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# PREDICTIVITY OF EARLY DEPRESSIVE SYMPTOMS FOR POST-STROKE DEPRESSION

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**Abstract:** *Objectives:* Depression is a frequent complication after stroke. However, little is known about the predictive value of early self-reported depressive symptoms (DS) for later development of post-stroke depression (PSD) 6 months after discharge. *Design:* Using a prospective longitudinal design, we investigated the prevalence of DS and examined their predictive value for depressive disorders 6 months after stroke while statistically controlling major established PSD risk factors. *Setting and Participants:* During inpatient rehabilitation, 96 stroke patients were screened for DS. After 6 months, 71 patients were attainable for a follow-up. Measurements: DS was assessed using the 15-item Geriatric Depression Scale (GDS-15). At follow-up a telephone interview that included the Structured Clinical Interview for Psychiatric Disorders (SCID), which is based on DSM-IV criteria, and the GDS-15 was conducted. Patients with major depression (MD) at the follow-up were considered to have PSD. *Results:* Regression analyses were conducted to examine the influence of early DS on PSD after 6 months while controlling for age, premorbid depression, and functional and cognitive impairments. The percentage of patients who scored above the GDS-15 cut-off for clinically relevant DS increased significantly, from 37% to 44%, after 6 months. According to the SCID, 27% of stroke patients fulfilled the criteria for MD, and another 16% fulfilled those for minor depression. Logistic regression showed that DS at baseline significantly predicted PSD at follow-up (odds ratio: 1.43; 95% CI: 1.15–1.8). *Conclusion:* Self-reported DS during inpatient rehabilitation are predictive for PSD 6 months after discharge. Assessment of early DS contributes to identifying stroke patients at risk for PSD, thereby facilitating prevention and treatment.

**Key words:** Prospective longitudinal study, post-stroke depression, PSD, regression analysis, Geriatric Depression Scale.

## Introduction

It has been established that about 30% of stroke survivors develop depressive symptoms (DS) during the first weeks after stroke onset (1). The high rate of DS in patients shortly after stroke can be understood as a reaction to a highly stressful medical illness, especially when patients are confronted with the consequences of their stroke (2). Additionally, high levels of DS have been attributed to early organic dysthymia, which presumably results from stroke-induced neurobiological alterations (3).

The course of DS has been investigated by several prospective studies, which have reported conflicting results (4). As most of these studies used a 12-month or longer follow-up period (5, 6), less is known about the development of DS in the first 6 months after stroke. Research regarding major depression (MD) in the general population has shown that most patients recover within 3–6 months and that the rate of recovery slows toward 12 months (7). Given that the duration of MD after stroke is thought to be about 9 months (8) and given that DS may initially emerge after the acute phase (9), it is important to increase our understanding of the evolution of DS within the first year after stroke. However, research in this post-acute phase is hindered by transitions in the care chain (e.g., from inpatient rehabilitation to ambulatory care).

To our knowledge, only two studies have assessed DS both during inpatient stroke rehabilitation and at 6 months after discharge (10, 11). Nys et al. (10) assessed DS in an acute clinic and 6 months later using the Montgomery–Asberg Depression Rating Scale (MADRS; 12), which is completed by professionals. They reported an increase in the percentage of patients scoring above the MADRS clinical cut-off (49.5–52.7%), but the change was not statistically significant. However, the high initial rate of clinically relevant DS may be have been artificially inflated, as MADRS items addressing somatic symptoms (e.g., sleep disorders, fatigue, etc.) may overestimate DS, as has been shown in studies with patients with brain lesions (13, 14). In a study conducted by Aström et al. (1993) (11), the DSM-III criteria for depressive disorders were applied before and after discharge from inpatient rehabilitation. The authors noted an increase in MD rates from 25% to 31% at a 3-month follow-up, but the increase was not significant, probably due to the small sample size. Apart from these two studies, no evidence of the association between DS in rehabilitation and a later diagnosis of post-stroke depression (PSD), defined as a disorder that fulfils the criteria for depression "occurring in the context of a clinically apparent stroke," has been published (15).

From a psychosocial perspective, discharge from inpatient rehabilitation to ambulatory care represents a critical transition in the care chain (16, 17). During inpatient rehabilitation, high self-efficacy and self-perceived social support may act

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as protecting factors (18). However, after the patients return home and realise the impact of their remaining deficits on their everyday lives after returning home, DS may increase and reach clinically significant levels that meet criteria for PSD (19). However, to our knowledge, no longitudinal study has investigated the predictive value of DS in a rehabilitation clinic for later PSD. Questions about whether early DS are a valid predictor of later PSD are highly relevant for clinical practice, as PSD is associated with a worse prognosis (i.e., reduced quality of life (11) and increased mortality (20). If early DS during inpatient rehabilitation were known to be predictive of later PSD, assessing these symptoms and conveying this information to ambulatory care providers could contribute to the timely prevention or treatment of depressive disorders.

When examining the relationship between early DS and later PSD, several other well-known PSD risk factors should be controlled, such as premorbid depression, impaired activities of daily living (ADLs), impaired cognitive functioning, younger age, and site of lesion (21; for a review see 22).

### *Aims*

Our prospective study investigated the predictive value of DS assessed during inpatient neurological rehabilitation for the development of PSD 6 months later. Based on previous reports, we assumed that the prevalence of DS would increase at 6 months. The diagnosis of PSD was based on the DSM-IV criteria for depressive disorders, which reflect the state-of-the-art approach to the diagnosis of PSD (5, 23, 8). Our study went beyond earlier research in two ways. First, we used the 15-item Geriatric Depression Scale to measure DS in older patients, as this instrument omits somatic items and relies on an easily understandable dichotomous rating system (24, 14). Second, other previously reported major PSD risk factors were statistically controlled (25, 26, 10).

## Methods

### *Participants*

A total of 96 stroke patients recruited at the Neurological Rehabilitation Centre (Brandenburg Klinik, Bernau, Germany) over a period of 6 months participated in this study. Only patients with ischaemic stroke were included in the sample to control for other neurological causes of negative affective outcomes and prolonged recovery, such as surgery or clipping following haemorrhagic stroke. Inclusion criteria were a) at least 4 weeks after stroke, b) sufficient verbal comprehension (fluent in German, Token Test score >12), c) no severe comorbidities (e.g., diabetes), and d) at least 8 years of education. Consenting patients were asked to complete a standardised assessment form in the presence of study personnel not involved in rehabilitation. Patients with motor impairments received assistance in filling out the questionnaires. The study was approved by the Ethics Committee of the Department of Psychology, Humboldt Universität zu Berlin, Reg.-No 2010-13.

At baseline, consecutive patients who had undergone a multidisciplinary neurological rehabilitation programme were assessed shortly before discharge. At the 6-month follow-up, 71 patients were attainable for follow-up. Patients who participated in the follow-up did not differ from those who did not, with respect to demographic variables, cognitive functioning, and ADL (all $p > .05$).

### *Predictor variables*

At baseline, DS were assessed using the 15-item short form of the Geriatric Depression Scale (GDS-15, 23), with higher GDS-15 scores indicating higher levels of DS. A cut-off of ≥5 points was defined as clinically relevant DS in our study sample (27, 28, 29), in accordance to a large German validation study. As other studies had proposed cut-offs of 6 (30) and 7 (31), we conducted an additional analysis to examine sensitivity and specificity in our population. The cut-off of 5 was confirmed as optimal for detecting MD (sensitivity = .893 and specificity = .853), in comparison to the cut-off of 6 (sensitivity = .821, specificity = .897) and the cut-off of 7 (sensitivity = .786 and specificity = .926.

In addition to the self-report questionnaire, an interview was conducted to obtain demographic and clinical data, including history of mental disorders. As a measure of lesion site, the hemisphere in which the stroke had occurred (right, left or both hemisphere) was taken from each patient's medical records. ADLs were assessed using the Barthel Index (BI; 32). As a global measure of cognitive functioning, the Mini-Mental State Examination (MMSE; 33) was administered.

### *Outcome measures*

At the 6-month follow-up, standardised telephone interviews were conducted to reassess current DS according to the GDS-15, and a German version of the Structured Clinical Interview for DSM Disorders (SCID; 34) was used to diagnose depression according to DSM-IV criteria (35). Only patients with major depression according to DSM-IV criteria at the 6-month follow-up (MD-6m) were considered to have PSD, representing a conservative estimate of depressive disorders.

### *Statistical analysis*

Forward logistic regression analysis was used to determine the predictive value of GDS-15 at baseline (GDS-15-BL) for the presence of MD-6m. Independent variables were entered stepwise into the model; GDS-15-BL scores were entered in the first step, and GDS-15-BL scores and covariates (premorbid depression, ADLs, cognitive functioning, and age) were entered in the second model to control for the effect of potentially confounding variables on MD-6m. Finally, hierarchical multiple linear regression analysis was performed to ascertain the predictive value of the GDS-15-BL for DS at follow-up applying a similar two-step approach. Antidepressant medication was not included as a control variable, as only

12.5% of participants received antidepressants. Exploratory correlations between the hemisphere of the lesion and dosage of antidepressant medication did not reveal any significant relationship and were thus not entered in the analysis.

The assumptions for these regression analyses were checked separately. The Bonferroni correction for multiple testing was used in the regression analyses. All statistical analyses were performed using the Statistical Package for Social Sciences version 19.0 (SPSS Inc., Chicago, IL, USA). A two-tailed p-value <0.05 indicated statistical significance.

## Results

### *Depressive symptoms at baseline and at 6-month follow-up*

The demographic and clinical characteristics of participants at baseline and at the 6-month follow-up are displayed in Table 1.

The percentage of patients whose scores exceeded the cut-off on the GDS-15 increased significantly (t(70) = -2.16, p = 0.03), from 36.5% at baseline (M = 3.85, SD = 3.47) to 43.7% 6 months later (M = 4.63, SD = 4.29). The follow-up SCID interview revealed that 26.8% of patients (n = 19) fulfilled the criteria for MD, and 15.5% (n= m) the criteria for minor depression. Thus, 72.3% fulfilled the DSM-IV criteria for depressive disorders.

Of those patients whose scores exceeded the cut-off at baseline 54.5% (n= 12) met the criteria for major and 22.7% (n= 5) met those for minor depression at the follow-up visit.

### *Risk of major depression at 6-month follow-up*

According to the Receiver Operating Characteristics (ROC) analysis, the discriminant ability for major depression at follow-up revealed to be high, with areas under the ROC curves of .766 for GDS-15-8 L. For GDS-15, further analysis confirmed reliable detection of MD-6m with sensitivity = 1.00 nd specificity = 769 for the recommnded cut-off of 5 (27, 28, 29). The PPV was .371 and the NPV was .885.

The logistic regression analysis (Table 2) showed that patients with higher scores on the GDS-15-BL were at higher risk for MD-6m (95% CI = 1.20–2.00, p < 0.001), with an odds ratio (OR) of 1.54. Pre-stroke depression (p = 0.19), ADLs (p = 0.39), cognitive functioning (p = 0.22), and age (p = 0.08) were not significant predictors of MD-6m.

Further hierarchical multiple regression analysis confirmed that the GDS-15-BL was an independent significant predictor of MD-6m (Figure 1). In the first model, the GDS-15-BL accounted for 49% of the variability in MD-6m (F(1,69) = 67.07, p < 0.01). In the second model, other known risk factors, such as premorbid depression, ADLs, cognitive functioning and age, did not significantly improve the model (F(5,65) = 14.91, p < 0.01), explaining no more than 4% of unique variance in MD-6m.

**Figure 1**

Summary of hierarchical regression analyses of variables predicting depressive symptoms at 6-month follow-up

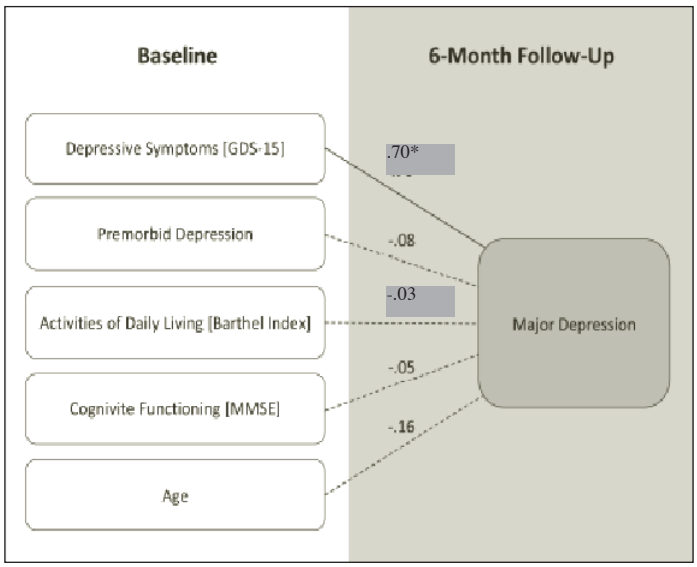


**Table 1**

Demographic and clinical characteristics at baseline and at 6-month follow-up

| | Baseline (N = 96) | | | Follow-up (N = 71) | | |
|---|---|---|---|---|---|---|
| Sex | f: 47% | | | f: 46% | | |
| Premorbid depression | 13.5% | | | 11.3% | | |
| | **M** | **SD** | **Range** | **M** | **SD** | **Range** |
| Age | 67.03 | 10.56 | 50–90 | 66.51 | 10.47 | 51–90 |
| Years of education | 11.03 | 3.24 | 9–18 | 11.3 | 3.44 | 9–18 |
| Weeks since stroke | 6.66 | 4.41 | 4–37 | 6.63 | 4.72 | 4–37 |
| GDS-15 | 4.33 | 3.61 | 0–14 | 4.63 | 4.27 | 0–15 |
| ADLs | 80.89 | 22.09 | 25–100 | 81.41 | 21.96 | 25–100 |
| Cognitive functioning | 28.10 | 2.41 | 18–30 | 28.18 | 2.37 | 18–30 |

Abbreviations: f = female; M = mean; SD = standard deviation; GDS-15 = depressive symptoms according to the Geriatric Depression Scale, 15-item version; ADLs = activities of daily living.

**Table 2**
Summary of logistic regression analysis for variables predicting major depression at 6-month follow-up

| Baseline predictors | MD-6m | | |
|---|---|---|---|
| | OR | 95% CI | P |
| GDS-15-BL | 1.73 | 1.95–1.80 | <0.002 |
| Premorbid depression | 1.43 | 0.07–2.7 | 0.37 |
| ADLs | 1.02 | 0.98–1.06 | 0.36 |
| Cognitive functioning | 0.89 | 0.69–1.17 | 0.41 |
| Age | 0.97 | 0.90–1.04 | 0.35 |
| R2 | 0.39 | | |
| GOF | p = 0.76 | | |

Abbreviations: MD-6m = major depression at 6-month follow-up; OR = odds ratio; CI = 95% confidence interval; p = level of significance; GDS-15-BL = depressive symptoms according to the Geriatric Depression Scale; 15-item version at baseline; ADL = activities of Daily Living; GOF = Hosmer–Lemeshow goodness-of-fit test. R2 = Nagelcobre

## Discussion

The main finding of our study was that self-reported DS during inpatient rehabilitation reliably and significantly predicted PSD 6 months later. Almost half of the patients who scored above the cut-off on the GDS-15-BL (42.43%) met DSM-IV criteria for a depressive disorder at 6 months after discharge. More than half of the subsample with clinically relevant DS according to the GDS-15-BL (54.5%) fulfilled the criteria for MD at follow-up. Regression analysis indicated that patients with early DS had a 43% increased risk of developing MD 6 months later. Notably, the strong predictive value of early DS remained stable even when the influence of other well-established risk factors, such as premorbid depression, impaired ADLs, impaired cognitive functioning, and younger age (21, for a review see 22), were controlled. To our knowledge, this is the first study to investigate the predictive value of DS for later PSD after statistically controlling for relevant risk factors.

Our results regarding the prevalence of PSD at follow-up are in accordance with those of previous studies reporting a pooled prevalence of 30% for PSD after discharge (1, 35). Indeed, 26.8% of our sample fulfilled criteria for MD at 6 months. Our result is also consistent with Bour (36), who found that 26.7% of the sample met DSM-IV criteria for depression at 6 months post stroke. Similarly, Aström et al. (11) reported a 31% prevalence of MD at a 3-month follow-up assessment.

Another important finding of our study involves the significant increase in DS at the 6-month follow-up, which supports the hypothesis that the transition from inpatient rehabilitation to outpatient settings may reinforce DS (25), probably due to increasing awareness of the negative effects of stroke on everyday life. In contrast, previous studies (10, 11) have reported a non-significant increase in DS within the first 6 months post-stroke (8, 10, 11). We suggest that this discrepancy may be attributable to the use of different assessment scales, as the previous studies were comparable to ours in terms of study population, sample size, and drop-out rates. The MADRS used by Nys et al. is easily influenced by physical problems (10). Thus, higher rates of somatic and autonomic symptoms shortly after stroke may have artificially increased baseline MADRS scores. In fact, the reported rates of DS (49%) at the 1-month follow-up were rather high compared with those in other studies using different diagnostic criteria (4, 14). In our study, we avoided this problem by using the GDS-15 scale, which omits somatic items, as reflected in lower baseline DS.

The study conducted by Aström et al. (1993) (10) found an increase in MD measured according to DSM-IV criteria (from 25% to 31%), although this change was not significant. We assume that a sample of 76 patients at admission was too small to detect significant differences.

Despite the aforementioned clear results, several limitations of our study should be considered. First, patients with haemorrhagic stroke were excluded due to their frequent need for surgery or other causes of prolonged recovery. Second, although aphasia was not a general exclusion criterion, patients with severe language comprehension deficits were excluded, although this subgroup may be at a significantly higher risk for DS (4). However, despite these restrictions in sampling, the rates of DS at baseline were consistent with those in the general stroke population (1). A further limitation of the study design was that patients were initially accessed during the inpatient rehabilitation phase. Future research should collect data in the acute phase. Finally, a small group of patients (n = 9) entered our study after more than 11 weeks (time elapsed since stroke ≥1 SD). These outliers were more depressed and functionally impaired and were younger than the average participant. An additional analysis excluding these outliers did not substantially change the results of either regression analyses, and self-reported DS during inpatient rehabilitation were still predictive of PSD 6 months after discharge.

Additionally, objections may be raised to our application of DSM-IV criteria for depression, which have been criticised for their exclusion of organic causes, time criteria, and inclusion of somatic symptoms (14). Nevertheless, we applied the DSM criteria for major depressive disorder to diagnose PSD because their hierarchical diagnostic approach is superior to rating scales that were designed to measure the severity of depression in those with a primary diagnosis of a depressive illness rather than to diagnose depression per se (37). As an alternative, the empirical evidence in support of the revised WHO criteria for depression reflects their superiority over DSM criteria for stroke (4), and these could be applied in future research.

In terms of practical implications, DS can be economically and validly assessed with self-report measures administered during the daily routine followed by rehabilitation clinics prior to discharge. Self-report measures of DS can contribute to identifying stroke patients at risk for PSD. Conveying this

information to ambulatory care settings can facilitate timely prevention and treatment (6) and thereby bridge the gap in the care chain. Based on our findings, we recommend the inclusion of a short self-report scale addressing depressive symptoms in standard rehabilitation assessments.

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*Declaration:* The study complies with the current ethic laws of Federal Republic of Germany in which they were performed. The study was approved by the Ethics Committee of the Department of Psychology, Humboldt Universität zu Berlin, Reg.-No 2010-13. The English in this document has been checked by at least two professional editors, both native speakers of English. For a certificate, please see: http://www.textcheck.com/certificate/elak7J

*Conflict of Interest:* None.

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