD.

CSD: Cornell Scale for Depression, MADRS: Montgomery and Åsberg depression rating scale.

Figure legend

Figure 1: Use of antidepressants at baseline and follow-up.

Figure 2: Poststroke depression and shift of gender.

Data given as number (percentage).

Figure 3: PSD in relation to functional and cognitive deficits.

Δ--Δ depressed, •…• non-depressed, x-axis: month 1,3,6,12 and 18, Y-axis: scale values.

Table 1: Questionnaire of psychosocial events in the last 18 months

Important person deceased in the family (spouse, children, grandchildren or parent(s))
Other Important person deceased (friend, brother, sister or other family members)
Oncological diagnosis established
Victim of an acute life-threatening condition
Chronic disorder present
Victim of a negative event with potential effect on mood (death, sick relative, financial problems, pension etc.)
Hospitalization (new event, additional or other health problems resulting from/or independently of stroke)
Relational problems since stroke onset
Caregivers present or available if needed (spouse, children or others)

Table 2: Patient's characteristics

Characteristics	Total group n = 201	Month 1 n = 94	Month 3 n = 170	Month 6 n = 99	Month 12 n = 116	Month 18 n = 156
Age mean (±SD)	70.1 (13.1)	68.7 (14.2)	69.9 (13.1)	68.0 (14.6)	69.0 (14.3)	69.7 (13.2)
median	74	73.5	74	71	74	74
range	(25-90)	(31-88)	(25-90)	(25-88)	(25-88)	(31-88)
Men/woman	115/86	52/42	100/70	56/43	66/50	94/62
Living alone/together	61/140	27/67	48/122	28/78	33/83	46/110
Pre-stroke employment status (working/not working)	38/163	27/67	35/135	24/75	26/90	32/124
Level of education (%) (with higher professional/university degree)	43 (21.4)	17 (18.1)	35 (20.6)	17 (17.2)	20 (17.2)	29 (18.6)
Location of stroke (%)						
Right hemisphere	87 (43.3)	39 (41.5)	75 (44.1)	41 (41.4)	49 (42.2)	68 (43.6)
Left hemisphere	101 (50.2)	47 (50)	90 (52.9)	52 (52.5)	54 (46.6)	77 (49.4)
Type of stroke (%)						
Ischemia	161 (80.1)	72 (76.6)	42 (83.5)	77 (77.8)	88 (75.9)	124 (79.5)
Haemorrhage	9 (4.5)	5 (5.3)	9 (5.3)	5 (5.1)	5 (4.3)	7 (4.5)
TIA	31 (15.4)	17 (18.1)	19 (11.2)	17 (17.2)	23 (19.8)	25 (16.0)
Use of antidepressant at baseline (before stroke) (%)	22 (10.9)	9 (9.6)	18 (10.6)	13 (13.1)	13 (11.2)	17 (10.9)
Use of antidepressant at follow-up (%)		20 (21.3)	43 (25.3)	38 (38.4)	41 (35.3)	48 (30.8)
Depressive symptoms present (%)		23 (24.5)	46 (27.1)	28 (28.3)	23 (19.8)	41 (26.3)

Data given as mean ± SD or as percentage.

Table 3: Comparing depressive and non-depressive stroke patients 18 months poststroke

Characteristics	Depression n = 41	No depression n = 115	*P* value of difference
Stroke severity			
NIHSS	2.8 ± 3.5	1.4 ± 2.5	**0.012**
Functional impairment			
FIM total	103.8 ± 27.3	113.7 ± 19.1	**0.003**
FIM motor	74.0 ± 21.9	81.7 ± 14.7	**0.030**
FIM cognitive	29.8 ± 6.7	32.0 ± 5.4	**0.002**
Level of independence			
BI	84.5 ± 27.5	91.1 ± 19.4	0.133
Cognition			
MMSE	26.4 ± 5.2	27.3 ± 3.8	0.461
Stroke outcome			
mRS	2.4 ± 1.1	1.6 ± 1.2	**<0.001**
Stroke impact			
SIS total	76.3 ± 16.4	88.4 ± 11.5	**<0.001**
SIS mobility	76.2 ± 24.1	87.3 ± 15.6	**0.016**
SIS memory	81.5 ± 21.0	90.5 ± 15.9	**0.003**
SIS emotion	73.4 ± 12.5	91.2 ± 7.5	**<0.001**
SIS communication	86.1 ± 19.1	92.2 ± 15.5	**0.016**
SIS activity	66.5 ± 20.4	82.7 ± 16.8	**<0.001**

Student t-test (independent) for continuous variables or the Mann Whitney Rank Sum test in case of a non-normal distribution or small numbers. Data given as mean ± SD.
NIHSS: National Institute of Health Stroke Scale, mRS: Modified Rankin Scale,
BI: Barthel Index, FIM: Functional Independent Measure Scale, MMSE: Minimental State Examination, SIS: Stroke Impact Scale.

Table 4: Correlations and univariate linear regression analysis of potential risk factors for developing PSD (MADRS)

	Month 1 n = 94	Month 3 n = 170	Month 6 n = 99	Month 12 n = 116	Month 18 n = 156
Stroke severity					
NIH	ρ = 0.338 *P = <0.001*	ρ = 0.278 *P = <0.001*	ρ = 0.210 *P = 0.022*	ρ = 0.156 *P = 0.041*	ρ = 0.205 *P = 0.013*
Stroke outcome					
mRS	ρ = 0.407 *P = <0.001*	ρ = 0.474 *P = <0.001*	ρ = 0.233 *P = 0.026*	ρ = 0.342 *P = 0.001*	ρ = 0.337 *P = <0.001*
Level of independence					
BI	ρ = - 0.418 *P = <0.001*	ρ = - 0.434 *P = <0.001*	ρ = - 0.150	ρ = - 0.178	ρ = - 0.239 *P = 0.014*
Functional impairment					
FIM total	ρ = - 0.423 *P = <0.001*	ρ = - 0.462 *P = <0.001*	ρ = - 0.276	ρ = - 0.258 *P = 0.014*	ρ = - 0.334 *P = 0.002*
FIM motor	ρ = - 0.362 *P = <0.001*	ρ = - 0.418 *P = <0.001*	ρ = - 0.209	ρ = - 0.216 *P = 0.036*	ρ = - 0.277 *P = 0.003*
FIM cognition	ρ = - 0.410 *P = <0.001*	ρ = - 0.410 *P = <0.001*	ρ = - 0.299	ρ = - 0.254	ρ = - 0.326 *P = 0.007*
Cognitive screening					
MMSE	ρ = - 0.113	ρ = - 0.291 *P = 0.002*	ρ = - 0.141	ρ = - 0.285 *P = 0.002*	ρ = - 0.130 *P = 0.046*
Stroke impact					
SIS total	ρ = - 0.481 *P = <0.001*	ρ = - 0.595 *P = <0.001*	ρ = - 0.478 *P = <0.001*	ρ = - 0.465 *P = <0.001*	ρ = - 0.542 *P = <0.001*
SIS mobility	ρ = - 0.341 *P = <0.001*	ρ = - 0.417 *P = <0.001*	ρ = - 0.199	ρ = - 0.314 *P = 0.002*	ρ = - 0.279 *P = <0.001*
SIS memory	ρ = - 0.431 *P = <0.001*	ρ = - 0.494 *P = <0.001*	ρ = - 0.433 *P = 0.050*	ρ = - 0.282 *P = 0.001*	ρ = - 0.388 *P = <0.001*
SIS emotion	ρ = - 0.691 *P = <0.001*	ρ = - 0.796 *P = <0.001*	ρ = - 0.783 *P = <0.001*	ρ = - 0.768 *P = <0.001*	ρ = - 0.812 *P = <0.001*
SIS communication	ρ = - 0.280 *P = <0.001*	ρ = - 0.268 *P = <0.001*	ρ = - 0.200 *P = 0.004*	ρ = - 0.164	ρ = - 0.364 *P = 0.005*
SIS activity	ρ = - 0.343 *P = <0.001*	ρ = - 0.475 *P = <0.001*	ρ = - 0.284 *P = 0.001*	ρ = - 0.398 *P = <0.001*	ρ = - 0.442 *P = <0.001*
SIS % recovery	ρ = - 0.409 *P = <0.001*	ρ = - 0.419 *P = <0.001*	ρ = - 0.193 *P = 0.003*	ρ = - 0.343 *P = 0.002*	ρ = - 0.243 *P = 0.027*
Depression					
CSD	ρ = 0.892 *P = <0.001*	ρ = 0.830 *P = <0.001*	ρ = 0.885 *P = <0.001*	ρ = 0.884 *P = <0.001*	ρ = 0.885 *P = <0.001*

ρ = Spearman rank correlation coefficient, *P*= p-value Linear regression, only significant p-values are shown. NIHSS: National Institute of Health Stroke Scale, mRS: Modified Rankin Scale, BI: Barthel Index, FIM: Functional Independent Measure Scale, MMSE: Minimental State examination, SIS: Stroke Impact Scale, CSD: Cornell Scale for Depression.

Table 5: Univariate logistic regression analysis of potential functional risk factors for developing PSD

	Month 1 n = 94	Month 3 n = 170	Month 6 n = 99	Month 12 n = 116	Month 18 n = 156
Stroke severity					
NIH	1.18 (1.06-1.33)				1.16 (1.03-1.30)
Stroke outcome					
mRS		1.93 (1.42-2.62)		1.64 (1.13-2.39)	1.72 (1.25-2.36)
Level of independence					
BI		0.97 (0.96-0.98)			
Functional impairment					
FIM motoric		0.96 (0.94-0.98)			0.97 (0.95-0.99)
FIM cognition		0.92 (0.87-0.96)			0.94 (0.89-0.99)
Cognitive screening					
MMSE				0.90 (0.81-0.99)	
Stroke impact					
SIS mobility		0.96 (0.94-0.97)		0.97 (0.94-0.99)	0.97 (0.95-0.98)
SIS memory		0.96 (0.94-0.97)		0.97 (0.94-0.99)	0.97 (0.95-0.99)
SIS emotion		0.83 (0.79-0.88)		0.69 (0.57-0.82)	0.85 (0.80-0.89)
SIS communication		0.97 (0.96-0.99)			
SIS activity		0.96 (0.94-0.97)	0.96 (0.94-0.99)	0.94 (0.92-0.97)	0.95 (0.93-0.97)

Data given as odds ratios and confidence interval, only significant associations are shown. NIHSS: National Institute of Health Stroke Scale, mRS: Modified Rankin Scale, BI: Barthel Index, FIM: Functional Independent Measure Scale, MMSE: Minimental State Examination, SIS: Stroke Impact Scale.

Table 6: One-way ANOVA of potential risk factors for developing PSD (significant *P*-values)

	Month 1 n=94		Month 3 n=170		Month 6 n=99		Month 12 n=116		Month 18 n=156	
	CSD	MADRS	CSD	MADRS	CSD	MADRS	CSD	MADRS	CSD	MADRS
Neurocognitive outcome measure										
Speech and/or language problems			0.019	0.001						
Aphasia	0.032	0.003		0.048	0.039	0.009				
Dysarthria			0.025	0.011						
Verbal apraxia	0.014	<0.001			0.003	0.003				
Agnosia			0.027	<0.001						
Neglect	0.004	<0.001						0.029	0.030	
Apraxia	0.048	0.001	<0.001	<0.001	0.003	0.003		0.011	0.043	0.006
Psychosocial factors										
Important person deceased									0.040	0.048
Victim of an acute life-threatening condition										0.045
Relational problems since stroke onset									<0.001	<0.001

CSD: Cornell Scale for Depression, MADRS: Montgomery and Åsberg Depression Rating Scale.

Figure 1: Use of antidepressants at baseline and follow-up

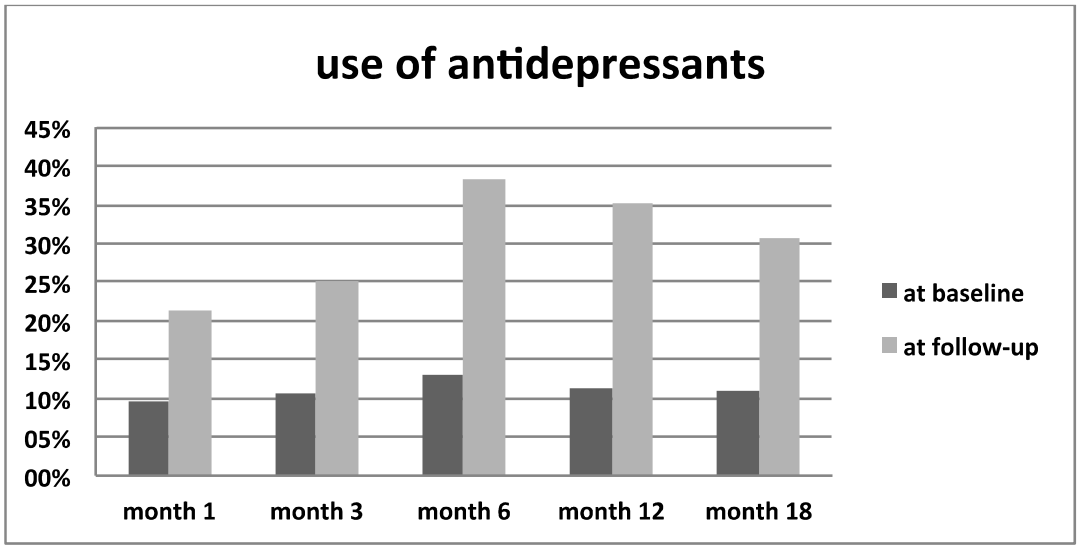
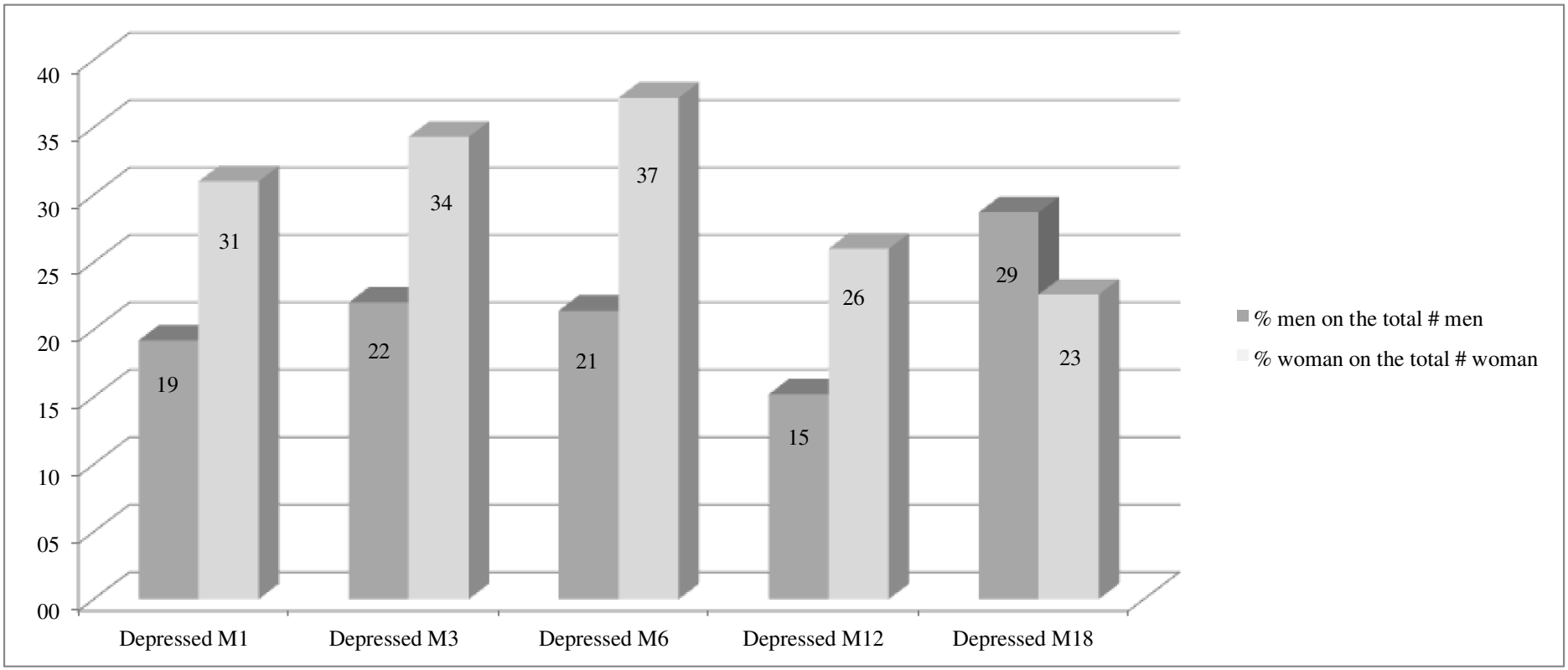


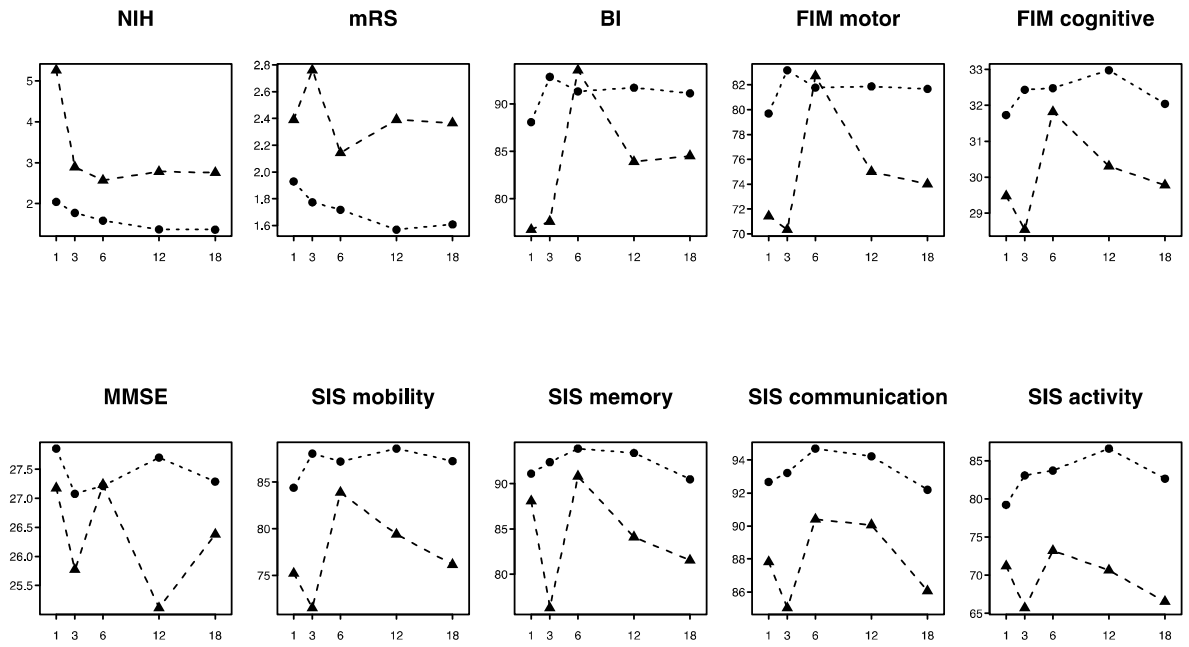
Figure 2: PSD and shift of gender



Data given as number (percentage).

Figure 3: PSD in relation to functional and cognitive deficits

Figure 3: PSD in relation to functional and cognitive deficits



Δ--Δ depressed, •…• non-depressed, x-axis: month 1,3,6,12 and 18, Y-axis: scale values.