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*Alexandros Argyriadis, Christodoulos Fylaktou, Panagiota Bellou-Mylona, Maritsa Gourni, Evanthia Asimakopoulou, Despina Sapountzi-Krepia*

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## REVIEW

## POST STROKE DEPRESSION AND ITS EFFECTS ON FUNCTIONAL REHABILITATION OF PATIENTS: SOCIO-CULTURAL DISABILITY COMMUNITIES

Alexandros Argyriadis<sup>1</sup>, Christodoulos Fylaktou<sup>2</sup>, Panagiota Bellou-Mylona<sup>3</sup>, Maritsa Gourni<sup>4</sup>, Evanthia Asimakopoulou<sup>5</sup>, Despina Sapountzi-Krepia<sup>6</sup>

1. RN, PhD, Assistant Professor, Frederick University, Cyprus
2. RN, MSc, Nurse, Frederick University, Cyprus
3. RN, PhD, Professor, Frederick University, Cyprus
4. RN, PhD, Professor, Frederick University, Cyprus
5. RN, PhD, Lecturer, Frederick University, Cyprus
6. RN, PhD, Professor, Frederick University, Cyprus

DOI:

**Abstract**

**Background:** Stroke is considered to be the third, most frequent cause of death and the leading cause of disability in Western societies. Apart from physical problems, stroke can cause psychological and social problems, too as post Stroke Depression (PSD) which is the most common emotional disorder that usually occurs in the first months, in about 1/3 of patients surviving after stroke.

**Aim:** To describe the frequency of post stroke depression (PSD) and its effects on functional recovery of patients.

**Method:** A systematic review was conducted on databases MEDLINE, PUBMED, CINAHL, and the web using Google Scholar.

**Results:** Thirty articles were retrieved, from 2000 and onwards which met the selection criteria. According to the results, PSD is a common and serious complication after stroke. Approximately 1/3 of the patients have a type of depression in the first year after stroke, with the risk increasing, the first months of the onset of stroke. The researchers suggest that there is a collaborative relationship between stroke and depression, which leads to inability to perform activities of daily living and slows the rehabilitation of patients.

**Conclusion:** Early detection of PSD and the implementation of appropriate therapeutic interventions in rehabilitation units help to speed up the recovery process and reintegration of patients into society.

**Key words:** Post Stroke Depression-PSD, stroke, functional rehabilitation, treatment.

**Corresponding Author:** Alexandros Argyriadis, 7 Yianni Fredericou, 1036, Nicosia, Cyprus, E-mail: hsc.arg@frederick.ac.cy

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## INTRODUCTION

Several studies in America and Europe have shown that depression is the most common emotional disorder occurring in one out of three patients after stroke.<sup>1-6</sup> Major depression occurs in 10-25% of patients after stroke and mild depression in 10-40% of patients.<sup>7,8</sup>

The period at a higher risk of developing depression after PSD is considered to be the first months after stroke.<sup>2</sup> As the incidence of PSD increases, it rises from the initial weeks after the stroke, up to three months. UK's National Clinical Guidelines for Stroke reports that the most appropriate time to evaluate depression is one month after stroke occurrence.<sup>9</sup>

PSD is associated with worsening physical disability and negative effects on patient recovery.<sup>1,10-13</sup> An improvement in depressive symptoms after antidepressant therapy appears to have a positive effect on the functional rehabilitation of patients.<sup>7</sup> Appropriate diagnosis and treatment of depression can bring significant results to those recovering from stroke, improving their health status, quality of life, while reducing pain and disability. Treatment for depression can also shorten the recovery process, leading to faster recovery and a quicker return to daily habits; it also reduce health costs.<sup>8</sup>

The literature review identifies various problems in assessing depression in patients with stroke, such as aphasic patients, which cannot be done in the same way as for those without aphasia; a different tool should be used like the Aphasic Depression Rating scale (ADRS), a scale of 9 points that measures depression in these patients.<sup>14</sup>

Another problem that makes it difficult to interpret and compare the results of different surveys is the use of different tools for assessing depression. However, what is supported by the majority of researchers is using two or three tools to evaluate PSD to avoid a misinterpretation of stroke symptoms of stroke that resemble symptoms of depression.<sup>2,15</sup>

Timely diagnosis and treatment are considered very important because depression prevents recovery, social reintegration, and motor and cognitive functions and affects quality of life. The involvement of the family as well as the structure of psychosocial rehabilitation are very important in treatment. Rehabilitation programs that include patient and family training, sleep

improvement, improved nutrition and frequent physical exercise significantly contribute to reducing the prevalence of PSD. When the patient co-operates, his participation in behavioral and cognitive psychotherapy, with or without drug therapy or short psychodynamic therapy and group and interpersonal psychotherapy, has encouraging results.<sup>13</sup> However, there is reduced research activity on that issue and this study aims to cover this research gap by recording articles about post stroke depression.

## AIM

The aim of the present review was to describe the frequency of post stroke depression (PSD) and its effects on functional recovery of patients.

## MATERIAL AND METHODS

A systematic review was conducted on MEDLINE, PUBMED, CINAHL, and the global web with Google Scholar. The key words used in all possible combinations were post-stroke depression (Post Stroke Depression - PSD), vascular stroke, functional rehabilitation, treatment.

### Inclusion criteria for studies

Articles were included from 2000 onwards in patients with a clinical diagnosis of stroke, who were evaluated for mood during rehabilitation at certain times. They had depressive disorder, depressive symptoms, major depressive disorder, mild depression or dysthymia according to DSM- III, III - R, IV (or other standardized diagnostic criteria). Also included were references to full texts accessed from the bibliographic review of the subject.

### Exclusion criteria for studies

Investigations referring to mixed diagnoses such as stroke and brain injury were not included. Studies published in other language than Greek or English were also not included. Studies not clearly mentioned in a diagnosis of depressive disorder were also rejected. Finally, articles which lack full access or they are written in another language than Greek or English, were also rejected.

### Detailed search process

The same search strategy was applied to all databases using

the same keywords. In the first phase, key words were introduced in different combinations to the databases. The search resulted in 1213 article titles, which were assessed to the extent that they belonged to the subject under investigation and whether access to the full text of the articles was available. Any articles deemed not relevant to the matter being investigated, and with no access to the full text, were rejected. From this process, a total of 750 articles were rejected and the remainder went on to the next stage. For articles for which there was no access to the full text, a study of the references was selected; those related to the subject were selected and the full text was accessed and passed to the next phase (total 15).

During the second phase, the summaries of the articles passed at this stage were studied. 124 articles were rejected because their summaries were not relevant to the subject under investigation and because they were published in a language other than Greek or English. The remaining 144 passed to the next stage.

In the third phase, the full text of the articles that were passed was studied. Of these, 96 were not relevant to the subject under investigation and were rejected. A total of 48 articles remained for review. In the fourth phase, the 48 articles were evaluated qualitatively on the basis of specific criteria and 18 were rejected. Thus, the totality of the articles included in the review was ultimately 30. The steps of the review of the literature are presented in Table 1.

## RESULTS

Of the 30 articles included in the review, 7 were cohort studies of which one was retrospective (Nanetti et al., 2005). The rest were descriptive studies, descriptive correlations, randomized clinical trials, cross-sectional and bibliographic reviews. The sampling method used in the majority of surveys was occasional. In the other surveys, a random sampling and random allocation to a control and intervention groups was followed. The participants ranged from 11 to 459.

### Frequency of PSD appearance

Badaru et al., in 2013, found through a cross-sectional study in Nigeria that evaluated fluctuations in functional independence in basic and functional daily activities in patients with stroke, of

the 65 patients who participated, 15 (23.1%) were diagnosed with PSD.<sup>16</sup>

Similarly, Matsuzaki et al., in 2015, in a prospective study from 2011-2013, involving 117 stroke patients hospitalized in a rehabilitation unit in a hospital in Japan, reported that 23.9% were diagnosed with depression.<sup>17</sup>

Brown et al., in 2012, conducted a prospective longitudinal study from 2003 to 2005, which included 182 patients with stroke. They found that 15 to 19% were depressed of which 58-59% are men. The percentage of patients with PSD did not differ significantly at the three time points of data collection: 2 weeks after discharge, and 3 and 12 months post-stroke. Also, while none of the three time points had an association with age in contrast to other studies, women were deemed more likely to develop PSD the first time, or 2 weeks after discharge.<sup>18</sup>

Cassidi et al., in 2004, studying 50 post-stroke patients in a rehabilitation unit in Ireland, found that 20% of the patients had depression, with women showing twice as many depressive symptoms as men. Gainotti et al., (2001), studying the data of 64 patients with stroke from an earlier prospective survey conducted in Italy from 1994-1997, found that 49 of them had PSD. Furthermore, Hama et al., (2007) conducted a study with a larger sample (N = 237) of people with stroke in Japan, aiming to investigate the effects of depression or apathy on functional rehabilitation. Of the 237 stroke patients, 75 (31.6%) had PSD.<sup>19</sup> Goodwin & Devanand in 2008, studied the data of a large population survey conducted in 48 US states from 1995-1996 to determine the relationship between stroke, depression and functional results. It showed that of the 24 people who had stroke, 7 had PSD.<sup>20</sup>

Greater PSD (47.1%) in patients 6 months after stroke was found by Unalan et al., (2008), with PSD being positively related to age and negatively with quality of life and functional status.<sup>21</sup>

### PSD Relationship and functionality

According to Gillen et al., in 2001, the increased number of depressive symptoms in the acute phase of stroke leads to the inefficient use of rehabilitation services by patients. In their research, 243 patients were enrolled in post-stroke rehabilita-

tion. They were assessed for depression symptoms at the beginning of the study, and for their ability to perform basic daily activities both at the beginning and the end upon their discharge. It was found that patients with high scores in GDS, compared to those with low scores, showed slower progress in regaining basic skills, such as movement, dressing and feeding.<sup>22</sup>

The above results seem to be consistent with Lai's research et al., in 2002, involving 459 post-stroke patients, of whom 131 were depressed. In particular, depressed patients were 0.3 times less likely to score  $\geq 95$  in normal daily activities (BADL) than the non-depressed and were 0.4 times less likely to be independent in three or more complex daily activities (IADLs). In six months, depressed patients showed slower progress in achieving independence in BADL and IADL compared with the non-depressed.<sup>23</sup>

Equally important are the research results of Žikić et al., in 2014, where two groups studied depression patients post-stroke (N = 30) and those without depression (N = 30). They concluded that there is relative depression and disability severity. In particular, PSD patients showed a more functional impairment than patients without depression ( $p < 0.001$ ).<sup>24</sup>

Similarly, Srivastava et al., in 2010, in a cross-sectional study of 51 patients following stroke in recovery units found that 18 experienced a depressive disorder. At one follow-up, the results showed that PSD was associated with functional ability, since PSD subjects showed a lower average on all scores of the functional parameter assessment scales, such as mental, equilibrium, mobility, walking ability and independence of basic functions compared to people who did not have PSD.<sup>25</sup>

Similarly, Brown et al., in 2012, showed that patients with severely depressed stroke had lower functionality. At the time of data collection, i.e., at 2 weeks, 3 months and 12 months after stroke, PSD had a statistically-significant correlation with functionality.<sup>18</sup>

In a survey by Badaru et al., in 2013, with a view to assessing fluctuations in functional independence in both basal and complex daily life activities in patients after stroke (N = 65), a negative correlation was found between PSD and functional rehabilitation.<sup>16</sup>

Chau et al., in 2010, found in that depression experienced by patients after stroke was associated with low levels of self-esteem and satisfaction with social support.<sup>26</sup>

Van De Port et al., in 2006, performing a prospective cohort study, they found that, out of the 205 patients with stroke who participated in the research, 21% experienced a progressive decline in mobility. They concluded that one-fifth of the patients had a significant reduction in mobility/long-term mobility even one year after stroke.<sup>27</sup>

Nannetti et al. in 2005, who followed up patients for three months, showed that depression did not affect kinetic and functional rehabilitation during this time. What they found, however, was that after the deprivation of the symptoms of depression increased, the degree of patient functionality diminished.<sup>28</sup>

Hama et al., studying in 2011 the effect of apathy and depression in the functional recovery of patients after stroke, point out that psychological symptoms do not cause functional disability but may be related to the interaction with the rehabilitation process. Apathy was a stronger prognostic factor for poor rehabilitation than depression, which should not be disregarded when rehabilitating patients. In a more recent survey, the researchers claim that improvements in day-to-day activities--the ability to walk--have a positive effect on mood disorders.<sup>29</sup>

### **Applying medication therapy to treat depression and the results in functional rehabilitation**

Hackett et al., in 2009, in a literature review, studied 17 trials, of which 13 were pharmaceutical clinical trials and 3 physiotherapy. The results showed that drug therapy was beneficial to the extent of a complete recession of depression and a decrease in scores on depression assessment scales as well as in the improvement of mental and functional rehabilitation. However, this comes with an increase in side effects. The types of drugs used primarily in clinical trials that were effective are tricyclic antidepressants and SSRIs.<sup>30</sup>

Robinson et al. in 2000, conducted a randomized, blind clinical trial that included 104 patients with stroke. Patients were administered randomly nortriptyline, a tricyclic antidepressant, fluoxetine, belonging to selective inhibitors of serotonin reuptake, and a placebo, for 12 weeks. The group of patients

taking nortriptyline showed significant improvement in HDRS at 77% compared to the other two groups (fluoxetine at 14% and a placebo at 31%).<sup>31</sup>

Narushima et al., in 2002, in a small-scale study that included 48 patients also looked at the same classes of drugs; their results showed that both were effective in preventing PSD. They found a higher rebound effect of depression after discontinuation of therapy in patients taking nortriptyline.<sup>32</sup>

Studying the effect of SSRIs on improving functional rehabilitation over a longer period (6 months) in 11 PSD patients, Bilge et al., in 2008, concluded that while at the start of the study, depressed patients had poor functional rehabilitation compared to the non-depressed ( $p < 0.05$ ), in the following months they showed depression recession and improved functional rehabilitation at similar rates to the non-depressive patients. The drug given was citalopram 20 mg.<sup>33</sup>

Gainotti et al., in 2001, studied the data of earlier cohort research. They chose 64 stroke patients who met the inclusion criteria. Of these, 49 people experienced depression and some had antidepressant therapy ( $N = 24$ ) and some ( $N = 25$ ). They concluded that patients with untreated depression had the lowest rates of improvement in functional rehabilitation, while those who were depressed and treated had the same improvement in functional rehabilitation as the patients with no symptoms. The drug of choice in this study was fluoxetine.<sup>34</sup>

For Llorca et al. in 2015, SSRIs are considered to be the safest drugs in the case of stroke patients because they have fewer side effects. Plus, they act more quickly with a latency period of 7-10 days and have an anxiolytic effect. They are first-class antidepressants for these patients who are mainly elderly with cardiovascular problems and other co-morbidities and are taking too many drugs with a risk of interaction.<sup>35</sup>

#### **Applying other interventions to treat depression and the results in functional rehabilitation**

There is a study that refers to the effect of cognitive behavioral therapy on depression treatment and, consequently, on improving the functioning of patients with stroke by Chang et al., in 2011. This randomized clinical trial randomly distributed 77 stroke patients into two groups: medication + rehabilitation training and the intervention group, where the patients re-

ceived conventional therapy + counseling (cognitive behavioral therapy). Patients in the intervention group experienced significant improvement in anger management, hostility, depression, quality of life and functionality in their day-to-day activities ( $p < 0.001$ ) relative to the control group.<sup>36</sup>

Mitchel et al., in 2009, additionally studied the duration of the effect of combining the psychosocial/behavioral treatment with antidepressant therapy to reduce depression and improve mobility and social participation. The 101 stroke patients enrolled were evaluated at 9 weeks, 21 weeks, 12 months and 24 months. One group received psychosocial/behavioral intervention and antidepressant therapy, while the control group got the usual care and antidepressant treatment. The results showed that the combination of psychosocial/behavioral treatment and antidepressants is very effective in reducing depression short term, and the result remains stable for 2 years. The control group experienced a decrease in depression in the first year but at a slower pace and to a lesser extent.<sup>37</sup>

#### **CONCLUSIONS**

In this systematic review, the PSD incidence rate estimate was not easy to determine due to the methodological differences in the investigations included. The percentage ranged from 15% to 47.1%, a result consistent with previous literature reviews.<sup>2,35</sup> Researchers use different diagnostic tools, although most of the investigations followed DSM - IV criteria. In addition, the evaluation time differs; in some surveys, the evaluation was done in the acute phase while in others in the subacute phase. Differences were also observed in the assessment area where the investigations took place in hospitals, as compared to rehabilitation units. All these factors may affect the correct diagnosis of PSD. All researchers have pointed out that PSD is a problem seen in the rehabilitation of SNE patients, but the diagnosis is often undecided. The time when the evaluation is performed affects the number of patients who are diagnosed with depression.<sup>22</sup> The results of the review are consistent with the above after a consideration of the difference in incidence rates of depression in the initial stages of stroke and later on.

The guidelines recommend the evaluation of depression in all patients with stroke and the application of antidepressant ther-

apy for 6 months for efficacy. Both during application and after discontinuation of treatment, they should be closely monitored by a trained health professionals. However, it is unclear whether treatment should be given prophylactically, what kind of drugs are most effective and their effect on patients' functional rehabilitation. This is why more research is needed in the field.

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There is a complex interaction between biological factors (the magnitude of damage and number of lesions) and experiential factors (individual history, social status and psychological state), leading to the pathophysiology of PSD. To address depression and apathy requires a multidisciplinary approach focused on the neuroanatomic/ neurobiological, emotional and physical aspects of patient rehabilitation.<sup>29</sup> Simple conventional therapies help, but the combination of these therapies with counseling and cognitive behavioral therapy gives better and time-resistant results.

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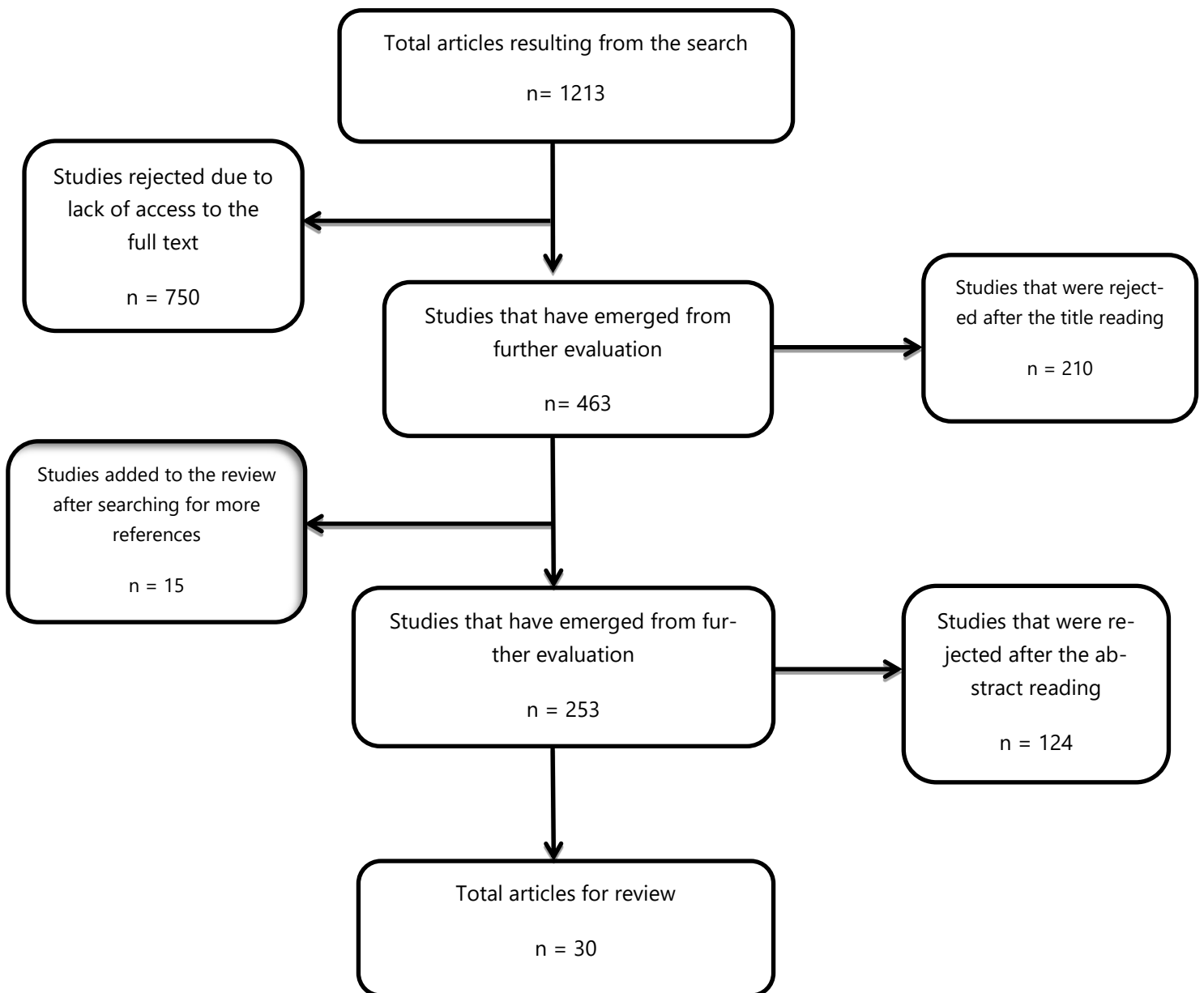


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## ANNEX

FIGURE 1. Flow chart displaying the steps conducted for the review.



**TABLE 1.** Characteristics of the studies investigating post stroke depression.

Researchers	Country	Purpose	Type of study	Sample	Results
1. Alfred & Beard, 2002	USA	Determine the relationship between depression and patient function after stroke and the strategic interventions for physical recovery and drug therapy	Metanalysis	31 Studies related to depression and functional status after stroke since 1989	Development of a theoretical model: depression and post-stroke functional status  1. Negative relation between depression and functional status  2. Physical recovery and drug therapy for depression increase the patient's functional status
2. Badaru et al., 2013	Nigeria	Evaluate fluctuations in functional independence and in the basic activities of everyday life of patients with depression after stroke	Synchronous	N = 65 patients who survived stroke	PSD patients showed reduced independence in basic and functional activities of everyday life during physical recovery
3. Bilge et al., 2008	Turkey	Study the differences in functional rehabilitation between depressed patients with stroke and non-depressed patients over 6 months	Clinical trial	Patients with stroke N = 40 Depressive N = 11 Non-depressant N = 29	Depressed patients had poor functional rehabilitation.  Depressed patients experienced depression in the first months after treatment and improvement in functional rehabilitation at similar rates to non-depressed patients
4. Brown et a ., 201	Sweden	Explore the PSD- related	Review	Patients after stroke	15-19% of the participants

2		factors to improve recovery efforts to reduce the incidence of PSD.		N = 181	were depressed.  The degree of dependence in day-to-day activities was related to the seriousness of the PSD. Age was not associated with PSD.
5. Cassidy et al., 2004	Italy	To investigate the prevalence of depressive symptoms and depressive disorder in Irish patients in a post-stroke rehabilitation unit  To investigate prognostic factors for PSD  Investigate the relationship between PSD and the outcome after transfer to a special unit.	Descriptive	N = 50 patients admitted to a post-stroke rehabilitation unit.	1. 20% of patients with stroke experienced PSD. 2. Women had twice as many depressive symptoms as men. 3. no relationship between injury and depression was found. 4. no relationship between previous psychiatric history and PSD was found 5. There was no relationship between depression and disability after SNE. 6. The best functional indicator of the effectiveness of rehabilitation was initial functional disability.
6. Chang et al., 2011	China	Exploring demographic variables related to anger and well-being in patients with stroke. Investigating the hypothesis that cognitive behavioral	randomized clinical trial	Patients with stroke N = 77  Control group: conventional therapy  Intervention team: conventional therapy +	Patients in the intervention group experienced significant improvement in anger management, hostility, depression and functionality in day-to-day activities

		therapy improves the emotional and physical well-being of patients. Discovering psychological variables associated with therapeutic effects.		counseling in a recovery unit	with respect to the control group.
7. Chau et al., 2010	China	To investigate the prevalence of PSD in patients with stroke 6 months after their discharge from a rehabilitation hospital and the relationship to psychological, social, physical outcomes and demographic characteristics.	Synchronous	N = 210 Patients with stroke Rehabilitation hospitals	Depression was associated with low levels of self-esteem, satisfaction with social support and functional capacity.
8. Flaster et al., 2013	USA	Analyze the complex pathogenesis of PSD and summarize options for pharmacological treatment	Review		PSD appears in 33% of stroke patients. It adversely affects functional rehabilitation and improvement and increases mortality. Antidepressants, especially early onset SSRI, reduces depression and helps improve functionality.
9. Gainotti et al., 2001	Italy	Assess the effects of PSD and antidepressant therapy on improving motor	Clinical trial	N = 64 stroke patients 49 with depression (24 received treatment and 25	PSD has a negative impact on functional recovery of stroke patients and antide-

		scoring and disability and see whether the negative effects of PSD on functional rehabilitation can be offset by antidepressant therapy.		without treatment) and 15 without depression	pressant therapy can reverse these effects.
10. Gillen et al., 2001	USA	Investigate how depressive symptoms, history of depression and cognitive functioning contribute to predicting the effectiveness of rehabilitation in patients with stroke.	Descriptive	N = 243 post-stroke patients in a recovery unit	The increased number of depressive symptoms in the acute phase of stroke leads to inefficient use of rehabilitation services by patients. Patients with a history of depression also experienced a prolongation of their stay in recovery facilities and difficulty in achieving basic day-to-day activities.
11. Goodwin & Devanand, 2008	USA	Determine the relationship between SNE, depression and functionality	Descriptive	N = 3032 24-75-year-olds N = 24 people with stroke (7 had depression in the last 12 months)	SNEs and depression were individually associated with disability in day-to-day physical activities
12. Hacket et al., 2005	Australia	Investigate the incidence of depression after stroke	Review		
13. Hacket et al., 2009 b	Australia	Determine whether pharmacological, psychological therapy or electroconvulsive therapy in	Review	16 surveys	Pharmacotherapy has been shown to be beneficial for depression, but it causes unwanted effects. There

		PSD can improve outcomes			has been no beneficial effect from psychotherapy. There is no research on electroconvulsive therapy.
14. Hama et al., 2007	Japan	To investigate the effects of depression or apathy on the functional rehabilitation of people after stroke	descriptive	N = 237 people with stroke (75 were depressed and 95 had apathy)	Apathy is a stronger prognostic factor for poor rehabilitation than depression.
15. Hama et al., 2011	Japan	Define the two dimensions of PSD: emotional depressive dimension and absurdity and the way they affect functional rehabilitation in patients with stroke	descriptive	N = 237 stroke patients	Depression and apathy overshadow each other and may coexist but may also exist independently after stroke. They adversely affect attention and memory, causing problems in functional rehabilitation.
16. Lai et al., 2002	USA	To investigate the relationship between depressive symptoms and the time of recovery of independence in BADL and IADL	Research	N = 459 stroke patients N = 131 depressants	Depressed patients had lower scores in BADL and IADL than non-depressed and slower progress in achieving independence after six months of follow-up.
17. Li et al., 2008	China	To investigate the efficacy and tolerability of Free and Easy Wanderer Plus (FEWP) in patients with PSD	randomized clinical trial	N = 150 patients with PSD Group 1 (n = 60): FEWP Group 2 (n = 60): Fluoxetine	In the second week, the group receiving FEWP showed more improvement in depression than the fluoxetine-treated

				Group 3 (v = 30): placebo	group. At the end of the study, the group receiving FEWP showed more improvement in baseline activities than the fluoxetine group. The FEWP shows good efficacy, safety and tolerability in patients with PSD.
18. Llorca et al., 2015	Spain	Determine the incidence of depression, how the different types of stroke affect depression, whether the injury area is related to depression, and what the appropriate drug is for PSD	Review		One in 3 stroke patients is depressed.  Several biological, behavioral and social factors are related to the pathogenesis of depression. Symptoms occur during the first 3 months after stroke. The best treatment for choice are SSRIs.
19. Mitchel et al., 2009	USA	Determine the effect of providing psychosocial / behavioral therapy in patients with depression and stroke. Describe the time it takes to reduce depression and determine the effect of the intervention on functional ability and the social participation of patients	randomized clinical trial	N = 101 stroke patients  Intervention team: psychosocial / behavioral therapy + antidepressants  Control group: routine care + antidepressants  Hospitals	The combination of psychosocial / behavioral therapy + antidepressants is very effective in reducing depression and thus improves functional abilities.



20. Matsuzaki et al., 2015	Japan	To investigate the relationship between PSD and physical rehabilitation in post-stroke patients at a rehabilitation nursing home.	Research	N = 117 stroke patients hospitalized in rehabilitation hospital	Depression and apathy can occur after stroke and affect rehabilitation independently. The number of patients with PSD decreased during hospitalization, and there was a difference in the results of self-complemented evaluation and observation tools.
21. Nannetti et a ., 2005	Italy	Assess the prevalence of PSD and its effect on kinetic and functional rehabilitation.	Research	N = 117 stroke patients	PSD does not seem to affect the kinetics and functional recovery in patients admitted to rehabilitation units in the first three months after stroke. However, after discharge, the symptoms of depression appear to increase and the degree of functionality decreases.
22. Narushima et al., 2002	USA	To investigate the effect of antidepressants on PSD prevention	Randomized clinical trial	N = 48 non-depressed stroke patients Groups IIA PEM Convention: 1. nortriptyline n = 13 2. Fluoxetine n = 13 3. Placebo n = 15 They took treatment for 3 months followed for 21	Nortriptyline and fluoxetine were effective in preventing depression; however, after nortriptyline discontinuation after discontinuation, patients had recurrence of depression.

				months	
23. Ojagbemi et al., 2014	Nigeria	Determine the frequency and prognostic factors of the Major Depressive Disorder in survivors of SNEs undergoing rehabilitation.	Cohort	N = 130 stroke patients N = 130 control group	PSD is common in patients after stroke in the process of recovery and is associated with cognitive impairment and the inability to perform daily activities. It affects the recovery process. The application of treatment not only affects mood but also physical and cognitive restoration
24. Paolucci et al., 2008	Italy	To describe the epidemiological and therapeutic approaches PSD	Review		
25. Robinson et al., 2000	Argentina	Compare the effect of nortriptyline, fluoxetine and a placebo in treating depression and restoring physical and mental disability	randomized clinical trial	N = 104 stroke patients <u>Depressed:</u> N = 23 Fluoxetine N = 16 Nortriptyline N = 17 Placebo	Nortriptyline was more effective in treating depression and in improving the recovery of daily activities as measured by the FIM.
26. Salter et al., 2013	Canada	Assess the prevalence, physical course and risk factors for PSD, as well as issues related to its evaluation and impact on rehabilitation	Review		PSD affects one third of stroke patients. The highest rates occur in the first few months after the SNE. While there may be improvement, depression may remain for years.

27. Srivastava et al., 2010	India	To assess :  A) the prevalence of depressive disorder in chronic stroke patients  B) PSD 's relationship to disability	Synchronous	N = 51 stroke patients	18 patients (35.29%) were depressed.  The variables associated with PSD were male sex, married, if subject lived in a nuclear family, if subject lived in the city and had a high score on HDRS.  PSD was associated with functional disability, but the results were not statistically significant ( $p > 0,05$ )
28. Unalan et al., 2008	Turkey	To investigate the relationship between depressive symptoms six months after stroke and quality of life, clinical and socio- demographic characteristics, functional status and severity of stroke.	Description	N = 70 stroke patients	47.1% were depressed.  PSD appears to be positively related to age and negatively with educational level, quality of life and functional status
29. Žikić et al., 2014	Serbia	To investigate the effect of PSD on the outcome of the disease, e.g. the degree of disability and quality of life after the SNE	Research	N = 60 two groups  N = 30 patients without depression in the acute phase of stroke  N = 30 patients with depression 2 weeks after stroke  Neurological department of hospital and rehabili-	PSD patients had a more severe disability than non-depressed patients both in the initial phase and after rehabilitation.  The prospect of improved functionality was lower in depressed than non-depressed.

				tation units	The quality of life was worse in the depressed areas of emotional functioning with social relationships being more affected.
30. Van De Port et al., 2006	Holland	To identify clinical determinants that affect patient mobility decline 1-3 years after stroke	preamble - prudential Cohort 3 years of para monitoring	N = 264 in the first year N = 205 in the third year	In one-fifth of patients, functional and mobility deteriorated 1-3 years after stroke.  Among the predisposing factors of deprivation of function was depression.