THE RELATIONSHIP OF INSOMNIA WITH MOTOR CLINICAL OUTCOMES IN ISCHEMIC STROKE PATIENTS

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ABSTRACT

Introduction: Insomnia is a sleep disorder in about 20% - 56% of patients. Insomnia is an indicator that predicts a poor prognosis of functional recovery. There is growing evidence about the importance of sleep in neuroplasticity and learning in stroke recovery, but sleep management has not generally been considered in stroke management and rehabilitation protocols. Aims: To determine the relationship between insomnia severity and serum BDNF levels and other factors, namely stroke location, stroke severity, gender, age and depression with motor clinical outcomes in ischemic stroke patients. Methods: Cross sectional study. Insomnia was evaluated by the Insomnia Severity Index (ISI) score, and clinical motor output was evaluated by the Barthel Index (BI) score and the Short-Fugl Mayer Assessment (S-FMA) score. Depression was evaluated with the Beck Depression Inventory score. Serum BDNF levels were measured at 5 - 7 days of onset. Stroke severity was assessed by the NIHSS score, and the location of the stroke lesion was assessed by a non-contrast head CT scan. Bivariate and multivariate analysis of each factor on motor clinical outcome and multiple linear regression of all factors associated with motor clinical outcome to assess the magnitude of the influence of these factors on motor clinical outcome in stroke patients. The results were significant if the p-value <0.05. Results: There was no significant relationship between insomnia severity and motor clinical outcome (p = 0.936 and p = 0.116). There was no significant relationship between serum BDNF levels and clinical motor output (p = 0.183 and p = 0.819). There was a statistically significant relationship between age, stroke location and NIHSS with motor clinical outcome (Barthel Index) were age, and NIHSS were more influential (p = 0.030 and p = 0.035) and had an effect of 48.5%. There was a significant relationship between gender, stroke location and NIHSS with motor clinical outcome (Short Fugl Mayer Assessment / S-FMA). NIHSS was more influential (p = 0.002) and had an effect of 62.2%. Discussion: There is no relationship between insomnia severity and motor clinical outcome in ischemic stroke patients. There is no relationship between serum BDNF levels and motor clinical outcomes in ischemic stroke patients. It was found that the relationship between other factors, namely age, gender, location of stroke lesions and NIHSS with motor clinical outcome of ischemic stroke patients, where age and NIHSS were the most influencing factors on the clinical outcome of ischemic stroke patients.

KEYWORDS Insomnia, age, NIHSS, motor clinical outcome, ischemic stroke
Introduction

Insomnia is a sleep disorder in about 20% - 56% of patients. In stroke, it affects between 20% - 56% of total stroke patients. One study by Leppavuori et al. observed that 56% of all stroke patients complained of insomnia, of which 37% met the criteria for insomnia determined by the DSM-IV. They also observed that 38.6% had experienced insomnia before the stroke and 18.1% as a new symptom of insomnia after stroke. Insomnia is an indicator that predicts a poor prognosis of functional recovery. Sleep function suggests an important role for sleep in the reorganization and repair of neural networks, especially with regard to learning and memory. There is increasing evidence about the importance of sleep in neuroplasticity and learning in stroke recovery, but sleep management has not generally been considered in stroke management and rehabilitation protocols.[1]

This study aims to determine the relationship between insomnia severity and serum BDNF levels as well as other factors, namely stroke location, stroke severity, gender, age and depression, with motor clinical outcomes in ischemic stroke patients.

Research methods

This study is a cross-sectional study, which was conducted at the inpatient installation of Tugurejo Hospital Semarang from February to June 2020. The subjects of the study were ischemic stroke patients who met the inclusion criteria, namely patients with a diagnosis of ischemic stroke for the first time according to the non-contrast head CT scan image that was treated hospitalized at Tugurejo Hospital, Semarang, aged 40-70 years and agreed to do the research.

This research has received permission from the Ethics Commission of the Faculty of Medicine UNDIP number 443 / EC / KEPK / FK UNDIP / X / 2019 dated 16 October 2019, and received permission from the Tugurejo Hospital Semarang with number 423.4 / 05259 dated December 5, 2019. The patient was examined for insomnia. Severity Index on days 5 - 7 of onset (when going home after hospitalization) to determine the presence or absence of insomnia and determine the degree of insomnia severity. Then the patient was taken a venous blood sample for BDNF serum examination, 10 cc of venous blood was taken.[2] Blood tests were carried out at the Prodia laboratory. Blood samples can be stored for up to 6 months prior to the BDNF serum examination.[2] Patients were examined for stroke severity using NIHSS, clinical motor output using the Barthel Index and Short Fugl Meyer Assessment and the level of depression using the Beck Depression Inventory II. Then the data was collected and analyzed.

Data were processed using SPSS Statistics for Windows version 22 program. Data analysis included descriptive statistics and hypothesis testing. Bivariate analysis to determine the relationship between insomnia severity and BDNF levels with motor clinical outcomes (Barthel Index score and Short-Fugl Mayer Assessment score) with the Kruskal Wallis or Mann Whitney test and multivariate test of these factors. To assess its effect on motor clinical outcomes by multiple regression trials, with a 95% confidence level. The p-value is considered significant if p <0.05.

Research result

This study included 30 subjects who met the inclusion and exclusion criteria.

Table 1 shows the characteristics of the research subjects, it was found that the most age group was ≤ 60 years as many as 16 subjects (53.3%) and ages> 60 years as many as 14 subjects (46.7%). 17 more female subjects (56.7%) than 13 male subjects (43.3%). Insomnia severity with ISI score found 3 subjects (10%) did not lead to insomnia, 15 subjects (50%) with mild insomnia ISI score, 12 subjects (40%) with moderate insomnia ISI score. Normal serum BDNF levels were 10 subjects (33.3%) and high serum BDNF levels were 20 subjects (66.7%). In this study, there were no subjects with low BDNF levels. The location of ischemic stroke lesions in this study found subcortical lesions in 19 subjects (63.3%) and subcortical lesions + thalamus in 11 subjects (36.7%). Stroke severity with NIHSS score obtained 25 subjects (83.3%) mild NIHSS, 5 subjects (16.7%) moderate NIHSS. Subjects with depressive symptoms obtained 3 subjects (10%) BDI scores showed mild mood disorders, and 27 subjects (90%) BDI scores were normal. The clinical motor output as measured by the BI and S-FMA scores obtained 1 subject (3.3%) mild dependent BI score, 5 subjects (16.7%) moderate dependent BI score, 16 subjects (53.3%) BI score weight dependence and 8 subjects (26.7%) BI score of total dependence. The average S-FMA score was 10.53 (SD = 6.40).

Table 2 shows the relationship between insomnia severity and motor clinical outcome. In this study, there was no statistically significant relationship between the degree of insomnia severity (Insomnia Severity Index / ISI score) and clinical motor output (Barthel Index score and Short Fugl Mayer Assessment) with p-values 0.936 and 0.116, respectively.

Table 3 shows the association of BDNF with motor clinical outcomes. In this study, there was no significant relationship between serum BDNF levels and clinical motor output (Barthel Index score and short Fugl Mayer Assessment score), with p values 0.183 and 0.819, respectively.

Table 4 shows the relationship between age and clinical motor output. In this study, a significant relationship was found with the Barthel Index score with a value of p = 0.035, with age affecting the Barthel Index of 0.403. Meanwhile, the Short Fugl Mayer Assessment score did not show a statistically significant relationship with a p-value = 0.188.

Table 5 shows the relationship between gender and clinical motor output. In this study, a significant relationship between gender and the Short Fugl Mayer Assessment score was obtained with a value of p = 0.023, with an effect of -0.460. Meanwhile, gender with the Barthel Index score did not show a statistically significant relationship with a p-value = 0.117. In this study, women appeared to have a worse clinical outcome.

Table 6 shows the relationship between stroke lesion location and motor clinical outcome. In this study, a significant relationship was found with the Barthel Index score and the Short Fugl Mayer Assessment score with p values 0.004 and 0.002, respectively. Where the location of the stroke lesion has more influence on the Barthel Index of 0.518 compared to the Short Fugl Mayer Assessment (-0.581).

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### Table 1 Characteristics of Research Subjects

| Variable        | F   | %    | Mean ± SD | Median (min – max) |
|-----------------|-----|------|-----------|--------------------|
| **Age**         |     |      |           |                    |
| ≤ 60 years old  | 16  | 53.3 |           |                    |
| > 60 years old  | 14  | 46.7 |           |                    |
| **Gender**      |     |      |           |                    |
| Male            | 13  | 43.3 |           |                    |
| Female          | 17  | 56.7 |           |                    |
| **ISI**         |     |      |           |                    |
| No insomnia     | 3   | 10.0 |           |                    |
| Mild Insomnia   | 15  | 50.0 |           |                    |
| Moderate Insomnia| 12  | 40.0 |           |                    |
| **BDNF**        |     |      |           |                    |
| Normal          | 10  | 33.3 |           |                    |
| High            | 20  | 66.7 |           |                    |
| **BI**          |     |      |           |                    |
| Mild dependence | 1   | 3.3  |           |                    |
| Moderate dependence | 5  | 16.7 |           |                    |
| Severe dependence | 16 | 53.3 |           |                    |
| Total dependence | 8  | 26.7 |           |                    |
| **Stroke location** | | | | |
| Subkortikal     | 19  | 63.3 |           |                    |
| Subkortikal + thalamus | 11 | 36.7 |           |                    |
| **NIHSS**       |     |      |           |                    |
| Mild            | 25  | 83.3 |           |                    |
| Moderate        | 5   | 16.7 |           |                    |
| **BDI**         |     |      |           |                    |
| Normal          | 27  | 90.0 |           |                    |
| Mild mood disorder | 3 | 10.0 |           |                    |
| SFMA            | 10.53 ± 6.40 | 12 (0-23) | | |

### Table 2 Relationship of insomnia severity to motor clinical outcome

| Variable                              | Barthel Index | P  |
|---------------------------------------|---------------|----|
|                                       | Mild          | Moderate | Severe | Total |
| Insomnia Severity Index               |               |         |        |       |
| No insomnia                           | 1             | 0        | 1      | 1     |
| Mild insomnia                         | 0             | 2        | 10     | 3     | € 0.936 |
| Moderate insomnia                     | 0             | 3        | 5      | 4     |

Note: *Significant (p < 0.05); € Kruskal Wallis

| Variable                              | Short Fugl Mayer Assesment | P  |
|---------------------------------------|----------------------------|----|
|                                       | Mean ± SD                  | Median (min – max) |
| Insomnia Severity Index               |                            |                |
| No insomnia                           | 11.67 ± 11.50              | 12 (0 – 23)     | € 0.116 |
| Mild insomnia                         | 12.27 ± 6.08               | 12 (0 – 23)     |
| Moderate insomnia                     | 8.08 ± 5.11                | 10.5 (0 – 12)   |

Keterangan: *signifik an (p<0.05); €Kruskal Wallis
In a study by Leppavuori et al. in 2002, they analyzed NIHSS and motor clinical outcome. In this study, age and NIHSS were factors that influenced the Barthel Index score of 48.5%, and NIHSS was also the dominant factor affecting the Fugl Mayer Assessment score of 62.2%.

**Table 7** shows the relationship between stroke severity (NIHSS) and motor clinical outcomes. In this study, a significant relationship was found with the Barthel Index score and the Short Fugl Mayer Assessment score with p-values 0.001 and 0.001, respectively where the NIHSS is more influential on the Barthel Index of 0.575 compared to the Short Fugl Mayer Assessment (0.748).

**Table 8** shows the association of depression with motor clinical outcomes. In this study, it was found that there was no significant relationship with the p-value 0.819 and 0.802, respectively.

**Table 9** shows how much influence the factors that have a significant relationship to motor clinical outcomes together. In this study, age and NIHSS were factors that influenced the Barthel Index score of 48.5%, and NIHSS was also the dominant factor affecting the Fugl Mayer Assessment score of 62.2%.

**Discussion**

In this study, the age group ≤ 60 years was slightly more than the age group > 60 years as many as 16 subjects (53.5%) for ≤ 60 years old and 14 subjects (46.7%) aged > 60 years. In a study by Leppavuori et al. in 2002, who analyzed insomnia in stroke patients, it was observed that insomnia was more common in older subjects than in younger ages. In another study, namely Heikki et al.’s study in 2003, showed that the frequency of post-stroke insomnia at younger ages tended to be less than in the elderly. Sleep architecture changes significantly in healthy elderly individuals. Sleep initiation is more difficult, total sleep time and sleep efficiency is reduced, delta waves or Slow Wave Sleep are reduced, sleep fragmentation is increased, and more time is spent in bed after waking up. With aging, REM sleep duration tends to be longer, but sleep latency is significantly reduced.

In this study, 17 subjects (56.7%) were more female than male (43.3%). In a study by Leppavuori et al. in 2002, they analyzed insomnia in stroke patients more often in women and from a multivariate analysis showed that female subjects with complaints of fragmented sleep were at risk of developing insomnia frequently in stroke patients.[4]

In this study, the degree of insomnia severity as measured by the Insomnia Severity Index (ISI) score found 3 subjects (10%) did not lead to insomnia, 15 subjects (50%) with mild insomnia ISI scores, 12 subjects (40%) with insomnia ISI scores. Moderate. In a study by Leppavuori et al. in 2002, it was observed that 56% of all stroke patients complained of insomnia. 18% of insomnia occurs de novo after stroke.[1,5] In the 2003 study of Heikki et al., it was shown that insomnia complaints in stroke patients often occur in the acute stage and the early recovery period.[6]

Insomnia in stroke that occurs can be caused by internal factors and factors. External. Internal factors are due to thalamic lesions, brainstem lesions (thalamo-mesencephalic, pontomesencephalic, and pontine tegmentum / pons paramedian) and the left dorsomedial prefrontal cortex. These lesions cause a sleep-wake cycle disorder, which results in sleep disturbances in the form of insomnia, nighttime agitation, and daytime hypersonnia.[1,7,8] Insomnia in stroke caused by external factors including environmental factors (such as light or noise during inpatient care or at home, when monitoring, when taking medications) and comorbidities / complications of the disease itself, such as depression, breathing problems during sleep, pain, or physical disorders, heart failure, lung disease, Sleep Disorder Behavior (SDB), the influence of drugs, infection, fever, lack of activity. In one study, the use of preexisting psychotropic drugs, anxiety, dementia and insomnia and the severity of stroke would be risk factors for insomnia in stroke.[1,7,9] Metabolic factors are widely thought to influence insomnia through dysregulation of the Pituitary Hypothalamic Axis, increased sympathetic activity, systemic inflammation and endothelial dysfunction, where these metabolic factors will also increase the risk of cardiovascular disease and the metabolic disease itself. The research of Ding Zhou et al., 2020, which examined 830 subjects with middle age (50-64 years), found 12.4% insomnia in the population and insomnia found with metabolic syndrome in 17.6% of the population more than non-metabolic patients. Subjects with sleep time less than 6 hours were found in 10.6% of the population, where 13.5% were found with more metabolic syndromes than non-metabolic syndromes.[10] In several other meta-analyses, it was found that subjects with poor sleep quality were significantly associated with increased blood pressure, abnormal lipid profiles, impaired dietary intake and impaired blood sugar control are all associated with metabolic syndrome. In this ding zhou study, it was found that insomnia was associated with high triglycerides and low HDL levels, which indicated dyslipidemia which was a characteristic sign of insulin resistance that would affect stress, cortisol, insomnia and other neuroendocrine disorders.[10]

In this study, 10 subjects (33.3%) had normal serum BDNF levels and 20 (66.7%) high serum BDNF levels. In this study, there were no subjects with low BDNF levels. In the research of Aline et al. in 2018, there was no significant difference in BDNF levels on the first, third and 8-10 days of ischemic stroke onset, which depends on the amount of brain damage that occurs during ischemic stroke.[11] Conducted by Yannick Bejot et al. in 2011, observed serum BDNF levels in rats carried out at 4 hours, 24 hours and the 8th day of stroke onset showed an increase in serum BDNF.[12] In this study, there were no subjects with low BDNF levels, possibly due to sampling. Blood is still in the acute phase, namely the 5-7th day of stroke onset, so it is estimated that there will be no low BDNF levels because, in this phase, the BDNF levels in the study subjects increase for neuroplasticity processes of nerves injured due to ischemic stroke.

In this study, the location of ischemic stroke was divided into 4 locations, namely cortical, subcortical, subcortical, accompanied by thalamus and brain stem. Cortical locations include the cerebral cortex. The subcortical location is the corona radiata, the internal capsule. Subcortical location accompanied by the thalamus and finally the location of the brain stem. From this study, it was found 2 locations, namely subcortical and subcortical, with lesions in the thalamus. In this study, the location of ischemic stroke lesions in 30 subjects of this study found 19 subjects (63.3%) subcortical lesions and 11 thalamus subcortical lesions (36.7%). In Chen et al.’s 2010 study, it was found that subjects with insomnia had lesions in the frontal lobe (12.4%), temporal lobe (8.1%), subcortical parietal lobe (10.2%) (29.0%), thalamus (8.1%), brainstem (23%).[13] Insomnia in stroke is due to lesions in the thalamic, brainstem(thalamo-mesencephalic, pontomesencephallic, and pontine tegmentum / pons paramedian) and left dorsomedial prefrontal cortex. These lesions cause sleep inversion - the wake cycle so that it will affect the stages of the sleep process, either the NREM stage or the REM stage or even both so that it will disrupt sleep patterns that will cause sleep disorders including insomnia.[1,7,8]

In this study, subjects with depressive symptoms with the Beck Depression Inventory (BDI) score found 3 subjects (10%) with BDI scores showing mild mood disorders and 27 subjects
### Table 3: Relationship between serum BDNF levels and motor clinical outcome

| Variable | Barthel Index | P      |
|----------|---------------|--------|
|          | Ringan | Sedang | Berat | Total |        |
| BDNF     |         |        |       |       |        |
| Normal   | 0      | 1      | 5     | 4     | € 0.183 |
| High     | 1      | 4      | 11    | 4     |        |

Note: *Significant (p < 0.05); € Kruskal Wallis

### Table 4: Relationship between age and motor clinical outcome

| Variable | Barthel Index | P      |
|----------|---------------|--------|
|          | Mild | Moderate | Severe | Total |        |
| Age      |       |         |       |       |        |
| ≤ 60 years old | 1   | 5      | 7     | 3     | £ 0.035 |
| > 60 years old  | 0   | 0      | 9     | 5     |        |

Note: *Significant (p<0.05); £ Mann Whitney

### Table 5: Relationship between gender and motor clinical outcome

| Variable | Barthel Index | P      |
|----------|---------------|--------|
|          | Mild | Moderate | Severe | Total |        |
| Gender   |       |         |       |       |        |
| Male     | 1    | 3      | 7     | 2     | £ 0.117 |
| Female   | 0    | 2      | 9     | 6     |        |

Note: *Significant (p<0.05); £ Mann Whitney
### Table 6: Relationship of stroke lesion location and motor clinical outcome

| Variable                        | Barthel Index |    |    | P  |
|---------------------------------|---------------|----|----|----|
|                                 | Mild | Moderate | Severe | Total |
| Stroke location                 |      |          |        |       |
| Subkortikal                     | 1    | 5        | 11     | 2     |
| Subkortikal/thalamus            | 0    | 0        | 5      | 6     |

Note: *Significant (p < 0.05); € Kruskal Wallis

### Table 7: Relationship of stroke severity with motor clinical outcome

| Variable | Barthel Index |    |    | P  |
|----------|---------------|----|----|----|
|          | Mild | Moderate | Severe | Total |
| NIHSS    |      |          |        |       |
| Mild     | 1    | 5        | 16     | 3     |
| Moderate | 0    | 0        | 0      | 5     |

Note: *Significant (p < 0.05); € Kruskal Wallis

### Table 8: Relationship of depression with motor clinical outcomes

| Variable | Barthel Index |    |    | P  |
|----------|---------------|----|----|----|
|          | Mild | Moderate | Severe | Total |
| BDI      |      |          |        |       |
| Normal   | 1    | 5        | 13     | 8     |
| Mild mood disorder | 0 | 0 | 3 | 0 |

Note: *Significant (p < 0.05); € Kruskal Wallis
In this study, there was no statistically significant relationship between the degree of insomnia severity (Insomnia Severity Index / ISI score) and motor clinical outcome (Barthel Index score and Short Fugl Mayer Assessment) with p-values 0.936 and 0.116, respectively. In Glozier et al.’s study in 2017, there was a higher level of disability (measured by WHODASI II score) in stroke subjects with insomnia (mean score 31.2 [SD 21.4]) than those without insomnia (21.7 [SD 19.4]).[16] Many factors contribute, including heterogeneity of stroke location and size, and sleep-wake characteristics before stroke. Insomnia may not yet affect clinical motor outcomes because insomnia occurs in the acute phase of stroke (5–7 days of onset). Differences in clinical outcomes occurred due to differences in stroke severity and location of stroke lesions.

In this study, there was no significant relationship between serum BDNF levels and motor clinical outcomes (Barthel Index score and short Fugl Mayer Assessment score), with p values 0.183 and 0.819, respectively. In the research of Alme et al. in 2019, it was found that there was a correlation between serum BDNF levels and the clinical outcome of subjects with ischemic stroke on day 3 of stroke onset.[17] The clinical outcome measures were the NIHSS score, Rankin scale and GSS score (swallow). In another study, which was conducted by Luo et al. In 2014-2015, serum BDNF levels were statistically but not clinically related to clinical motor output with a value of p = 0.004.[16] In this study, BDNF levels tended to be normal and high with no difference in clinical motor output. It is possible that during the acute phase BDNF levels will be normal or high at either clinical outcome or poor clinical outcome in response to the neuroplasticity of injured nerves after stroke.

In this study, the relationship between a number of factors that influence the clinical motor output of patients with ischemic stroke was analyzed. These factors include age, gender, location of the stroke lesion, stroke severity and depression.

The relationship between age and clinical motor output (Barthel Index score and short Fugl Mayer Assessment score) has a significant relationship with the Barthel Index score with a value of p = 0.035, with age influencing the Barthel Index of 0.403. Meanwhile, the Short Fugl Mayer Assessment score did not show a statistically significant relationship with a p value = 0.188. In the study of Stephen Bagg et al. In 2002, there was a statistically significant relationship between age and motor clinical outcome of ischemic stroke patients (P <0.001), this increase in age with the poor clinical outcome may be explained by the presence of additional disabilities and the presence of comorbid accompanying diseases the stroke state. In addition, it is also exacerbated by the absence of family support.[19]

The relationship between gender and clinical motor output (Barthel Index score and short Fugl Mayer Assessment score), obtained a significant relationship between gender and the Short Fugl Mayer Assessment score with p = 0.023, with an effect of -0.460. Meanwhile, gender with the Barthel Index score did not show a statistically significant relationship with p value = 0.117. In this study women appeared to have a worse clinical outcome. In a metaanalysis conducted by Gall et al. In 2011, 2 studies showed that women had a worse clinical outcome of stroke, such as in a study by Feigin et al. In 2010 which reported that women were more limited than men in mobility and physical independence. In another study, Lo et al. In 2008 reported that although there was no difference in overall disability, women had greater physical independence disabilities than men.[20] But in another study, namely Pu et al.’s 2017 study on differences in clinical outcomes by type, There was no significant difference between sex in patients with intracranial atherosclerosis in post-stroke clinical outcomes between women and men.[21]

The relationship between stroke lesion location and motor clinical outcome (Barthel Index score and short Fugl Mayer Assessment score) showed a significant relationship with the Barthel Index score and the Short Fugl Mayer Assessment score with p-values 0.004 and 0.002, respectively. Where the location of the stroke lesion has more influence on the Barthel Index of 0.518 compared to the Short Fugl Mayer Assessment (-0.581). In
Mahmoud’s study in 2009, there was a significant relationship between the location of the stroke lesion and the clinical motor output (Barthel Index score) where the inner stroke location (internal capsule or thalamus) would provide better clinical motor output compared to the location of subcortical stroke lesions. However, there are contradictions in some other studies that suggest otherwise.[22]

The relationship between stroke severity as assessed by the NIHSS and clinical motor output (Barthel Index score and Short Fugl Mayer Assessment score) showed a significant relationship with the Barthel Index score and the Short Fugl Mayer Assessment score with p-values 0.001 and 0.001, respectively. Where the NIHSS is more influential on the Barthel Index of 0.575 compared to the Short Fugl Mayer Assessment (-0.748), this is in accordance with the research of Abdul Rahim et al. In 2015, a study conducted on 6843 patients who underwent thrombolysis found a significant relationship between NIHSS and functional outcomes and mortality rates so that the NIHSS profile in stroke patients could be used as information to determine the patient’s prognosis in the future.[23]

The relationship between depression and clinical motor output (Barthel Index score and Short Fugl Mayer Assessment score) was not significant with p-values 0.819 and 0.802, respectively. In contrast to what was found in the Yoshida study in 2019, it showed a significant correlation between the presence of depressive symptoms and motor clinical outcomes in 135 ischemic stroke patients. The same thing was also shown in the research of Hermann et al. In 1998, which also showed the same thing.[24]

In this study, 3 subjects experienced mild mood disorders, and the others were normal. These mood disorders may not have much of an impact on clinical motor output in the acute phase. The presence of depression and clinical outcomes of good/bad motor skills is likely more due to the severity of the stroke and the location of the stroke lesions. In contrast, depression in this stroke can worsen the improvement of clinical motor output in the future.

Then an analysis of the factors that were significantly related to the clinical motor output of ischemic stroke was carried out together, showing that age and NIHSS influenced the Barthel Index score of 48.5%, and NIHSS was also the dominant factor affecting the Fugl Mayer Assessment score. 62.2%. The same thing in Abdul Rahim et al’s study in 2015, which showed that the severity of stroke as measured by the NIHSS score is a factor that can be used to predict the prognosis of clinical outcome in ischemic stroke patients, in this case including the clinical motor output of ischemic stroke patients.[23]

**Conclusion**

There is no relationship between insomnia severity and motor clinical outcome in ischemic stroke patients. There is no relationship between serum BDNF levels and motor clinical outcomes in ischemic stroke patients. It was found that the relationship between other factors, namely age, gender, location of stroke lesions and NIHSS with motor clinical outcome of ischemic stroke patients, where age and NIHSS were the most influencing factors on the clinical outcome of ischemic stroke patients.

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**Conflict of interest**

There are no conflicts of interest to declare by any of the authors of this study.

**References**

1. Ferre A, Ribó M, Romero O, Sampol G, Molina CA. Strokes and their relationship with sleep and sleep disorders. Neurol (English Ed. 2013;28(2):103–18.

2. Polyakova M, Schlögl H, Sacher J, Schmidt-kassow M. Stability of BDNF in Human Samples Stored Up to 6 Months and Correlations of Serum and EDTA-Plasma Concentrations. Int J Mol Sci. 2017;1–11.

3. Kamel NS, Gammack JK. Insomnia in the Elderly: Cause, Approach, and Treatment. Am J Med. 2006;463–9.

4. Rocha PC Da. Predictive factors of subjective sleep quality and insomnia complaint in patients with stroke: implications for clinical practice. An Acad Bras Cienc. 2013;85:1197–206.

5. Jennum P, Cano JS, Bassetti C, Clarenbach P, Mathis J, Poirier R, et al. Sleep disorders in neurodegenerative disorders and stroke. In: European Handbook of Neurological Management. Second. Blackwell Publishing Ltd; 2011. p. 529–43.

6. Palomaki H. Complaints of Poststroke Insomnia and Its Treatment with Mianserine. Karger. 2003;56–62.

7. Kim W, Jung H, Choi H, Kim E, Lee S, Ko S, et al. PT NU. J Psychosom Res [Internet]. 2017; Available from: http://dx.doi.org/10.1016/j.jpsychores.2017.02.008

8. Hermann DM, Bassetti CL. Role of sleep-disordered breathing and sleep-wake disturbances for stroke and stroke recovery. AAN. 2016;0:1–8.

9. Bassetti CL. Sleep and Stroke. Semin Neurol. 2005;25(1):1–28.

10. Zou D, Wennman H, Hedner J, Ekblom Ö, Drotz O, Arvidsson D, et al. Insomnia is associated with metabolic syndrome in a middle-aged population: the SCAPIS pilot cohort. Eur J Prev Cardiol. 2020;8–10.

11. Mourão AM, Vicente LCC, Abreu MNS, Vale Sant’Anna R, Vieira ELM, de Souza LC, et al. Plasma Levels of Brain-Derived Neurotrophic Factor are Associated with Prognosis in the Acute Phase of Ischemic Stroke. J Stroke Cerebrovasc Dis. 2019;28(3):735–40.

12. Bejot Y, Prigent-Tessier A, Cachia C, Giroud M, Mossiat C, Bertrand N, et al. Time-dependent contribution of non neuronal cells to BDNF production after ischemic stroke in rats. Neurochem Int. 2011;58(1):102–11.

13. Chen YK, Lu JY, Mok VCT, Ungvari GS, Chu WCW, Wong KS, et al. Clinical and radiologic correlates of insomnia symptoms in ischemic stroke patients. Int J Geriatr Psychiatry. 2011;26(5):451–7.

14. Rețnăningsih. Serum Serotonin , A Good Indicator of Insomnia and Depression In Elderly. J Med Biomed Appl Sci. 2019;7(5):230–40.
15. Villa RF, Ferrari F, Moretti A. Post-stroke depression: Mechanisms and pharmacological treatment. Pharmacol Ther. 2017;0–1.

16. Glozier N, Moullaali TJ, Sivertsen B, Kim D, Mead G, Jan S, et al. The Course and Impact of Poststroke Insomnia in Stroke Survivors Aged 18 to 65 Years: Results from the Psychosocial Outcomes in StrokE (POISE) Study. Cerebrovasc Dis Extra. 2017;7(1):9–20.

17. Aline, D'Mour, Mansueto D, Vicente C, Abreu NS, Romeu, D Anna VS, Vieira LM, Leonardo DM. Plasma Levels of Brain-Derived Neurotrophic Factor are Associated with Prognosis in the Acute Phase of Ischemic Stroke D103X Mery D107X Cruz de Souza, D1 0X PhD, o. Natl Stroke Assoc. 2018;1–6.

18. Luo W, Liu T, Li S, Wen H, Zhou F, Zafonte R, et al. The Serum BDNF Level Offers Minimum Predictive Value for Motor Function Recovery After Stroke. Transl Stroke Res. 2019;10(4):342–51.

19. Bagg S, Pombo AP, Hopman W. Effect of Age on Functional Outcome After Stroke Rehabilitation. Am Hear Assoc. 2002;33:179–85.

20. Gall SL, Tran PL, Martin K, Blizzard L, Srikanth V. Sex differences in long-term outcomes after stroke: Functional outcomes, handicap, and quality of life. Stroke. 2012;43(7):1982–7.

21. Pu Y. Sex Differences Do Not Exist in Outcomes among Stroke Patients with Intracranial Atherosclerosis in China: Subgroup Analysis from the Chinese Intracranial Atherosclerosis Study. Neuroepidemiology. 2017;10050:48–54.

22. Mahmoud, Ahmed Saadah EN, Mohammed Saadah L, Mustafa Trebinjac S. Acute ischemic stroke: Relationship of brain lesion location & functional outcome. Disabil Rehabil. 2009;31(18):1501–6.

23. Abdul-rahim AH, Fulton RL, Sucharew H, Kleindorfer D, Khatri P, Broderick JP, et al. National Institutes of Health Stroke Scale Item Profiles as. AHA/ASA. 2015;2779–85.

24. Yoshida HM, Lima FO, Barreira J, Appenzeller S, Fernandes PT. Is there a correlation between depressive symptoms and motor skills in post-stroke patients? Arq Neuropsiquiatr. 2019;77(3):155–60.