



Preliminary communication

The relationship between post-stroke depression and physical recovery



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ABSTRACT

Background: Post-stroke depression (PSD) is a serious and common complication of stroke. In this prospective study on the relationship between clinical PSD and physical recovery, we focused on (1) distinguishing between depression and apathy, (2) issues in assessment of PSD, and (3) timing of assessment.

Methods: Japanese stroke patients ($n=117$) were studied. We used self-rating scales [Zung Self-Rating Depression Scale (SDS) for depression; Apathy Scale (AS) for apathy] and observer-rating scales [Montgomery–Åsberg Depression Rating Scale (MADRS) for depression; Neuropsychiatric Inventory–Nursing Home (NPI-NH) for apathy] to assess psychological state. We assessed physical disability using the Functional Independence Measurement (FIM). Two-way analysis of covariance was used to determine effects of depression and apathy on functional outcome. We evaluated PSD twice, within 10 days after hospitalization and four weeks later.

Results: Objective scales gave higher prevalence than subjective scales for both depression and apathy. A significant effect of apathy on FIM recovery was seen with objective scale assessment during hospitalization; there was a marginal effect of depression at the same time.

Limitations: We did not consider the stroke size and location. In addition, we excluded patients with severe comprehension deficits or with a history of stroke.

Conclusions: Our findings indicate that depression and apathy could occur independently after stroke and could individually influence functional recovery. We obtained more accurate estimates of functional recovery using objective measures. Furthermore, our findings suggest that depression and apathy should be assessed not only at admission but also during hospitalization to estimate and enhance the functional recovery of stroke patients.

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1. Introduction

Post-stroke depression (PSD) is a serious and common complication of stroke, affecting one third of all stroke patients at any time during the follow up (Hackett et al., 2005). PSD has negative impacts on patient participation in rehabilitation at the most crucial time to functional recovery and leads to poor outcomes (Hinojosa et al., 2011). On the other hand, there is an increasing evidence that antidepressants do treat PSD effectively and improve

functional status (Gonzalez-Torrecillas et al., 1995; Dam et al., 1996; Miyai and Reding, 1998; Gainotti et al., 2001; Narushima et al., 2007). Therefore, early detection, correct diagnosis, and appropriate treatment of PSD are essential to enhance the functional recovery of stroke patients.

In this prospective study, we investigated the relationship between the clinical condition of PSD and physical recovery of stroke patients in a rehabilitation hospital. We focused on the following three issues. The first was to distinguish clearly between depression and apathy. Apathy is defined as the absence or lack of feeling, emotion, interest, or concern (Marin, 1990). The symptom has been considered to partially overlap with the expression of depression; however, several recent studies have revealed neuroanatomical and symptomatological differences between the two symptoms (Marin et al., 1994; Levy et al., 1998; Andersson et al., 1999). Apathy is also often observed after stroke and can interfere

Abbreviations: PSD, post-stroke depression; SDS, Zung Self-Rating Depression Scale; AS, Apathy Scale; MADRS, Montgomery–Åsberg Depression Rating Scale; NPI-NH, Neuropsychiatric Inventory–Nursing Home; FIM, Functional Independence Measurement; MMSE, Mini-Mental State Examination

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with patient's engagement in rehabilitation programs. Depression and apathy require completely different therapeutic approaches. Thus, it is necessary to analyze depression and apathy separately in order to evaluate the influences of PSD on the recovery of physical function.

The second issue we focused on is the assessment of PSD. In a review of the assessment of PSD, [Salter et al. \(2007\)](#) noted that the use of self-report measures may be limited by the reliance of such scales on personal insight, but administration of self-report measures requires few resources and represents little patient burden. In contrast, results obtained via observer-rating scales based on psychiatric interviews are more diagnostically accurate, but the amount of time and level of expertise required for their administration make them less feasible assessment tools in most clinical settings ([Salter et al., 2007](#)). As with depression, patients with apathy may also lack insight into their disease. Therefore, we evaluated depression and apathy after stroke using both self-report (subjective) scales and observer-rating (objective) scales.

The third issue is the timing of the assessment of PSD. The majority of cases of PSD were developed between one and six months post stroke ([Whyte and Mulsant, 2002](#)). Some patients may develop depression during hospitalization for rehabilitation. Because the mental status of patients might be different according to the time between admission and assessment, a single assessment at admission makes it difficult to evaluate the influence of PSD on the rehabilitation effect. Therefore, we evaluated depression and apathy twice using a first assessment at admission and a second one during hospitalization (four weeks after the first one).

2. Method

All procedures for the present study strictly followed the 2011 Clinical Study Guidelines of the Ethics Committee of Kumamoto Takumadai Rehabilitation Hospital (Kumamoto, Japan) and were approved by the internal Review Board. Written informed consent was obtained from all patients after a complete description of all procedures of the study was provided.

2.1. Subjects

This study was a prospective rehabilitation hospital-based cohort study. The subjects were consecutively selected from patients who were admitted to Kumamoto Takumadai Rehabilitation Hospital between July 2011 and June 2013. All patients underwent routine laboratory tests and standard neuropsychological examinations including the Mini-Mental State Examination (MMSE) ([Folstein et al., 1975](#)). The inclusion criterion in the present study was hospitalization for sub-acute stroke rehabilitation. The exclusion criteria were as follows: 1) patients with a rehabilitation plan to be finished within four weeks, 2) patients after sub-arachnoid hemorrhage or transient ischemic attack, 3) history of previous stroke, 4) presence of severe aphasia that would make screening test for PSD difficult, 5) history of major psychiatric illness, such as major depression, bipolar disorder, schizophrenia, or schizoaffective disorder, 6) complication of dementia based on DSM-III-R criteria ([American Psychiatric Association, 1987](#)), and 7) inability to obtain informed consent.

2.2. Assessment

In this study, we assessed depression and apathy separately using both subjective and objective scales. The assessments were performed twice, first within 10 days of the admission and then again at four weeks after the first assessment. Depression and apathy were assessed by two experienced neuropsychiatrists

(M.S. and Y.S.). Patients with severe depression were treated appropriately through medication by the experienced neuropsychiatrists.

2.2.1. Assessment of depression

2.2.1.1. Subjective assessment. We used the Japanese version of the Self-rating Depression Scale (SDS) to examine the subjective severity of depression ([Zung, 1965](#); [Fukuda and Kobayashi, 1973](#)). The SDS scale consists of 20 items and patients choose their answer to each item from 4 categories: always, often, sometimes, or rarely. The total score is the sum of the 20 items and the SDS scores ranged from 20 to 80. We classified the patients into two groups according to their score: a non-depressed group (SDS score < 40 points) and a depressed group (SDS score \geq 40) ([Zung, 1965](#); [Fukuda and Kobayashi, 1973](#)).

2.3. Objective assessment

We used the Japanese version of the Montgomery–Åsberg Depression Rating Scale (MADRS-J) to examine the objective severity of depression ([Montgomery and Asberg, 1979](#); [Takahashi et al, 2004](#)). The MADRS-J consists of 10 items, each of which is scored on a scale that ranges from 0 to 6. The total score is the sum of the 10 items and the MADRS-J scores range from 0 to 60. We classified the patients into two groups according to their score: a non-depressed group (MADRS-J score < 12 points) and a depressed group (MADRS-J score \geq 12) ([Montgomery and Asberg, 1979](#); [Takahashi et al, 2004](#)).

2.3.1. Assessment of apathy

2.3.1.1. Subjective assessment. To quantify the apathetic state subjectively, we used the Japanese version of the Apathy Scale (AS) ([Starkstein et al., 1992](#); [Okada et al., 1998](#)). The AS consists of 14 questions concerning spontaneity, initiation, emotionality, activity level, and interest in hobbies. This scale is self-assessed. The answers to each question are scored against four grades (0–3) and the total score was used for the analysis. We classified the patients into two groups according to their score: a non-apatetic group (apathy score < 16 points) and an apathetic group (apathy score \geq 16 points) ([Starkstein et al., 1992](#); [Okada et al., 1998](#)).

2.4. Objective assessment

We assessed the patients' apathetic state objectively using a Japanese version of the Neuropsychiatric Inventory–Nursing Home (NPI-NH) ([Wood et al., 2000](#); [Shigenobu et al., 2008](#)). The NPI-NH is a structured interview with professional caregivers in which 10 neuropsychiatric symptoms are assessed: delusions, hallucinations, agitation/aggression, dysphoria, anxiety, euphoria, apathy, disinhibition, irritability/lability, and aberrant motor behaviors. In this study, we focused on the apathy item on the NPI-NH and interviewed patients' primary nurses, physiotherapists (PT), or occupational therapists (OT). Screening questions are asked to determine whether apathy is present. In the case of a positive answer, further questions are asked and the severity and frequency of the symptom are determined. Frequency is rated on a five point scale from 0–4 and severity is rated on a four point scale from 0–3: the larger the score, the higher the severity or frequency. The NPI-NH score (severity \times frequency) was calculated (range of possible scores, 0–12).

2.5. Physical function

Physical function was assessed with the Functional Independence Measurement (FIM) ([Data Management Service of the Uniform Data System for Medical Rehabilitation and the Center](#)

for Functional Assessment Research, 1990; Chino, 1997). The FIM is widely used as a measure of disability in stroke patients. The maximum total FIM score is 126; the lower the score, the greater the disability. The FIM was conducted at the time of admission and at discharge by the patients' PT or OT. In the present study, the recovery of physical function was expressed as the change of the FIM score during hospitalization, which was calculated as follows: [(FIM recovery)=(FIM score on discharge)–(FIM score on admission)].

2.6. Data analysis

The relationship between the clinical condition of PSD and physical recovery was assessed in a two-way analysis of covariance (ANCOVA) model with FIM recovery as a dependent variable, depression (depressive versus non-depressive) and apathy (apathetic versus non-apathetic) as main effects, and (depression) × (apathy) as an interaction term, adjusted for the appropriate covariates (gender, age, length of hospitalization, FIM score on admission and MMSE score). The analysis was performed separately on the basis of assessment measures (subjective or objective) and assessment timings (at admission or during hospitalization). All tests were 2-tailed and significance was set at the $p < 0.05$ level. All statistical analyses were performed using IBM SPSS Statistics 21 (IBM Japan, Tokyo, Japan).

3. Results

Of the 153 patients who participated this prospective study, 36 patients withdrew during the study because of discharge within 4 weeks ($n=25$) or worsening physical condition ($n=11$). Thus, 117 patients were enrolled for this study, with 64 women and 53 men. The mean age of these patients was 71.9 ± 13.8 years, the mean time to hospitalization from the onset was 21.0 ± 14.2 days, the mean length of hospitalization was 80.3 ± 39.0 days, the mean MMSE score was 25.0 ± 5.2 , the mean FIM score on admission was 85.9 ± 29.5 , and the mean FIM score on discharge was 104.7 ± 25.3 . Ten patients with depression received antidepressant drug therapy during hospitalization.

Fig. 1 shows the frequency of depression and apathy based on each assessment scale and timing. The frequency of depression measured by MADRS-J was significantly higher than that by SDS at both timings. The second assessment during hospitalization showed a lower frequency of depression compared with that on admission for objective assessments. The objective scale (NPI-NH) gave a significantly higher prevalence than the subjective one (AS) in apathy, just as in depression.

Depression and apathy coexisted in some, but not all patients, and could exist independently, as shown in Table 1. The objective scales gave higher estimates of depression, apathy, and overlapping apathy and depression than the subjective scales. The pattern of overlap between depression and apathy during hospitalization was similar to that on admission.

A two-way ANCOVA (depression × apathy) revealed a significant main effect of apathy ($p=0.025$) on FIM recovery when the symptom was assessed by objective scale and during hospitalization (Table 2). The main effect of depression on FIM recovery was marginal ($p=0.095$) and was assessed only by objective scale and during hospitalization. There was no significant interaction effect of depression and apathy in either assessment scale or timing.

4. Discussion

Depression and apathy are common neuropsychiatric consequences of stroke. Some form of depression is considered to occur

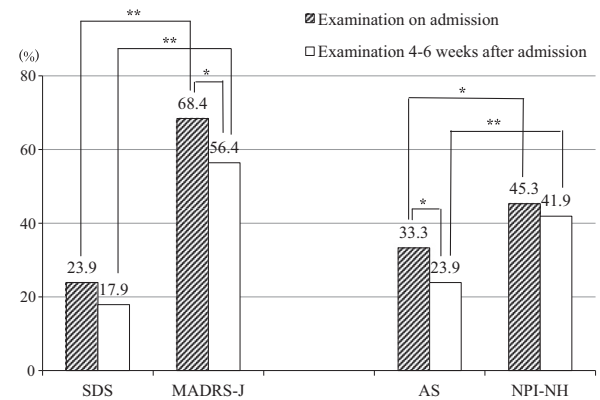


Fig. 1. Prevalence of depression and apathy presented as the percentage using cutoff scores noted in Section 2. The McNemar's test was used to calculate the differences in prevalence between the assessments (** $p < 0.01$, * $p < 0.05$). SDS: Japanese version of the Self-rating Depression Scale, MADRS-J: Japanese version of the Montgomery-Åsberg Depression Rating Scale, AS: Japanese version of the Apathy Scale, NPI-NH: Japanese version of the Neuropsychiatric Inventory-Nursing Home.

in at least one-quarter of patients in the first year after acute stroke (House, 1987; Burvill et al., 1995; Johnson, 1991). In the present study, depression was observed in 23.9% of patients using SDS, and apathy in 33.3% using AS on admission, which were comparable to a previous study conducted by Hama et al. (2007) in a rehabilitation hospital. They assessed psychological status using SDS for depression and AS for apathy in Japanese stroke patients and showed the prevalence of depression (31.6%) and apathy (40.1%).

Depression and apathy can appear simultaneously in the same patient after stroke. In this study, subjective measures revealed 50 patients (42.7%) with depression and/or apathy. Among them, 17 patients (34%) certainly had both depression and apathy at admission while two-thirds of patients had only one of them. This result suggested that depression and apathy could occur independently after stroke.

While investigating the relationships between the clinical condition of PSD and physical recovery after stroke, we also focused on the difference of assessment tools (subjective or objective measure) and timing of assessment (on admission or during hospitalization). There was a considerable discrepancy for prevalence of depression and apathy between self-report measures and observer rating scales. This finding stresses the need to analyze depression and apathy separately and to use appropriate measures for evaluating the influences of PSD on the recovery of physical function.

Apathy had a significant effect on FIM recovery, and depression showed a similar trend. There was no significant interaction effect between depression and apathy. This suggests that apathy and depression may influence functional recovery after stroke independently. It is noteworthy that the influence of apathy and depression on functional recovery was seen only when the symptoms were assessed using an objective scale and during hospitalization, indicating that later objective assessment may be more sensitive in detecting detrimental psychological states. The use of self-report measures to identify the presence of depression or to assess the level of depression has been the focus of considerable debate. It has been suggested that the discrepancies resulting from sole use of self-report measures were due to underreporting of depressive symptomatology compared with observer ratings. Gordon et al. (1991) suggest that either patients tend to minimize the severity of their mood disorders or examiners are sensitive to patients' behaviors. Based on results of the current study, assessment using objective scales is essential for

Table 1Comparisons of the assessments of PSD between groups, *n* (%).

		Depression (–) Apathy (–)	Depression (+) Apathy (–)	Depression (–) Apathy (+)	Depression (+) Apathy (+)
Examination on admission	Subjective assessment	67 (57.3%)	11 (9.4%)	22 (18.8%)	17 (14.5%)
	Objective assessment	33 (28.2%)	31 (26.5%)	4 (3.4%)	49 (41.9%)
Examination 4–6 weeks after admission	Subjective assessment	80 (68.4%)	9 (7.7%)	16 (13.7%)	12 (10.3%)
	Objective assessment	39 (33.3%)	29 (24.8%)	12 (10.3%)	37 (31.6%)

PSD: post-stroke depression.

Table 2

Influences of PSD on the recovery of physical function.

		Depression		Apathy		Depression	Apathy	Interaction
		Non-existence	Existence	Non-existence	Existence	<i>F</i>	<i>F</i>	<i>F</i>
Examination on admission	Subjective assessment	17.2(17.5)	22.2(22.4)	18.8(17.9)	17.6(20.8)	1.6	1.6	2.9
	Objective assessment	15.3(13.4)	19.8(20.8)	19.5(18.1)	17.0(19.7)	1.2	0.04	0.3
Examination 4–6 weeks after admission	Subjective assessment	17.5(17.2)	22.1(25.1)	19.2(16.7)	15.9(24.5)	0.4	1.0	1.2
	Objective assessment	18.3(15.0)	18.4(21.4)	19.5(18.2)	16.7(19.6)	2.8 [†]	5.2 [*]	0.2

Values are mean of FIM recovery (SD).

FIM recovery: (FIM score on discharge)–(FIM score on admission).

PSD: post-stroke depression.

FIM: Functional Independence Measurement.

Two way analysis of covariance (ANCOVA).

* $p < 0.05$.† $p < 0.1$.

identifying the impact of psychological state on functional recovery.

Our results demonstrated the impact of the timing of assessment after stroke onset and suggested the efficacy of psychological symptom assessment during hospitalization for estimating functional recovery. Why do apathy and depression have a relationship to poor functional recovery only when assessed during hospitalization? Two possible factors might provide an answer to the question. We performed our first assessment of depression and apathy within 10 days after hospitalization. Patients interviewed during the sub-acute phase may still be adjusting to their stroke experience, and depression in these patients may reflect this transition stage. Bhogal et al. (2004) reviewed 26 reports about PSD and showed that the highest rates of depression were noted in patients assessed within the first 28 days of stroke. In fact, the number of patients with depression decreased during hospitalization in this study. Another is the factor on the side of examiners. Performing assessment too early after hospitalization complicates proper PSD screening because medical staff do not have enough time to adequately evaluate patients.

5. Limitations

A few methodological limitations of this study should be acknowledged. First, we did not consider the stroke size and location. Many studies have demonstrated a relationship between left anterior frontal damage and depression soon after an ischemic stroke or intracerebral hemorrhage. On the other hand, right-sided stroke has been associated with the development of anosognosia of depression (denial or unawareness of illness) (Ramasubbu, 1994, Carota et al., 2002). These factors could cause depression or apathy and lead to a poor rehabilitation effect. Further study is needed to examine the influence of lesion site and size on functional recovery. Second, because patients with severe aphasia and patients with a history of stroke were excluded from the study, the results may not be applicable to all stroke patients.

6. Conclusion

Our findings demonstrate that depression and apathy could occur independently after stroke and they could individually influence functional recovery. While we employed both objective and subjective assessment scale, objective measures gave a more accurate estimate of functional recovery. Furthermore, these findings suggest that depression and apathy should be assessed not only at admission but also during hospitalization to estimate and enhance the functional recovery of stroke patients.

Role of funding source

None.

Conflict of interest

None of the authors has a conflict of interest to disclose.

Contributors

Shiho Matsuzaki designed this study, collected data, worked on data analysis, and drafted the article. Seiji Yuki helped in collecting data. Asuka Koyama helped to conduct a statistical analysis. Mamoru Hashimoto, Yoshifumi Hirata and Manabu Ikeda designed this study and contributed to supervise and edit the final version of manuscript. All authors revised the paper critically and have approved the final manuscript.

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