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研究名稱：腦幹與大腦半球梗塞對情緒狀態之影響：
長期追蹤研究

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Effects of Brainstem and Hemispheric Infarction on Emotional Status: A Longitudinal Study (II)

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摘要:

本研究主要的目的是探討腦幹中風患者的情緒狀態。總共 6 組受試,其中 5 組中風患者與 1 組正常受試參加本研究。5 組中風患者包括了左與右大腦皮質中風患者、左與右腦皮質下中風患者、以及腦幹中風患者。各組受試在人口學變項上, 年齡、教育程度、與性別上相互配對。每位受試接受一組測量情緒功能之測驗。從受試、受試重要照顧者, 以及主試者三方面所得到有關患者情緒功能之資料的分析, 結果顯示腦幹患者明顯呈現憂鬱等與身體化的問題。除此以外, 患者重要照顧者觀察到患者有強迫性思考與行爲, 以及焦慮症狀。儘管透過有限患者之追蹤研究發現其情緒功能的改變似乎具持續的特性, 不過由於樣本數的限制, 進一步採取大樣本來探討與驗證本研究關心的問題以及目前的發現有其必要性。

關鍵字：憂鬱、 情緒狀態、 腦幹中風

ABSTRACT

The aim of the study was to examine the emotional status of the patients with brainstem stroke. An emotional function test battery was administered to five groups of the adult patients with cerebral hemispheric, subcortical, and brainstem strokes, and one group of normal control adults. Members of these six groups were matched in terms of age, educational level, and sex. Comparing the test results derived from three sources including patients, patients' significant informants, and the examiner's ratings revealed that depression was remarkably evident in the patients with brainstem stroke. Somatization was also reported by both of the patients with brainstem stroke and their significant informants. Obsessive-compulsive problem and anxiety symptom were only noticed by the significant informants of the patients with brainstem stroke while psychotic problems were reported by the patients with brainstem stroke. Since our findings were based on the limited data, further investigation is necessary. However, there was no remarkable evidence of emotional disturbances in otherwise stroke patients. The emotional disturbances evident in the patients with brainstem stroke seemed to be persistent based on the limited follow-up data. Further study on a large scale, thus, is mandatory.

Key words: Depression, Emotional Status, Brainstem Stroke

Stroke is a common disease of central nervous system. In Taiwan this disease has been the second leading cause of death for all ages (Huang, Chiang & Lee, 1997). Physical disability, and a variety of cognitive impairments, such as aphasia, amnesia, apraxia, agnosia, aprosodia, dysarthria, attentional problem, neglect, and visuospatial disorientation are frequent consequences of cerebral hemispheric stroke (Heilman & Valenstein, 1993; Lezak, 1995; Walsh, 1994). In addition to these deficits, emotional changes are also a common sequela (Hosking, Marsh & Friedman, 1996). The disturbances include depression, emotional lability, apathy, irritability, agoraphobia, social withdrawal, self-neglect, and anxiety (House, Dennis, Mogridge, Warlow, Hawton & Jones, 1991;Morris, Robinson, & Raphael, 1993; Nelson, Cicchetti, Satz, Sowa & Mitrushina, 1994).

The implied clinical and economic impacts of these emotional disturbances on the stroke patients are multifold (Spencer, Tompkins & Schultz, 1997). First, the patients with emotional problems undertake more negative thinking and stress negative results (Ingram, Kendall, Smith, Donnell & Ronan, 1987). Consequently, sundry cognitive function changes in these patients might be exaggerated though cognitive impairments tend to co-occur with emotional problems (Seibert & Ellis, 1991; Speedie et al., 1990). Secondly, sundry cognitive function changes, such as depression can be a vital hindrance to rehabilitation (Reynolds, 1992). Finally, the quality of life of the patients

and their caregivers might be changed tensely by these emotional sequelae (Spencer et al.,1997). Therefore, in order to offer the patients the supreme opportunity for treatment profits, a great care for their emotional disturbances is merited.

Depression has generally been considered to be the most common emotional consequence of cerebral hemispheric stroke (Nelson, 1994; Price, 1990). The prevalence rate of poststroke depression, however, varies extensively from less than 25% up to more than 60% (Astrom, Adolfsson & Asplund, 1993). Methodological discrepancies mainly including the selection of patients, the time of evaluation since the stroke and the duration of the assessment period, as well as diverse diagnostic criteria and psychopathological measures have a significant contribution to this variation (Astrom et al., 1993; Hosking et al., 1996). Furthermore, the proportion of poststroke depression does not keep steady throughout the poststroke period (Astrom et al., 1993). The manifestations of otherwise emotional problems, such as agoraphobia, social withdrawal, anxiety, mania, catastrophic reactions, and apathy recently have also been observed in the patients following cerebral hemispheric stroke (e.g., House et al., 1991; Morris et al., 1993; Robinson & Starkstein, 1997). The issue regarding whether or not depression is the most frequent emotional result of cerebral hemispheric stroke, thus, becomes controversial and awaits further investigation.

Emotional abnormalities are also evident in the patients with subcortical stroke

though the literature in this area is less extensive than that of cerebral hemispheric stroke. Generally, depression is significantly related to lesions of left basal ganglia (Starkstein, Robinson, Berthier & Price, 1988). However, mania, bipolar affective disorders, and psychosis are highly associated with right subcortical (basal ganglia or thalamus) lesions (Robinson et al., 1988; Starkstein et al., 1991; Starkstein, Robinson & Berthier, 1992; Trimle & Cummings, 1981). Anxiety and apathy have a high frequency of lesions involving the posterior limb of the internal capsule (Robinson & Starkstein, 1997; Starkstein et al., 1993a) while catastrophic reactions are notably related to anterior subcortical lesions (Starkstein et al., 1993b).

The dysfunction of the biogenic amine system has been hypothesized to be one of the mechanisms that may play an important role in the cause of depression (Beatty, 1995; Conn, 1995). Both noradrenergic and serotonergic cell bodies are located in the locus coeruleus and raphe nucleus of the brainstem, and send ascending projections to the frontal cortex through the median forebrain bundle. The ascending pathways then arc posteriorly and travel longitudinally through the deep layers of the cortex, arborizing and sending terminal projections into the superficial cortical layer (Morrison, Molliver, & Grzanna, 1979). On the basis of neuroanatomical evidences and clinical findings, Robinson and his colleagues (1984) proposed that poststroke depression might be the result of severe depletions of norepinephrine and/or serotonin

due to lesions in either the frontal cortex or basal ganglia. If this is the case, depressive symptoms should also be evident in the patients with brainstem stroke involving the rostral pons and caudal mesencephalon which are sites for the serotonergic raphe nucleus and the noradrenergic locus coeruleus (Lang, 1991).

The literature of emotional disturbances in the patients following brainstem stroke, however, is very limited. Trimble and Cumminings (1981) reported that manifestations of suicidal ideation, unstable mood, euphoria, depressive feelings, and emotional lability were noted in two patients with brainstem stroke. However, the definite lesioned areas of both patients determined by the CT scan were located in the thalamus rather than the brainstem. Starkstein, Robinson, Berthier and Price (1988) found that patients with posterior circulation lesions involving the brainstem and/or cerebellum had a remarkably low frequency of depression, and a significantly short duration of depressive symptoms. Unfortunately, since no otherwise psychopathological measures, with the exception of depression and anxiety tests, were used in their study, the issue of whether or not other emotional sequelae might also be manifested in patients following brainstem stroke remains unknown.

The report of emotional disturbances in poststroke patients in Taiwan is lacking. In order to explore the above unclear issue, and to document the literature in Taiwan, we design this two-year longitudinal study. In our study, 6 groups of the participants,

that is, 5 patient cohorts and 1 group of normal controls will be included. 5 patient groups consist of 1 group of patients following brainstem stroke, 1 with left and 1 with right cortical stroke, and 1 with left and 1 with right basal ganglion stroke. The first-year study goal is to complete 1- and 6-monthss poststroke assessment of emotional function; the second-year study goal is to complete 1-year poststroke evaluation of emotional status. The specific aims of the study, thus, are to examine the following questions: 1) Is there an impairment of emotional status in patients with brainstem stroke? 2) If so, does the deficit only involve depression, as Starkstein et al's observation (1988), or also include otherwise emotional function tested? 3) If depression or/and otherwise emotional changes does/or occur in the patients with brainstem stroke, is/are the deficit(s) transient or persistent?

METHOD

Participants. Because of a very high dropout rate of the participants, 6 groups with only 74 volunteer adults were included in the study. There were 56 stroke patients including 16 with brainstem (Group 1), 5 with left cortical (Group 2), 7 with left subcoritcal (Group 3), 11 with right cortical (Group 4), and 17 with right subcortical (Group 5) lesions, and 18 normal control subjects (Group 6). The lesion locations were verified by MRI, and all of these patients were victims of the first stroke in the absence of any other CNS, and systemic disease (e.g., diabetes and hypertension with

drug treatment), and psychiatric history. The patients were also free of dementia, confusional state, anosognosia, and moderate or severe comprehension deficits.

The mean differences in age were not significantly different, with the exception of Groups 4 and 5 ($F_{5,68}$=4.85, p<.05) and Groups 4 and 6($F_{5,68}$=4.85, p<.05). That is, the mean age of the patients with right cortical stroke was significantly younger than that of the patients with right subcortical stroke and of the normal controls. The mean differences in education were also not significantly different. All participants were right-handed in which hand dominance was ascertained by the history that the participant has always used his/her right hand preferentially for doing skillful activities, such as writing and holding chopsticks.

Tests and procedure. After giving informed consent, each participant will receive a series of neuropsychological tests. They included cognitive function and emotional status measures. The Temporal Orientation Test (Benton, Hamsher, Varney & Spreen, 1983), the Orientation to Personal Information and Place (Hamsher, 1983), Object Naming Test (Spreen & Benton, 1969), and Aural Comprehension (Benton & Hamsher, 1978) were used to rule out the participants suspectable for dementia, moderately or severely receptive aphasia, confusional state, and anosognosia. The test battery of emotional status consisted of Symptom Checklist-90-R (Derogatis, 1977), Beck Depression Inventory (Beck, 1987), Neurobehavioral Rating Scale (Levin et al.,

1987), and a semi-structured Standard Neurobehavioral Interview Inventory (Hamsher, 1983). In addition, Canadian Neurological Scale and Barthel Index (Mahoney & Barthel, 1965) were also used to measure the severity of the patient's physical disability, and evaluate the degree of his/her independence in basic activities of daily living respectively. The assessment was administered in an examining room between 11 AM and 2PM to minimize any possible effects of diurnal mood variation on interview responses, as Starkstein, Cohen, Fedoroff, Parikh, Price, and Robinson (1990). All measures were Chinese versions.

In order to obtain reliable and valid ratings of the patient's emotional status, we also asked the participant's significant others, particularly family caregivers of the patient, to rate the emotional status of the participant. All of the significant informants of the patients will be free of emotional disturbances, dementia, and psychiatric history. For the present, our available patients only received the first examination, that is, they were examined at the poststroke periord of 1 month while a few (2 patients) received the second examination, that is, 6 months after the onset of stroke.

RESULTS

One-way analysis of variance (ANOVA) was used to analyze the score differences of the subject groups on the non-emotional function measures and Beck Depression Inventory. Since the measures of emotional status are ordinal scales, Kruskal-Wallis

one-way analysis of variance by Ranks (Marascuili and McSweeney, 1977) was used to determine whether the performance of the patient groups on the SCL-90-R was different from that of the normal control participants. On the Beck Depression Inventory, the patients with brainstem stroke had the highest mean rank followed by the patients with left subcortical stroke, the patients with right subcortical stroke, the patients with right cortical stroke, the patients with left cortical stroke, and the normal controls. The mean differences among the participant groups did reach a statistically significant level ($F_{5,68}$=5.07, $p<.001$). Scheffe's post-hoc pairwise comparisons revealed that only the differences between patients with brainstem stroke and the controls reached a statistical significance ($p<.001$).

Likewise, on the SCL-90-R, the highest mean rank to the lowest on the Somatization subscale was the patients with brainstem stroke, the patients with left subcortical stroke, the patients with right cortical stroke, the patients with right subcortical stroke, the normal controls, and the patients with left cortical stroke. On the Obsessive-Compulsive subscale, the patients with brainstem stroke had the highest mean rank followed by the patients with right cortical and subcortical stroke, the patients with left subcortical and cortical stroke, and the normal controls. On the Interpersonal Sensitivity subscale, the highest mean rank to the lowest was the patients with brainstem stroke, with left subcortical stroke, with right cortical and

subcortical stroke, the normal controls, and the patients with left cortical stroke. The patients with brainstem stroke had the highest mean rank on the Depression subscale, followed by the patients with right and left subcortical stroke, with right cortical stroke, left cortical stroke, and the normal controls,. On the Anxiety subscale, the patients with brainstem stroke had the highest mean rank followed by the patients with right cortical stroke, with right and left subcortical stroke, the normal controls, and with left cortical stroke. The highest mean rank on the Hostility subscale was the patients with brainstem stroke, followed by the patients with left and right subcortical stroke, the normal controls, and the patients with right and left cortical stroke. On the Phobia subscale, the highest mean rank to the lowest was the patients with brainstem stroke, with right cortical stroke, with left and right subcortical stroke, the normal controls, and the patients with left cortical stroke. The highest mean rank to the lowest on the Paranoid Ideation subscale was the patients with right cortical stroke followed by the patients with brainstem stroke, the normal controls, the patients with left and right subcoritcal stroke, and with left cortical stroke. On the psychoticism subcalse, the highest mean rank score was the patients with brainstem stroke, followed by the patients with right cortical stroke, with left subcortical stroke, the normal controls, the patients with right subcortical stroke, and the patients with left cortical stroke.

The differences of the mean rank over these subcales, however, only involved

Somatization (X^2=19.20, df = 5, p<.002), Obsessive-Compulsive Symptom (X^2=12.52, df=.05, p<.02), Depression (X^2=13.95, df=5, p<.02), Paranoid Ideation (X^2=14.26, df=5, p< .02), Psychoticism (X^2=22.28, df =5, p<.001)), and Global (X^2=13.99, df =5, p<.02) reached a statistically significant level. Nemenyi's post-hoc pairwise contrasts were subsequently performed and revealed that the ratings of patients with brainstem stroke on the somatization and depression subscales were significantly different from the controls. On the Psychoticism subscale, the rating differences between patients with brainstem and with right subcortical stroke were significnatly different.

The highest to the lowest mean scores of the significant informants of the participants on the BDI were the patients with brainstem stroke, followed by the patients with right and left subcortical stroke, the patients with right and left cortical stroke, and the normal controls. The mean differences, analyzed by one-way ANOVA revealed, did reach a statistical significant level ($F_{5,68}$=3.75, p<.005). Scheffe's post-hoc pairwise comparisons were subsequently performed, and revealed that only the differences between patients with brainstem stroke and the controls reached a statistically significant level (p<.007).

The ratings of the significant informants of the participants on the subscales of the SCL-90-R was as followed. On the Somatization subscale, the patients with brainstem stroke had the highest mean rank, followed by the patients with left subcortical stroke,

with right cortical and subcortical stroke, the patients with left cortical stroke, and the normal controls. The highest to the lowest mean ranks on the Obsessive-Compulsive subscale were the patients with brainstem stroke, followed by the patients with left and right cortical stroke, with right subcoritcal and left subcortical stroke, and the normal controls. On the Interpersonal Sensitivity subscale, the patients with left subcortical stroke, followed by brainstem stroke, with right cortical and subcortical stroke, the normal controls, and the patients with left cortical stroke. The highest to the lowest mean ranks on the Depression subscale were the patients with the patients with brainstem, followed by the patients with right and left subcortical stroke, with left and right cortical stroke, and the normal controls. On the Anxiety subscale, the patients with brainstem stroke had the highest mean rank, followed by with left cortical stroke, the patients with right subcortical stroke, with right cortical and left subcortical stroke, and the normal controls. On the Hostility subscale, the patients with brainstem stroke had the highest mean rank, followed by the patients with right cortical and left subcortical stroke, with right subcortical and left crotical stroke, and the normal controls. The highest to the lowest mean ranks on the Phobia subcale were the patients with brainstem stroke, followed by patients with right subcortical and left cortical stroke, with right cortical and left subcortical stroke, and the normal controls. On the Paranoid Ideation subscale, the patients with brainstem stroke had the highest

mean rank, followed by the patients with left subcortical and right cortical stroke, with right subcortical stroke, and the normal controls. The highest mean rank on the Psychoticism subscale was the patients with brainstem stroke, followed by the patients with left subcortical and right cortical stroke, with right subcortical stroke, with left cortical stroke, and the normal controls.

The data analysis by Kruskall-Wallis one-way ANOVA revealed that the mean rank differences of Somatization (X^2= 17.22, df=5, p<.005), Obsessive-Compulsive (X^2=15.73, df=5, p<.008), Depression (X^2=18..33, df=5, p<.003), Anxiety (X^2=13.97, df=5, p<.02), Paranoid Ideation (X^2=11.66, df=5, p<.04), and Psychoticism (X^2=11.62, df=5, p<.04) subscales among these subject groups reached a statistically significant level. Subsequent Nemenyi's post-hoc pairwise contrasts revealed that the ranking differences between patients with brainstem stroke and the controls on the Somatization, Depression, Obsessive-Compulsive, and Anxiety subscales were statistically significant.

In order to determine whether or not the ratings of the participants and their significant informants on the BDI and SCL-90-R were different. On the BDI, the discrepant score between the participant and his/her significant informant for each subject group was calculated, and then a match-paired t test was used to analyze the data. The result revealed that the differences did not reach a statistically significant

level. For each subject group, most of the ranking differences between the participant and his/her significant informant, with the exception of patients with right cortical and subcortical, and with left subcortical stroke, on each of the subscales of the SCL-90-R were not statistically significant. For patients with right cortical stroke, the rank differences between the patients and their significant informants on the Hostility subscale was statistically significant ($p<.008$). For patients with left subcortial stroke, the rank differences between the patients and their significant informants on the Paranoid Ideation subscale were statistically significant ($p<.04$). For patients with right subcortical stroke, the rank differences between the patients and their significant informants on the Paranoid Ideation ($p<.03$) and Psychoticism ($p<.03$) subscales were statistically significant.

On the Neurobehavioral Rating Scale, most of the rating scores of patients with brainstem stroke were higher than that of other patients and the normal controls. However, only the ranking differences among these subject groups on the Memory Deficits ($X^2=14.53$, $df=5$, $p<.02$), Depression ($X^2=17.53$, $df=5$, $p<.005$), Motor Retardation ($X^2=13.01$, $df=5$, $p<.03$), and Poor Planning scales ($X^2=15.18$, $df=5$, $p<.02$) were statistically significant. Nemenyi's posthoc pairwise contrasts were performed and revealed that the differences were not statistically significant.

DISCUSSION

Is there an impairment of emotional status in the patients with brainstem stroke? Because of the high dropout of the patients, our results based on the limited data did reveal that the patients with brainstem stroke had remarkably emotional impairments compared with their normal counterparts. Starkstein and his co-workers' findings (1988) in which they noted the patients with brainstem stroke having a significant low frequency of emotional changes. Our results seemed to be inconsistent with their findings. The discrepancy between Starkstein and his Colleagues' and our findigns might be attributed to different emotional measures and the sample size of patients. In Starkstein and his co-workers' study, only depression rating scale was used in measure patients' emotional status while in the present study we employed a comprehensive test battery of emotional function. Furthermore, emotional changes were not only determined by our patients' self report, but also included the ratings of patients' significant informants and of the examiner. However, in Starkstein and his colleagues' study, depression was only determined by the examiner's ratings, which might have a bias of sampling the patients' emotional status. Since our results were based on a small sample size of subjects, further investigation is merited.

If so, does the deficit only involve depression, as Starkstein and his colleagues' observation (1988), or also include otherwise emotional function tested? Our patients with brainstem stroke not only had depression, but also had other emotional

changes including somotization. In addition, otherwise emotional problems involving obsessive-compulsive problems, and anxiety symptom were also noticed by our patients' significant informants. These emotional changes seemed to be persistent despite that the follow-up results were based on the small sample size of patients.

Most of the literature showed that depression was major emotional changes evident in the patients with cerebral hemispheric lesions (e.g., Nelson, 1994; Price, 1990). Our findings based on the patients with either the left or right cerebral hemispheric stroke, however, were not consistent with these earlier observations. Again, the small sample size of our study might account for this disparity. Depression has often been seen in the patients with lesions of the subcortical regions, particularly the areas of left basal ganglia (Starkstein Robinson, Berthier & Price, 1988). Generally, our results did find patients with subcortical stroke with a tendency of having a depressed mood compared with their normal counterparts. However, the results were not statistically significant. Moreover, we also did not note our patients having any remarkably asymmetric manifestation between the two subcortical hemispheric strokes in terms of this specific aspect of emotional changes. Robinson and Starkstein (1997), and Starkstein and his co-workers (1993) reported that the patients with lesions involving the posterior limb of the internal capsule were often evident of anxiety. However, we did also notice our patients with the subcortical

stroke having the symptom of anxiety. The lesion areas in our patients not only involved the subcortical white matters, but also the adjacent subcortical gray regions. The findings of mania, bipolar affective disorders, psychosis, apathy, and catastrophic reactions have been reported in the patients with subcortical lesions (e.g., Robinson et al., 1988; Starkstein et al., 1991; Starkstein, Robinson, & Berthier, 1992; Trimble & Cummings, 1981; Starkstein et al., 1993). We did not observe these emotional changes in our patients with the subcortical stroke. Nevertheless, the manifestation of paranoid ideation tended to be manifest in our patients.

The dysfunction of the biogenic amine system has been hypothesized to be one of the mechanisms that may play an essential role in the cause of depression (Beatty, 1995; Conn, 1995). Since both noradrenergic and serotonergic cell bodies are located in the locus coeruleus and raphe nucleus of the brainstem, depressive symptoms should be evident in the patients with brainstem stroke involving the rostral pons and caudal mesencephalon which are sites for these two nuclei. In fact, depression was the cardinal psychopathological symptom in our patients with brainstem stroke. Accordingly, our results seemed to be in accordance with the hypothesis of the dysfunction of the biogenic amine system. In addition, somatization, was also evident in these patients.

In line with this hypothesis and on the basis of neuroanatomical evidences and

clinical findings, Robinson and his co-workers (1984) also claimed that poststroke depression might be as a result of depletion of norepinephrine and/or serotonin due to lesions in either the frontal cortex or basal ganglia. A tendency of having a depressed mood evident in our patients with subcortical stroke seemed to partially substantiate these researchers' proposition.

In summary, our preliminary results revealed that emotional changes could be evident in the patients with brainstem stroke, and depression was the cardinal psychopathological symptom. In addition, otherwise slightly to mildly emotional changes including somatization, obsessive-compulsive problems, and anxiety symptom were also noticed in these patients. Since the available data were limited, the proposed questions await further investigation.

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