

Chronic posttraumatic stress symptoms after nonsevere stroke

Laure Bruggimann^{abd}, Jean-Marie Annoni^a, Fabienne Staub^a, Nicole von Steinbüchel^b, Martial Van der Linden^c, Julien Bogousslavsky^a

^aService of Neurology, University Hospital of Lausanne, Switzerland

^bClinic of Geriatric Psychiatry, University Hospitals of Geneva, Switzerland

^cF.P.S.E., University of Geneva, Switzerland

^dService of Neurology, University Hospital of Lausanne, Bugnon 46, 1011 Lausanne, Switzerland

KEYWORDS: Affect, Anxiety, Cerebrovascular Accident, Chronic Disease, Depression, Memory Disorders, Post-Traumatic Stress Disorders

ABSTRACT

Objective: To determine whether posttraumatic stress disorder (PTSD)-related symptoms were present 1 year after a nonsevere stroke and, if so, to examine the relationship between PTSD, coexisting cognitive variables, and infarct localization *Methods:* The authors assessed 49 patients using standard measures of memory, trauma experience, neuro-logic deficit, depression, anxiety, and PTSD. *Results:* Fifteen (31%) patients had significant PTSD symptoms on the Impact of Event Scale (IES > 30). PTSD-like syndrome was independent of neurologic impairment, peristroke amnesia, long-term memory impairment, nosognosia, hypochondriac preoccupations, and physical pain during hospitalization, but was more frequent in women, less educated patients, and patients with more negative appraisals of the stroke experience. Intrusions were increased after basal ganglia strokes, suggesting that the re-experiencing phenomena may be modulated by frontosubcortical pathways. *Conclusions:* Posttraumatic stress disorder symptoms seem frequent in patients with nonsevere stroke and were associated with the subjective intensity of the stroke experience and accompanied by a depressive and anxious state.

Studies on the chronic phase of stroke have mainly focused on the frequency of depressive disorders (20 to 60%), whereas anxious symptoms have been less explored.^{1,2} Twenty to 30% of patients in the chronic phase of stroke have anxious disorders, independent of stroke severity.³ More recently, posttraumatic reactions following strokes have been reported.⁴⁻⁶ According to the Diagnostic and Statistical Manual of Mental Disorders (4th rev. ed.), the characteristic symptoms of posttraumatic stress disorder (PTSD) include intrusions (persistent re-experiencing of the traumatic event in distressing recollections or dreams), avoidance of stimuli evoking the trauma, and symptoms of increased arousal (e.g., exaggerated startle response).⁷ Partial, or subsyndromal, PTSD is frequent and may be regarded as a specific nosologic category.⁸ Two key processes seem to be involved in

the development of PTSD: excessively negative appraisals of the trauma and disturbance in autobiographical memory characterized by poor intentional recollection of the trauma.⁹

In this study, we aimed to determine the frequency of PTSD-like syndrome 1 year after a minor stroke, we explored the link between PTSD and memory impairment in terms of recollection of the stroke event and current episodic memory capacities, which are an indicator of memory functioning during the stroke, and we examined the relationship between PTSD and negative appraisals in assessing the subjective experience during the acute event (traumatic intensity and awareness of the medical condition measured retrospectively) and the patients' actual understanding of the etiologic factor for their condition. Lesion localization, likely to influence the occurrence of memory dysfunction and PTSD symptoms, was also considered. Symptoms of depression and nonspecific anxiety were concurrently evaluated.

Methods

One hundred forty-two patients younger than age 70 were enrolled after a first-ever nonsevere ischemic or hemorrhagic stroke (National Institute of Health Stroke Scale [NIHSS] < 6). Patients were subsequently excluded during follow-up if they had a persistent severe or moderate neurologic deficit (NIHSS > 3), were discovered to have a major psychiatric illness before stroke, or had a neurologic comorbidity. All 105 patients remaining after application of the exclusion criteria were evaluated using the Barthel Index, which provided an estimate of functional deficit (100 indicating no deficit, 0 indicating maximal deficit).¹⁰ Neurobehavioral assessment included a long-term memory assessment using a French version of the Rey Auditory Verbal Learning Test (RAVLT) in which the subject is asked to learn 15 unrelated words and to recall as many as possible after a delay of 40 minutes.¹¹ Mood alterations were evaluated using the French versions of the Hospital Anxiety and Depression Scale (HAD) and the Hamilton Depression Rating Scale (HDRS).^{12,13} The HAD is a brief 14-item, self-reported questionnaire used to detect symptoms of depression (HADD) and anxiety (HADA); the suggested cutoff score in stroke patients is 8 for depression, and we used the same cutoff for anxiety.¹⁴ The HDRS version used in this study was the 17-item scale, which was completed by an experienced psychiatrist; the recommended cutoff score of 12 was used.¹⁴ Patients were divided into two groups with educational levels of <11 years and ≥11 years of schooling (11 years was the median score in our population).

All patients were given three questionnaires to complete at home and return by mail. PTSD symptoms were assessed using the Impact of Event Scale (IES), a 15-item scale measuring intrusion (IESI) and avoidance (IESA) symptoms, which is available in French.^{15,16} An item of intrusion is, for instance: "Any reminder brought back feelings about it" (item 14). Example of an item concerning avoidance is: "I tried not to talk about it" (item 9). The recommended global score of 30 was considered as indicative of PTSD, and a cutoff score of 19 was used for each subscale.¹⁵ The patients also had to complete the six-item Trauma Experience Questionnaire (TEQ), which explores the subjective traumatic value of a severe medical event.¹⁷ With use of 4-point scales for each item

(1 = not at all, 4 = a lot), this questionnaire assesses patients' retrospective perceptions of helplessness, hopelessness, loss of control, pain, distress, and concerns about death during their hospitalization. Additional questions about the acute event were asked using a formal questionnaire developed for the current study. In particular, patients had to qualify the nature of their memories about the stroke onset (1 = precise and full recollection; 2 = fragmented or poor recollection; 3 = emotional re-experiencing without recollection of the event) and to determine the moment at which they first became aware of their condition (1 = at the time of the first stroke symptoms; 2 = when informed of the diagnosis; 3 = a few days later). We also tested the patients' knowledge of the etiologic factor for their condition in an open written question.

Lesion localization was determined on the basis of MRI data collected during the acute phase. With use of anatomic templates specifically designed for, and validated in, vascular diseases, six anatomic groups were constituted (frontal, parietal, temporal, occipital, basal ganglia/thalamus, brainstem/cerebellum).^{18,19} Although the strokes were minor, some lesions simultaneously affected two areas (i.e., frontal and temporal); in this case, both areas were recorded, with the result that the total number of lesions is greater than the total number of patients.

STATISTICAL METHODS.

All variables were found to have non normal statistical distributions and were therefore evaluated using appropriate nonparametric methods (medians, Mann-Whitney *U* test). Correlations between measures were estimated using the Pearson coefficient. Significance was set at the conventional 5% level, but the Bonferroni correction was applied in the case of multiple tests. Statistical analyses were performed using S PLUS 6.1 for Windows.

Results

DESCRIPTIVE DATA

Population.

Fifty-five of the 105 (52%) selected patients returned the three questionnaires (IES, TEQ, and questionnaire about the acute event); six were discarded because the data were incomplete. The analysis were therefore performed on 49 patients (16 women and 33 men; age mean 51.4 ± 16.2 ; 37 of whom had an educational level of at least 11 years of schooling). The group of 56 patients excluded from analysis were similar to the group of 49 included patients in terms of gender ($\chi^2 = 0.27$, $p = 0.604$), neurologic deficit measured by NIHSS 1 year after stroke ($t = 0.053$, $p = 0.958$), as well as mood disorders assessed using the HADD ($t = 1.432$, $p = 0.156$) and the HADA ($t = 1.118$, $p = 0.242$).

Among the 49 included patients, lesion localization was frontal in 11, temporal in 6, parietal in 13, occipital in 6, basal ganglia/thalamus in 13, and brainstem/cerebellum in 16. One year after stroke, the mean NIHSS score was $0.83 (\pm 0.98)$, indicating a minor neurologic deficit. On the Barthel Index, 1 patient had a mild physical disability, and the other 48 scored 100 (full ability).

Memory assessment.

In the delayed recall section of the RAVLT, the patients recalled 9.45 ± 4.42 words (mean and SD) out of a maximum of 15.

PTSD symptoms.

Fifteen of the 49 (31%) patients scored higher than the cutoff for PTSD on the IES (IES > 30). Considering the two subscales of the IES, 11 of the 49 (22%) patients reported significant symptoms of intrusion (IESI > 19), and the same proportion mentioned significant symptoms of avoidance (IESA > 19) (table). Of the 15 patients scoring >30 on the IES, 7 (47%) had PTSD symptoms in the absence of significant anxiety or depression as measured by the HAD and HDRS.

Table Scores of 49 patients with stroke on the IES measuring PTSD symptoms

	Mean (SD)	Percentage in clinical range*
IES: total score (0–75)	21.67(17.57)	31
IESI: intrusions (0–35)	11.45 (9.81)	22
IESA: avoidance (0–40)	10.20(10.00)	22

* The cutoffs for “abnormality” were as follows: IES total score > 30; IESI > 19; IESA > 19.

IES = Impact of Event Scale; PTSD = posttraumatic stress disorder; IESI = Impact of Event Scale for intrusions; IESA = Impact of Event Scale for avoidance.

Mood disorders.

With use of the HAD subscale for depression, 6% of patients reached the cutoff for depression (HADD ≥ 8), whereas 10% were depressed according to HDRS (HDRS ≥ 12). On the HAD subscale for anxiety, 12 of the 49 (24%) patients showed nonspecific anxious symptoms (HADA ≥ 8).

Trauma experience.

When questioned retrospectively on their perceptions during stroke onset, a minority of patients reported physical pain (25% reporting “moderate” or “severe” pain on the pain subscale of the TEQ) or concerns about death during the acute event (32% of them reporting “moderate or “severe” concern on the concern subscale of the TEQ). In terms of retrospective appraisal of helplessness, hopelessness, loss of control, and distress, answers were distributed relatively homogeneously across the four response categories of each subscale of the TEQ, with about 25% of subjects falling into each response category from 1 (not at all) to 4 (a lot).

Questions about the acute event.

Most of the patients claimed to have an excellent recollection of the stroke onset: 74% reported a complete memory, 22% a poor recall, and 4% had no recollection at all. No patient reported an emotional re-experiencing without recollection of the event. Regarding awareness of the medical

condition, 72% of the patients said they first became aware of their condition at the time of the first stroke symptoms, 24% when informed of the diagnosis, and 4% a few days later. Regarding their understanding of the etiologic factor, 51% reported that they still did not have an explanation for their stroke.

STATISTICAL ANALYSIS.

Demographic data and PTSD.

The occurrence of significant poststroke PTSD symptomatology was independent of age ($p = 0.129$, $p = 0.376$), but women scored higher on the IES total score ($t = 3.816$, $p < 0.001$), as did subjects with a lower educational level ($t = 2.671$, $p = 0.010$).

Memory and PTSD.

There was no correlation between delayed recall in the RAVLT and the IES total score ($r = 0.179$, $p = 0.270$). Furthermore, the quality of the memory of stroke onset was not a predictor of PTSD symptoms: There was no statistical difference in terms of PTSD score between subjects with an intact memory of the event ($n = 36$) and those with fragmented or absent recollection of the stroke ($n = 13$) ($t = -0.141$, $p = 0.888$). Thus, no relationship was found between PTSD and memory measures.

However, when the subscores of the IES were analyzed separately, intrusions (IESI) were associated with better verbal memory performance ($p = 0.329$, $p = 0.038$).

Lesion site and PTSD.

No specific lesion localization was associated with the global PTSD score. However, the intensity of intrusions was higher in the case of lesions involving the basal ganglia and thalamus ($t = 5.027$, $p = 0.030$).

Trauma experience and PTSD.

A higher total subjective trauma appraisal score was associated with greater PTSD symptomatology ($p = 0.661$, $p < 0.001$). When two groups of subjects were constituted on the basis of their responses for each item of the questionnaire (“no or some concerns about death” vs “moderate or a lot of concerns about death”) and compared in terms of PTSD symptomatology, differences were found in the IES total score for every item (helplessness: $t = 3.860$, $p < 0.001$; hopelessness: $t = 5.791$, $p < 0.001$; loss of control: $t = 2.910$, $p = 0.006$; distress: $t = 2.896$, $p = 0.006$, concerns about death: $t = 2.226$, $p = 0.033$), except physical pain ($t = 1.359$, $p = 0.062$).

Questions about the acute event and PTSD.

Nosognosia during hospitalization, assessed retrospectively by asking the subjects when they first became aware of their condition, had no effect on PTSD symptomatology, as subjects who were aware of their condition from the first stroke symptoms ($n = 35$) did not have a greater PTSD score than those who became aware of their condition at a later date ($n = 14$) ($t = 0.315$, $p = 0.754$). In addition, being aware of the etiologic factor responsible for the stroke had no effect on the

development of PTSD symptomatology, as there was no difference between subjects who had an explanation for their stroke ($n = 24$) and those who did not ($n = 25$) ($t = 1.610, p = 0.114$).

Neurologic deficit and PTSD.

The occurrence of significant poststroke PTSD symptomatology was independent of neurologic impairment assessed using the NIHSS ($p = 0.180, p = 0.215$). In contrast, the NIHSS was correlated with depression measured using the HAD scale ($p = 0.313, p = 0.029$).

Mood disorders and PTSD.

The scores on both depression scales and anxiety scale were correlated with PTSD symptomatology (HADD: $p = 0.420, p = 0.003$; HADA: $p = 0.339, p = 0.017$; HDRS: $p = 0.514; p < 0.001$). Post-hoc analysis of the HDRS item concerning hypochondriac anguish (HDRS, item 15) showed that such fear was not a good predictor of PTSD, as subjects with a tendency to hypochondriac preoccupations ($n = 17$) did not score higher on the PTSD measure than those who did not ($n = 32$) ($t = -1.510, p = 0.138$).

Discussion.

PTSD-like symptoms were found in 31% of the patients. The presence of such symptoms was associated with the subjective intensity of the traumatic experience measured retrospectively and was accompanied by an increased depressive and nonspecific anxious state. Our results indicate that a neurobiological substrate may exist for intrusion symptoms.

The percentage of patients with PTSD symptoms in our study was higher than the 21% reported by others using the same measure on a group of 61 patients.⁵ A large proportion (53%) of patients were excluded because of no or incomplete response to questionnaires, raising concerns about bias. Given the strong correlation between depression, anxiety, and PTSD, the fact that included patients are neither more depressed nor anxious on HAD scales than excluded ones suggests that PTSD symptoms are not necessarily overestimated in patients who returned questionnaires. Moreover, gender, which also influenced PTSD scores in our study, is equally distributed in the excluded and included groups.

In contrast with the current stroke literature,^{3,20} we found that poststroke anxious symptoms were more frequent than depression after stroke. Indeed, on the basis of the HAD scale, 24% of the patients had nonspecific anxiety symptoms, but only 6% had significant depressive complaints. However, the risk of having a second stroke did not seem to be a determinant factor for PTSD-related symptoms, as hypochondriac anguish was not predictive of PTSD symptoms. This observation goes against the idea that PTSD after stroke may result from a specific fear of a cerebrovascular recurrence.

The strong correlation between the results of the TEQ and the IES found in our study supports the role of subjective appraisal of the trauma experience in the development and maintenance of PTSD. Physical pain reported during stroke was not related to posttraumatic reactions, underlying the preponderant role of the emotional experience (feeling of helplessness, distress, etc.). PTSD symptoms were not influenced by the patient's current understanding of the etiologic factor

responsible for their condition, as patients who did not have an explanation for their stroke did not have more PTSD symptoms than those who did. However, it is recognized that having identified an origin of the stroke leads to better psychological adjustment.²¹ This issue should be specifically addressed in further studies.

Contrary to our expectations, subjects with fragmented or incomplete memory of the stroke onset did not score higher in PTSD measures. Furthermore, we found that subjects with a lower verbal memory capacity had fewer intrusion symptoms than others. The role of memory in the generation of PTSD symptoms is far from being fully understood. Our study only tackled the question of explicit verbal memory ability. Other types of memories, such as nonverbal or implicit learning, as well as the ability to encode emotional experience, should be examined in further cohort studies.

Concerning possible correlation with the infarct site, we found greater intrusions in patients with basal ganglia stroke ($n = 13$), suggesting that the phenomenon of re-experiencing may be modulated by thalamocortical pathways. This result is in agreement with those of studies indicating a possible role for basal ganglia and thalamic dysfunction in flashbacks.²²⁻²⁴ Basal ganglia lesions have been reported in other psychiatric conditions, such as depression, addiction, and obsessive compulsive syndrome, in which the obsessive thoughts evoke, in some respects, the intrusive and repetitive nature of the flashbacks in PTSD.²⁵⁻²⁷ No significant correlation was found between the PTSD score and lesions in cortical areas involved in memory. This may be due to the small sample size, as post-hoc analysis showed that only two patients had internal temporal lesions coupled with significant memory difficulties.

PTSD-like manifestations have been also described after other medical conditions and treatment. Most studies have focused on cancer, myocardial infarction or traumatic brain injury.²⁸⁻³⁰ The only study comparing stroke patients with patients having other physical problems suggests that a stroke is not more associated with PTSD problems than any other serious medical condition.⁶

References

1. Andersen G, Vestergaard K, Lauritzen L. Effective treatment of post-stroke depression with the selective serotonin reuptake inhibitor citalopram. *Stroke* 1994;25:1099–1104.
2. Beekman AT, Penninx BW, Deeg DJ, et al. Depression in survivors of stroke: a community-based study of prevalence, risk factors and consequences. *Soc Psychiatry Psychiatr Epidemiol* 1998;33:463–470.
3. Starkstein SE, Cohen BS, Fedoroff P, Parikh RM, Price, TR, Robinson RG. Relationship between anxiety disorders and depression disorders in patients with cerebrovascular injury. *Arch Gen Psychiatry* 1990;47:246–251.
4. Berry E. Post-traumatic stress disorder after subarachnoid haemorrhage. *Br J Clin Psychol* 1998;37:365–367.
5. Sembi S, Tarrrier N, O'Neill P, Burns A, Faragher B. Does post-traumatic stress disorder occur after stroke: a preliminary study. *Int J Geriatr Psychiatry* 1998;13:315–322.
6. Sampson MJ, Kinderman P, Watts S, Sembi S. Psychopathology and autobiographical memory in stroke and non-stroke hospitalised patients. *Int J Geriatr Psychiatry* 2003;18:23–32.
7. American Psychiatric Association. *Diagnostic and statistical manual of mental disorders*. 4th rev ed.

- Washington, DC: American Psychiatric Press, 2000:463–468.
8. Mylle J, Maes M. *Partial posttraumatic stress disorder revisited. J Affect Disord* 2004;78:37–48.
 9. Ehlers A, Clark DM. *A cognitive model of posttraumatic stress disorder. Behav Res Ther* 2000;38:319–345.
 10. Mahoney F, Barthel D. *Functional evaluation: the Barthel ADL Index. Maryland State Med J* 1965;14:61–65.
 11. Spreen O, Strauss E. *A compendium of Neuropsychological testing: administration, norms and commentary. Vol 2. New York:Oxford University Press, 1998.*
 12. Lépine JP, Godchau M, Brun P, Lemperière T. *Evaluation of anxiety and depression among patients hospitalized on an internal medicine service. Ann Med Psychol (Paris)* 1985;143:175–189.
 13. Guelfi JD, Dreyfus JF, Ruschel S, Blanchard C, Pichot P. *Factorial structure of the Hamilton Depression Scale, I. Ann Med Psychol (Paris)* 1981;139:199–214.
 14. Aben I, Verhey F, Strik J, Lousberg R, Lodder J, Honig A. *Validity of the Beck Depression Inventory, Hospital Anxiety and Depression Scale, SCL-90, and Hamilton Depression Scale as screening instruments for depression in stroke patients. Psychosomatics* 2002;43:386–393.
 15. Horowitz M, Wilner N, Alvarez W. *Impact of Event Scale: a measure of subjective stress. Psychosom Med* 1979;41:209–218.
 16. Hansenne M, Charles G, Pholien P, Panzer M. *Mesure subjective de l'impact d'un événement: traduction française et validation de l'échelle d'Horowitz. Psychol Med* 1993;25:86–88.
 17. Widows MR, Jacobsen PB, Fields KK. *Relation of psychological vulnerability factors to posttraumatic stress disorder symptomatology in bone marrow transplant recipients. Psychosom Med* 2000;62:873–882.
 18. Tatu L, Moulin J, Bogousslavsky J, Duvernoy H. *Arterial territories of the human brain: cerebral hemispheres. Neurology* 1998;50:1699–1708.
 19. Tatu L, Moulin J, Bogousslavsky J, Duvernoy H. *Arterial territories of the human brain: brainstem and cerebellum. Neurology* 1996;47:1125–1135.
 20. O'Rourke S, MacHale S, Signorini D, Dennis M. *Detecting psychiatric morbidity after stroke: comparison of the GHQ and the HAD scale. Stroke* 1998;29:980–985.
 21. Thompson SC. *The search for meaning following a stroke. Basic Appl Soc Psychol* 1991;12:81–96.
 22. Lanius RA, Williamson PC, Hopper J, et al. *Recall of emotional states in posttraumatic stress disorder: an fMRI investigation. Biol Psychiatry* 2003;53:204–210.
 23. Liberzon I, Taylor SF, Fig LM, Koeppe RA. *Alteration of corticothalamic perfusion ratios during a PTSD flashback. Depression Anxiety* 1996;97;4:146–150.
 24. Lucey JV, Costa DC, Adshead G, et al. *Brain blood flow in anxiety disorders: OCD, panic disorder with agoraphobia, and post-traumatic stress disorder on 99mTcHMPAO single photon emission tomography (SPET). Br J Psychiatry* 1997;171:346–350.
 25. Mayberg H. *Depression and fronto-subcortical circuits: focus on prefrontal-limbic interactions. In: Lichter, DG, Cummings JL, eds. Frontal-subcortical circuits in psychiatric and neurological disorders. New York: Guildford Press, 2001:177–206.*
 26. Capote HA, Flaherty L, Lichter D. *Addictions and frontal-subcortical circuits. In: Lichter, DG, Cummings JL, eds. Frontal-subcortical circuits in psychiatric and neurological disorders. New York: Guildford Press, 2001:231–259.*

27. Baxter LR, Clark EC, Iqbal M, Ackermann RE. Cortico-subcortical systems in the mediation of obsessive-compulsive disorder: modelling the brain's mediation of a classic "neurosis." In: Lichter DG, Cummings JL, eds. *Frontal-subcortical circuits in psychiatric and neurological disorders*. New York: Guilford Press, 2001:207-230.
28. Tedstone JE, Tarrier N. Post-traumatic stress disorder following medical illness and treatment. *Clin Psychol Rev* 2003;23:409-448.
29. Kangas M, Henry JL, Bryant RA. Post-traumatic stress disorder following cancer. A conceptual and empirical review. *Clin Psychol Rev* 2002; 22:499-524.
30. McMillan TM, Williams WH, Bryant R. Posttraumatic stress disorder and traumatic brain injury: a review of causal mechanisms, assessment, and treatment. *Neuropsychol Rehabil* 2003;13:149-164.