Comprehensive Psychiatry 99 (2020) 152171

Contents lists available at ScienceDirect

Comprehensive Psychiatry

journal homepage: www.elsevier.com/locate/comppsych

Post-stroke depression and functional impairments – A 3-year prospective study

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ARTICLE INFO

Keywords:
Post-stroke depression
Functional impairments
Social support
Stroke
Prospective design

ABSTRACT

Background: Post-Stroke Depression (PSD) is a severe condition, affecting about 30% of stroke survivors within a five-year period after stroke. Post-stroke functional impairments (FI) and social support are associated with PSD. It is inconclusive, whether one of the factors, post-stroke FI and PSD, shows a stronger predictive value on the respective other over time. The aims of the present study were to 1) investigate the relationship between PSD, FI, and social support of stroke patients in a 3-year prospective design, and 2) address methodological shortcomings of previous studies.
Methods: We investigated 174 stroke survivors and assessed PSD with a structured clinical interview and a dimensional symptom rating scale. We conducted regression analyses and applied the approach of multiple imputations (MI) for missing data due to dropout during follow-up.
Results: PSD prevalence was 32.2% in the acute phase after stroke. Individuals with a PSD in this phase revealed a fivefold higher risk for PSD 3 years later. FI in the acute phase did not additionally contribute to the prediction of PSD at follow-up. Compared to individuals without PSD in the acute phase, individuals with PSD had an increased risk for FI at follow-up. Limitations regarding sample characteristics, design, and dropout are discussed.
Conclusions: Results indicate that PSD rather than FI represents a crucial risk factor for negative long-term consequences regarding physical and psychological health after stroke. Post-stroke treatment might be optimized by a routine assessment of PSD and FI after stroke and considering the results for personalized treatment options.

1. Introduction

Stroke is the second leading cause of death worldwide. In 2010, there were an estimated 17 million strokes globally [1]. As a common cause of long-term disability, stroke provokes considerable burden for affected individuals and health systems [2]. Many stroke survivors remain dependent on caregivers regarding activities of daily living [3]. In 2017, stroke made up the third-leading cause of disability-adjusted life-years (DALYs) worldwide, with a total of 132 million DALYs [4].

Depressive disorders caused 43 million DALYs worldwide in 2017 [4]. Post-Stroke Depression (PSD) is another frequent complication after stroke which affects about 30% of patients within a five-year period after stroke [5,6]. PSD is associated with a reduced quality of life and higher mortality [7,8]. The causes for PSD appear to be a multifactorial combination of biological and psychosocial factors such as alterations in neurotransmitter systems or the psychosocial reaction to poststroke functional impairments (FI), respectively [9]. The severity of post-stroke FI was identified as the most consistent factor associated with PSD [10]. Most previous studies investigated PSD and post-stroke FI separately regarding their predictive power for long-term effects on physical and psychological health.

Results of some studies imply that PSD worsens post-stroke FI as PSD patients use rehabilitation services less efficiently and show less adherence to required changes in their life style [11,12]. Nevertheless, the recent meta-analysis of Blöchl et al. [13] challenges this common assumption, as there was no consistent association between PSD and the effectiveness of stroke rehabilitation in the acute phase after stroke. The authors claim that the characteristics of previous studies and a publication bias have led to an overestimation of the effect of PSD on the effectiveness of physical rehabilitation and functional improvements during recovery. However, PSD was associated with a two-fold increased risk for long-term disability [13]. Thus, the authors hypothesize that depressive mood unfolds its negative impact on physical disability rather in the long run than in the first months after stroke.

Other studies investigated the relationship between PSD and functional outcome vice versa. Results imply that post-stroke FI constitute

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https://doi.org/10.1016/j.comppsych.2020.152171

a significant risk factor for the development of PSD. The systematic review of De Ryck et al. [14] identifies the level of FI in 14 of 15 examined studies as a crucial risk factor for PSD. In the longitudinal study of Singh et al. [15], FI one month post-stroke made up the strongest predictor for depressive symptoms three months post-stroke but did not predict the level of depressive symptoms one year post-stroke. In the longitudinal study of Schepers et al. [16], FI six months post-stroke did neither predict depressive symptoms one nor three years post-stroke. The results of previous studies substantially differ regarding the predictive power of post-stroke impairments on the development of PSD [17].

These inconclusive results might be explained by varying methodical factors, such as different measures for relevant predictors and outcomes, different settings, and time of measurements [10]. Further, there are only a few longitudinal PSD-studies with multiple assessments and a follow-up period longer than one year [18,19]. As a stroke rather occurs in elderly people and is accompanied by physical impairments, longitudinal study designs face the challenge of a high dropout rate in such individuals. In most studies on PSD, these individuals were excluded from statistical analyses (listwise deletion), albeit it has been shown that this approach increases the risk for biased results, even under optimal conditions when missingness is generated by a missing at random (MAR) process [20,21].

Hadidi et al. [17] argued that the strength of the association between PSD and impairment after stroke might depend on the duration since the stroke. Accordingly, straightforward conclusions regarding time sensitive relationships between PSD and other variables, such as FI, remain challenging. Present research suggests a bidirectional relationship between PSD and post-stroke FI [10,12]. However, to date, it remains uncertain whether one of the factors, post-stroke FI and PSD, shows a stronger predictive value on the respective other over time.

In addition to FI, a lack of social support is associated with a higher risk for PSD [22]. In most studies addressing this topic, social support was operationalized indirectly as a demographic or socioeconomic characteristic, such as the marital or resident status of stroke survivors. However, the subjectively perceived social support (PSS) after stroke rather than the social support according to objective markers might be crucial for the development of PSD [23–25]. To our knowledge, no longitudinal study has yet investigated the influence of PSS on the association between PSD and FI.

Knowledge about aetiological mechanisms of PSD and their interaction with FI and PSS is necessary for the development and optimizing of prevention and treatment strategies for PSD. Therefore, the aim of the current study is to investigate the direction and strength of the relationship between PSD, FI and PSS in a 3-year prospective design. Further, we aim to address the methodological shortcomings of previous research on PSD in longitudinal designs by applying the approach of multiple imputations (MI) for missing data (i.e. study participants who dropped out during the 3-year follow-up). MI is an excellent tool to assess data with missing values because the effect of the imputed data is directly measurable, MI performs equally or even better than other techniques in case of missingness not at random (MNAR), and has been shown to be suitable in cases of up to 50% missing data in complex models [20,21,26,27].

We hypothesize that a diagnosis of PSD in the acute phase after stroke more powerfully predicts higher FI after three years than vice versa. Second, we expect that PSS influences the relationship between FI and PSD.

2. Material and methods

2.1. Participants

186 stroke patients from three German rehabilitation clinics participated in the study. Inclusion criteria were a diagnosis of either acute cerebral infarction or intracerebral haemorrhage, documentation of neurological symptoms exceeding 24 h, the patient's physical capacity to attend the study procedure and to take part in a structured interview. Exclusion criteria were the need for intensive medical treatment, artificial respiration, intensive treatment of body injuries and heightened intracranial pressure, and severe aphasia. Patients with aphasia were included if their communication skills were sufficient. The final sample consisted of 174 participants ($M_{age} = 67.51$, 50.0% female) after excluding 12 participants (5 due to missing dates of the stroke, T1, or T2 assessment, 7 with >24 weeks between the stroke and T1 assessment; as a consistent definition of acute phase is lacking in the literature in this field, we chose 23 weeks as a maximum duration for inclusion). 113 participants (64.9%) were married and 46 (26.4%) widowed. 122 participants (70.1%) were living with their partner, 50 (28.7%) alone. At 3-years follow-up, the T2 assessment data of 84 individuals were included. Seventeen individuals refused to participate, $n = 23$ revealed severe health impairments, $n = 21$ addresses were unknown, $n = 28$ had deceased since T1 assessment, and datasets of 6 participants were incomplete for specific measures. Sample sizes for the individual analyses are reported, respectively.

2.2. Measures

2.2.1. Primary measures

PSD was assessed with the structured clinical interview, Axis 1 Disorders (*SCID-I* [28,29]) according to the diagnostic criteria for Major Depression of the fourth version of the *Diagnostic and Statistical Manual of Mental Disorders* (*DSM-IV*; [30]). Additionally, depression was measured dimensionally using the German version of the *Cornell Scale for Depression* (*CDS*; [31,32]), a clinician rating scale for depressive symptoms in patients with organic brain lesions. The sum score of the 19 items, ranging between 0 and 38, was used with higher scores indicating higher depression levels.

FI was measured by the *Barthel-Index* (*BI*; [33]). The BI is a commonly used rating instrument consisting of 10 weighted items measuring the patient's performance in activities of daily living. The total score ranges from 0 to 100, with lower scores indicating higher FI. Quinn et al. [34] suggest the following interpretation of BI scores: BI scores <40 represent “complete dependence on others”, scores >60 “transition from complete dependence to assisted independence”, and scores >85 “independence with minor assistance”. This categorization does not define scores between 40 and 60. Thus, we used the continuous total scores for the analyses.

PSS was assessed with the three subscales “emotional support”, “practical support” and “social integration” of the self-report questionnaire *Social Support Questionnaire* (*F-SozU*; [35]). Subjects rated their PSS on a five-point Likert scale. The mean score of the 38 items was used with higher mean scores indicating higher PSS.

2.3. Procedure

Informed consent was obtained from all patients after the study procedure had been fully explained. The study complied with the local ethics committees and the three rehabilitation clinics. The initial assessment took place in the acute phase after stroke (weeks between stroke and T1: $M = 6.53$, $SD = 4.34$) and the follow-up assessment was carried out three years after the initial assessment ($M_{month} = 37$; $SD = 6.73$). The assessments were conducted by three trained clinical psychologist and supervised by the first author.

2.4. Data analyses

All data analyses were conducted using IBM SPSS Statistics software version 25. For the prediction of PSD_{T2}, we performed a blockwise logistic regression on the basis of demographic predictors (age, sex) and the focal predictors (PSD_{T1}, FI_{T1}, and PSS_{T1}), as well as the $FI_{T1} * PSS_{T1}$ interaction. For the prediction of CDS_{T2} and FI_{T2}, we used ordinary least squares regression, respectively. The model for predicting CDS_{T2} was

analog to the PSD_{T2} model. For the FI models, we omitted PSS_{T1} and the interaction as predictors, since we did not have any specific hypotheses for these variables. For all models we used a blockwise regression approach, i.e. entering the predictors in a predefined order on the basis of theoretical considerations. By contrast, automated step-wise procedures may capitalize on chance and elevate the type 1 error rate. For better interpretability and to remedy potential non-essential multicollinearity of zero order predictors, all continuous predictor variables were mean-centred.

To account for the dropout at T2, we used the SPSS built-in MI algorithm with 100 imputations for each missing data value. We submitted all outcome and predictor variables of the models to the MI algorithm, including the interaction term, which has been calculated before the MI, to preserve the internal structure [36]. The following auxiliary variables were additionally used to predict missingness and impute missing values but were not part of the final models: living situation, marital status, health-related characteristics, such as status of psychotropic medication, current and past use of alcohol, diabetes, hypertonia, obesity. Analyses of the relationships between missingness in model variables at T2 and all other variables revealed that missingness could at least partly be predicted by age, PSS_{T1}, FI_{T1}, and status of past use of alcohol. Higher age, lower PSS_{T1}, lower FI_{T1} but no past alcohol use (vs. mild use vs. abuse) predicted higher missing data rates. This indicated that at least some amount of missingness is accounted for by a MAR process and not entirely by a MNAR process [20,37]. Where possible and provided by SPSS, we report pooled estimates of the coefficients of interest, according to Rubin's rule [38], otherwise we report median values of the coefficients from the 100 imputations. There is no consensus how to calculate standardized regression coefficients from logistic regression. To be able to compare regression coefficients within the path diagram, we calculated *fully standardized regression coefficients* [39,40], for which the interpretation is most comparable to standardized coefficients from OLS regression.

3. Results

3.1. Post-stroke depression, functional impairments, and perceived social support

Means and SDs as well as intercorrelations of the measures for depression, FI and PSS are presented in Table 1. The prevalence of PSD at T1 was 32.2% ($n = 56$) and 36.9% ($n = 31$) at T2. CDS sum scores indicated low depressive symptoms at T1 and clinically relevant symptoms at T2 across all participants. The BI scores represented the range of transition from complete dependence to assisted independence across all patients. According to the PSS scores, participants experienced average social support. As evident in Table 1, correlations between PSD and FI were medium, correlations between PSD and PSS small to medium.

3.2. Prediction of PSD at 3-year follow-up

A blockwise logistic regression analysis predicting PSD_{T2} was conducted with age, sex, PSD_{T1}, FI_{T1}, PSS_{T1}, and the $FI_{T1} * PSS_{T1}$ interaction as predictors (see Table 2 for analyses with the original data and Table A1 for results of MI based analyses). PSD_{T1} was the strongest predictor, indicating that individuals with (vs. without) PSD at T1 had a 5.3times higher risk for PSD at follow-up. The MI based analyses revealed similar results, even though the effect decreased to OR = 2.11 [95% CI 0.56–8.04]. Fig. 1a) presents the standardized regression coefficients for both, original and MI data. In addition to PSD_{T1}, the $FI_{T1} * PSS_{T1}$ interaction significantly predicted the risk for PSD at follow-up in the blockwise logistic regression analysis on PSD_{T2} according to DSM-IV (Table 2), indicating that the strength of the PSS moderated the relationship between FI at T1 and the PSD-risk at follow-up. However, the moderator effect decreased to a non-significant level in MI based analyses as well as the regression analysis according to the CDS (see next section, Table 3, and supplementary material).

The blockwise OLS regression analysis predicting CDS_{T2} (i.e. dimensional measurement of depressive symptoms) with the predictors age, sex, CDS_{T1}, FI_{T1}, PSS_{T1}, and the $FI_{T1} * PSS_{T1}$ interaction revealed CDS_{T1} as strongest predictor (see Table 3 for original data and Table A2 for MI based analyses) and therefore supported the results for PSD_{T2}. The interaction did not reach significance, neither in the original sample, nor in the MI based analyses.

3.3. Prediction of FI at 3-year follow-up

The blockwise OLS regression analysis predicting FI_{T2} was conducted with age, sex, FI_{T1}, and PSD_{T1} as predictors (see Table 4 for analyses with the original data, Table A3 for results of MI based analyses, Tables A4 and A5 for the models with CDS as predictor instead of PSD). Age, FI and a PSD at T1 were significant predictors for FI at follow-up, indicating higher FI at T2 for individuals with higher age, higher FI at T1, and a PSD at T1. FI at T1 was the strongest predictor. The MI based analyses supported these findings. The standardized regression coefficients for both, original and MI data, are displayed in Fig. 1b).

4. Discussion

The aim of the present study was to investigate the direction and strength of the relationship between Post-Stroke Depression (PSD), functional impairments (FI), and perceived social support (PSS) of stroke patients in a 3-year prospective design. We investigated 174 stroke survivors and used two measures on PSD, a structured clinical interview and a dimensional symptom rating scale. Diagnoses according to DSM-IV criteria revealed a PSD prevalence of 32.2% in the acute phase after stroke. This number is in line with the results of previous studies and meta-analyses [5,6,41].

Table 1
Bivariate correlations, means and standard deviations for demographics and primary outcome measures for the original sample.

Time	Measure	Age	T1				T2				M	SD
			PSD	CDS	FI	PSS	PSD	CDS	FI	PSS		
	Sex	0.15	0.10	−0.06	0.01	−0.19	0.02	0.12	0.07	−0.19	0.5	0.5
	Age		0.00	−0.02	−0.12	−0.03	0.13	0.22	−0.30	−0.13	67.51	11.63
T1	PSD			0.31	−0.29	−0.12	0.28	0.39	−0.39	−0.17	0.32	0.47
	CDS				−0.46	−0.03	0.23	0.32	−0.44	−0.24	4.59	5.12
	FI					−0.09	−0.01	−0.15	0.58	0.01	67.05	30.51
	PSS						0.04	−0.08	−0.06	0.33	3.94	0.62
T2	PSD							0.81	−0.28	−0.32	0.38	0.49
	CDS								−0.38	−0.36	10.85	8.23
	FI									0.20	79.29	25.71
	PSS										4.15	0.47

Note. PSD = Post-Stroke Depression according to DSM-IV criteria, CDS = depressive symptoms according to the Cornell Scale for Depression, FI = functional impairment according to the Barthel Index, PSS = perceived social support according to the Social Support Questionnaire.

Table 2
Logistic regression predicting PSD_{T2} based on the original sample ($n = 78$).

Variable	*B*	*SE(B)*	*OR*	95% *CI* of *OR*		*p*	−2 Log-Lik	$R^2_{C\&S}$	R^2_N	X^2_{Model}	X^2_{Block}
Block 1							102.656	0.027	0.037	2.169	2.169
Sex	−0.261	0.476	0.771	[0.303,	1.958]	.584					
Age	0.028	0.022	1.028	[0.984,	1.074]	.212					
Block 2							96.888	0.097	0.131	7.937	5.768
Sex	−0.154	0.495	0.858	[0.325,	2.264]	.757					
Age	0.027	0.023	1.027	[0.983,	1.073]	.234					
PSD_{T1}	1.217	0.515	3.376	[1.231,	9.258]	.018					
Block 3							95.957	0.107	0.145	8.869	0.932
Sex	−0.056	0.509	0.945	[0.349,	2.563]	.912					
Age	0.029	0.023	1.030	[0.984,	1.077]	.204					
PSD_{T1}	1.397	0.558	4.043	[1.353,	12.076]	.012					
FI_{T1}	0.009	0.009	1.009	[0.991,	1.027]	.342					
Block 4							95.568	0.112	0.151	9.257	0.388
Sex	−0.099	0.513	0.906	[0.331,	2.477]	.847					
Age	0.029	0.023	1.030	[0.984,	1.078]	.203					
PSD_{T1}	1.447	0.567	4.250	[1.397,	12.924]	.011					
FI_{T1}	0.009	0.009	1.009	[0.991,	1.027]	.312					
PSS_{T1}	0.304	0.493	1.355	[0.516,	3.560]	.537					
Block 5							90.376	0.169	0.229	14.450	5.192
Sex	0.178	0.542	1.195	[0.413,	3.453]	.743					
Age	0.030	0.023	1.030	[0.984,	1.078]	.205					
PSD_{T1}	1.669	0.613	5.309	[1.596,	17.662]	.006					
FI_{T1}	0.023	0.012	1.024	[1.000,	1.048]	.054					
PSS_{T1}	0.601	0.574	1.825	[0.593,	5.617]	.295					
Interaction	−0.046	0.021	0.955	[0.916,	0.996]	.031					

Note. *B* = regression coefficient, *SE(B)* = standard error, *OR* = odds ratio, *95% CI* of *OR* = 95% confidence interval of the odds ratio, $R^2_{C\&S}$ = Cox and Snell's R^2, R^2_N = Nagelkerke's R^2, PSD = Post-Stroke Depression according to DSM-IV criteria, FI = functional impairment according to the Barthel Index, PSS = perceived social support according to the Social Support Questionnaire, Interaction = interaction $FI_{T1} * PSS_{T1}$.

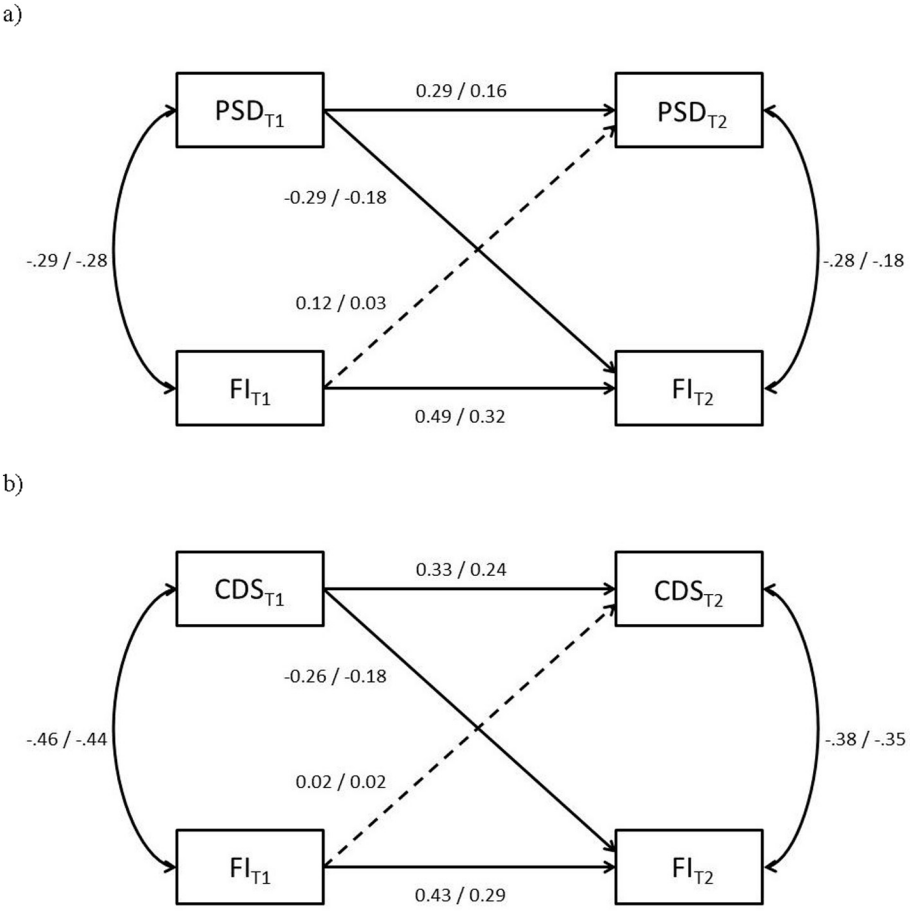

Fig. 1. Standardized Regression coefficients for the prediction of a) Post-Stroke Depression (PSD) and functional impairment (FI) at T2 and b) depressive symptoms according to the Cornell Depression Scale (CDS) and FI at T2. Standardized regression coefficients based on the original data are presented first, medians for the standardized regression coefficients based on MIs second.

Table 3
OLS Regression predicting CDS_{T2} based on the original sample ($n = 78$).

Variable	*B*	*SE(B)*	*β*	*95% CI of B*		*p*	R^2	*adj.* R^2	ΔR^2
Block 1							0.046	0.020	0.046
Sex	1.988	1.868	0.121	[−1.734,	5.710]	.291			
Age	0.121	0.082	0.169	[−0.042,	0.285]	.142			
Block 2							0.145	0.110	0.099
Sex	2.115	1.781	0.129	[−1.434,	5.664]	.239			
Age	0.111	0.078	0.154	[−0.045,	0.267]	.161			
CDS_{T1}	0.460	0.158	0.316	[0.145,	0.775]	.005			
Block 3							0.146	0.098	0.000
Sex	2.054	1.818	0.125	[−1.570,	5.679]	.262			
Age	0.111	0.079	0.154	[−0.046,	0.268]	.162			
CDS_{T1}	0.474	0.173	0.325	[0.129,	0.819]	.008			
FI_{T1}	0.007	0.033	0.024	[−0.060,	0.073]	.842			
Block 4							0.146	0.086	0.000
Sex	2.080	1.839	0.127	[−1.586,	5.746]	.262			
Age	0.111	0.079	0.155	[−0.047,	0.269]	.164			
CDS_{T1}	0.477	0.176	0.327	[0.127,	0.828]	.008			
FI_{T1}	0.007	0.034	0.026	[−0.060,	0.075]	.829			
PSS_{T1}	0.256	1.740	0.016	[−3.213,	3.726]	.883			
Block 5							0.178	0.107	0.032
Sex	1.305	1.877	0.080	[−2.438,	5.049]	.489			
Age	0.103	0.078	0.144	[−0.053,	0.260]	.192			
CDS_{T1}	0.527	0.176	0.361	[0.175,	0.878]	.004			
FI_{T1}	0.039	0.039	0.140	[−0.038,	0.116]	.318			
PSS_{T1}	0.608	1.733	0.039	[−2.848,	4.064]	.727			
Interaction	−0.113	0.068	−0.209	[−0.249,	0.024]	.104			

Note. B = regression coefficient, $SE(B)$ = standard error, β = standardized regression coefficient, *95% CI* of B = 95% confidence interval of the regression coefficient, R^2 = variance, *adj.* R^2 = adjusted variance, ΔR^2 = incremental proportion of variance explained by each regression block, CDS = depressive changes according to the Cornell Depression Scale, FI = functional impairment according to the Barthel Index, PSS = perceived social support according to the Social Support Questionnaire, Interaction = interaction $FI_{T1} * PSS_{T1}$.

The PSD status in the acute phase significantly predicted the PSD status 3 years later, with individuals experiencing a PSD in the acute phase exhibiting a fivefold higher risk for PSD at follow-up. The extent of FI in the acute phase after stroke did not additionally contribute to the prediction of PSD status at follow-up. Thus, in line with the results of Schepers et al. [16], the current study does not support the hypothesis that stroke survivors develop a PSD as a psychosocial reaction on new FI after stroke. However, FI were found to predict PSD status in other studies [15,42]. A possible reason for these divergent findings might be the short follow-up intervals up to one year after stroke in those studies. Robinson and Jorge [10] discussed that the influence of FI on the PSD risk might decrease in the course of time since stroke.

Importantly, compared to stroke survivors without PSD in the acute phase, individuals with PSD had an increased risk for FI at the 3-year follow-up. This result supports meta-analytic findings of Blöchl et al. [13], who discussed that a PSD might unfold its negative impact rather in the long run than in the first months after stroke. Additionally, the fivefold higher long-term PSD-risk of stroke survivors with a PSD in the acute phase after stroke emphasizes the high risk for chronicity of depressive symptoms after stroke. Thus, in line with our expectations, our results imply that rather PSD than FI in the acute phase after stroke makes up an important risk factor for both, long-term disability and depression. Notably, both measures for post-stroke depression, the structured clinical interview to diagnose PSD and the clinician rating scale for depressive symptoms (i.e. CDS), revealed the same pattern of results – in the original data and in the MI data as well as in models with depression as predictor and outcome. The similarity of results in MI versus original data indicates that MI is a reasonable and valid method to deal with missing values. The similar patterns of results for the different measures on depression underline the robustness and goodness of fit of the models. However, alternative explanations for changes in the PSD status and/or functional impairments may be considered. Such changes over a time course of three years may be influenced by cognitive disability or the impact of other interventions, to mention two potential influences. Accordingly, the results on FI at T2 revealed age and FI at T1 as significant predictors (not only PSD at T1). It seems likely that these predictors are associated with health-related or other factors, which we did not account for in the current study.

The PSS of stroke survivors influenced the relationship between FI and PSD in the current sample. However, contrary to our expectations,

Table 4
OLS Regression predicting functional impairment at T2 based on the original sample ($n = 79$).

Variable	*B*	*SE(B)*	*β*	*95% CI of B*		*p*	R^2	*adj.* R^2	ΔR^2
Block 1							0.113	0.089	0.113
Sex	6.748	5.724	0.128	[−4.652,	18.149]	.242			
Age	−0.745	0.252	−0.320	[−1.248,	−0.243]	.004			
Block 2							0.415	0.391	0.302
Sex	2.441	4.730	0.046	[−6.981,	11.864]	.607			
Age	−0.649	0.207	−0.279	[−1.061,	−0.237]	.002			
FI_{T1}	0.477	0.077	0.557	[0.324,	0.630]	.000			
Block 3							0.494	0.467	0.079
Sex	4.576	4.472	0.087	[−4.334,	13,486]	.310			
Age	−0.639	0.194	−0.274	[−1.024,	−0.253]	.001			
FI_{T1}	0.416	0.074	0.486	[0.269,	0.564]	.000			
PSD_{T1}	−16.470	4.835	−0.292	[−26.105,	−6.836]	.001			

Note. B = regression coefficient, $SE(B)$ = standard error, β = standardized regression coefficient, *95% CI* of B = 95% confidence interval of the regression coefficient, R^2 = variance, *adj.* R^2 = adjusted variance, ΔR^2 = incremental proportion of variance explained by each regression block, FI = Functional impairment according to the Barthel Index, PSD = Post-Stroke Depression according to DSM-IV criteria.

stroke survivors with major (vs. minor) FI were at lower risk for PSD at follow-up when perceiving low social support in the acute phase after stroke. As this result is not consistent with previous findings [24,25], future research may follow up on this topic. Longitudinal studies assessing changes in FI, PSD symptoms and PSS appear necessary.

4.1. Limitations

For the interpretation of our results several limitations have to be considered. One limitation of this study is that the generalizability to the general stroke population is restricted by several factors, such as the rehabilitation setting, which does not represent individuals with severe morbidity after stroke. Another limitation of the current study is the dropout rate of 45%. The dropout in a 3-year prospective design studying an elderly and impaired population is high and presumably systematic (i.e. caused by for example age or health status). The comparative analyses of the raw data and the data with MI help to compensate the dropout rate.

Across all analyses, the MI results resemble the results from the original sample with listwise deletion. The only exception was the significant interaction FI * social support in the PSD regression, which attenuated to non-significance in the MI analyses and could not be found for the CDS analysis. Generally, the MI results showed attenuated estimates for the regression coefficients but remained coherent with the same patterns, not only in comparison to the original sample but also across the different models (PSD vs. CDS as predictors and outcome variables), which fortifies the overall findings. Nonetheless, we cannot rule out that some part of the drop-out generating process is MNAR driven and may bias the results in an increasing or decreasing manner. Therefore, we recommend using the attenuated MI results as estimates and starting points for future research.

Additionally, multiple assessments would be beneficial for future studies with long follow-up periods, as well as the application of survival analyses to identify factors predicting the drop-out. Moreover, multiple assessments would help to display the course of PSD more accurately, as affective disorders rather take an episodic than a chronic course [43]. Based on our findings, future studies may include an age-matched control group without stroke and assess further potentially relevant factors (e.g., life events, other treatment such as psychotherapy, pharmacotherapy, rehabilitation programs).

5. Conclusion

The results of the 3-year prospective investigation of PSD, FI and PSS indicate that PSD rather than FI represents a crucial risk factor for negative long-term consequences regarding physical and psychological health after stroke. Further investigations regarding time-sensitive relationships between PSD, FI, and PSS after stroke would contribute to a better understanding of the needs of stroke patients. For the clinical practice, the routine assessment of PSD, FI, and PSS after stroke might facilitate the evaluation of individual long-term risks and thereby contribute to optimize individualized post-stroke treatment.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Contributors

All persons who met authorship criteria are listed as authors. All authors contributed significantly to the study and approved the final version of the manuscript.

Declaration of competing interest

All other authors declare that they have no conflicts of interest.

Acknowledgements

None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.comppsych.2020.152171.

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