William Feinberg Lecture 2002
Emotions, Mood, and Behavior After Stroke
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Abstract—While emotional outcome is a critical factor influencing early evolution and late prognosis after stroke, few relevant studies have been performed on this subject. However, mood changes, modified judgment, and emotional reactions may also dramatically alter recruitment into clinical trials; for instance, up to one third of patients with acute stroke may have altered time perception, inappropriate self-evaluation of their condition, and attentional or memory dysfunction, with a subsequent increase in referral-to-hospital delays. In addition, the value of the “informed” consenting process may be questionable in the setting of urgent randomization into an acute stroke clinical trial. Data from ongoing studies suggest that behavior and emotional reactions in acute stroke patients may be classified into a few broad categories, with considerable overlap. Correlations between mood changes and the type, location, and severity of stroke may provide useful information for improving patient management, including the prediction of functional evolution and late prognosis. While depressive reactions have been widely studied in the recovery-rehabilitation phase after stroke, significant depression is uncommon shortly after stroke. On the other hand, related, though different, emotional behavioral changes may be more frequent; these have often been confused with depression and include catastrophic reaction, emotionalism, and athymhormia. Late depression is the most common mood alteration during the first year after stroke and has specific characteristics that differentiate it from classic endogenous and reactive depression, thus emphasizing the critical role of brain damage in the pathogenesis of poststroke depression. Early recognition and management of mood disorders after stroke are critical for the functional improvement of individual patients. However, little is known about specific indications for different antidepressant drugs in poststroke depression and related disorders. Ongoing research has identified a “new” emotional-behavioral disorder, poststroke fatigue, which is clearly distinct from depression in most instances. It is especially disabling and frustrating in that it typically involves patients with total or near-total neurological recovery, who should have been able to go back to their previous activities but who become severely disabled because of early and persisting exhaustion. Preliminary neuropsychological and MR and PET imaging studies suggest that disruption of subtle mechanisms underlying attention, in the absence of significant cognitive and mood alterations, may be responsible. Research projects are now being launched to better delineate poststroke fatigue and its management. (Stroke. 2003;34:1046-1050.)

Key Words: behavior ■ depression ■ mood disorders

It is an honor to give the 2002 lecture and a pleasure to be able to contribute to Bill Feinberg’s memory.

Emotions, mood, and behavior is perhaps an unusual topic for this kind of lecture, but I have chosen it because I think it is of utmost importance and certainly underrecognized by clinicians. The trauma and individual drama of acute stroke actually start by active injury to the self, although, in many cases, the patient does not fully recognize this injury as such. There is also an important change in sensory-motor interactions with both the internal and external world. What is particularly ill recognized, especially during the acute phase, is some kind of “modified mental processing,” which actually leads to altered judgment in many instances. A very good example is what can be called “acute memory or acute remembering impairment” in patients with acute stroke: there was a very interesting study by Grotta et al1 on this topic, which we subsequently confirmed, showing that up to one third of stroke patients have no, or only a poor, memory of what actually happened during the acute phase. The interesting aspect is that this usually occurs without specific damage to the classic anatomical structures known to be involved in memory processing. This is a very acute phenomenon, perhaps linked to something like “sideration” of brain function. Another issue is the poor recognition of the condition or neurological impairment. We often call this anosognosia, although this term lumps together quite different conditions, which can include the patient being convinced that he is not ill, does not have motor impairment, does not have a potentially severe medical condition, or does not have a brain problem. There are also rather subtle variants, eg, patients

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1046
with so-called denial behavior may try to get out of bed in order to go home because they deny their own illness. This has several consequences. The first is the potentially important delay before the patient receives care, especially if denial is already present very early in the course of the disease. The second consequence is the effect on the informed consent process, as, although investigators are keen to include patients in clinical trials, it may not be appropriate to consider patients with poor memory, altered judgment, and modified mental processing as being able to give informed consent. This deserves some concern, as increasing emphasis is being placed on informed consent. It is quite interesting that, in many of these patients, alterations of mental processing can also occur with lacunar infarction, for instance, in patients with pure motor stroke, in whom this is not expected. A third consequence is false memories, which can be annoying or distracting during patient follow-up, especially if the same physician is involved in acute care and follow-up. For all these reasons, it is important to emphasize that emotions, mood, and behavior can be markedly affected during the acute phase of stroke, and this can have consequences, such as poststroke depression.

**Acute Versus Chronic Stages**

Some of the differences between the results of studies that have addressed the problem of poststroke depression may be due to the fact that pseudodepressive mood disorders are often classified simply as “depression.” These pseudodepressive manifestations include emotionalism, catastrophic reaction, pathological crying, anxiety, apathy, and loss of psychic self-activation (athymhormia). Another problem is that this classification lumps together the acute and chronic consequences of stroke. For instance, mania and mania-like states are really acute phase problems, as is catastrophic reaction, seen in some patients very early in the course of stroke, whereas depression, by definition, is a chronic manifestation. One of the main issues is that, in contrast to the plethora of studies on poststroke depression several weeks, months, or years after stroke, emotion and behavior during the acute stroke phase have received very little attention.

At Lausanne, we have developed an index, the Emotional Behavioral Index (Table 1), which can be completed by nurses in continuous care units. Its advantage is that it provides a description, rather than an interpretation, of behavior in acute stroke patients. In principle, depression already is a diagnosis, ie, it is already an interpretation of the facts rather than a simple description that the patient looks sad or is crying. This measurement of behavior may be much closer to reality, especially in patients with communications problems, eg, aphasics, who are usually systematically excluded from studies because of their communication problems. The Emotional Behavioral Index bypasses the need for language communication. In our experience in over 300 acute patients, overt sadness is the most common manifestation (72%), followed by disinhibition (56%), lack of adaptation (44%), environmental withdrawal (40%), crying (27%), anosognosia (24%), passivity (24%), and aggressiveness (11%). Overt sadness is more frequently associated with left (86%) rather than right (61%) hemisphere lesions ($P<0.05$), and the association is even greater in the case of crying (50% versus 20% for left and right hemisphere lesions, respectively; $P=0.02$). With right-side lesions, anosognosia is clearly associated with neglect (95% versus 34% for neglect

<table>
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<th>Category</th>
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| Overt Sadness| 1. Cries  
2. Looks sad  
3. Complains  
4. Screams  
5. Sighs |
| Environment Withdrawal | 1. Gives up  
2. Isolated |
| Aggressiveness | 1. Tensed  
2. Agitated  
3. Angry  
4. Rebellious  
5. Opposition  
6. Aggressive  
7. Revolted |
| Passiveness   | 1. Indifferent  
2. Neglected  
3. Apathetic |
| Disinhibition | 1. Jokes  
2. Disinhibited  
3. Laughs  
4. Impatient |
| Denial        | 1. Minimizes  
2. Total denial  
3. Partial denial |
| Adaptation    | 1. Smiles  
2. Socializes  
3. Quiet  
4. Patient  
5. Founded emotions  
6. Decent  
7. Interested  
8. Look serious  
9. Interactive  
10. Helpful  
11. Collaborant |

Observational methods. The Lausanne Emotion in Acute Stroke Study (LEASS). Observation: every day for the first 4 days after onset by acute stroke unit nurses.
versus nonneglect, respectively; *P*=0.01). However, with right hemisphere lesions, both sadness and indifference are also more frequent in anosognosic patients.

It is interesting to see that, even in right hemisphere stroke, sadness is not absent by any means. Moreover, anosognosia may coexist with severe sadness, which, at first sight, may seem paradoxical. However, it is obvious that sadness, even leading to depression in some cases, can actually develop in patients who are not really aware of their own condition.3

Another important issue is to try to link these early behavioral changes with brain tissue changes during the first hours of stroke, which is not easy in humans. We have bypassed some technical and feasibility difficulties linked to the use of MRI by developing perfusion CT techniques (using 4 contiguous 10-mm slices) allowing us to determine the mean transit time, cerebral blood flow, and cerebral blood volume according to simple equations.4 Figure 1 shows perfusion CT in a patient with severe right hemiparesis and global aphasia with catastrophic reaction. What we are doing using this approach is to develop maps of tissues (shown in red in Figure 1) that will inevitably undergo infarction, ie, tissues below the threshold for both cerebral blood flow and cerebral blood volume undergo infarction, while tissues below the threshold for cerebral blood flow, but not below that for cerebral blood volume, approximate to penumbra (shown in green in Figure 1).4 In this patient, imaged within 2 hours after stroke, the penumbra is still extensive in the speech areas, although coexisting with very severe aphasic disturbances. This patient had a rather favorable evolution of aphasia with complete disappearance of the catastrophic reaction, corresponding to a small residual infarct in the posterior parietal region, while the penumbra tissue identified by perfusion CT did not evolve toward infarction.

Another example, shown in Figure 2, is a patient with a right hemisphere stroke and severe hemineglect, anosognosia, and flattening of affect. Within 3 hours, a rather large penumbra area was seen on perfusion CT. The patient had a middle cerebral artery stem occlusion on CT, which reperfused with thrombolysis. Actually, both the penumbra and the entire area of ischemic tissue decreased, and the MRA showed persistence of middle cerebral artery patency, delayed diffusion-weighted imaging demonstrating that the final infarct corresponded well with the “red area” (ie, future infarction) on the initial perfusion CT.

**Chronic and Delayed Emotional Behavior**

During the nonacute phase, depression is the prototype of mood disturbances and chronic behavioral abnormalities. Indeed, if one follows the psychiatric *DSM-IV* criteria, depression is a condition that can be assessed in patients without an acute brain condition. It is possible to speak of sadness or behavioral depressive changes during the acute phase, but not really of depression, because it is not possible to assess items such as the lack of interest or pleasure in activities or loss of self-esteem in patients sitting in intensive care units. Poststroke depression is not rare, occurring in around 40% of stroke victims,5–10 with minor and major poststroke depression occurring in equal proportions. Clinically, this shows important differences from what psychiatrists call endogenous depression. Even severe cases of poststroke depression are not identical to endogenous depression, as they have much more reactive diurnal mood variation and emotionalism, show an absence of guilt, and are rarely suicidal, despite the fact that these patients are also disabled from a physical point of view; however, the death rate is nevertheless increased in these patients.5
The importance of studying poststroke depression is the strong link between its occurrence and a poor functional outcome of the patients (Figure 3). This is well demonstrated in the literature, and our own data show a strong correlation between the development of depression and a poor Rankin Scale or Barthel Index. The problem is that we do not know which occurs first, but it is probable that either can, ie, depression can lead to a worse functional outcome and vice versa, although we do not know all the subtleties of the interaction. The patient-linked factors that can lead to depression are rather controversial. Table 2 summarizes the different studies that have assessed the relationship between depression and factors such as age and gender; positive and negative findings have been found in equal proportions.

Things are simpler when we consider stroke features (Table 3). Stroke severity and functional prognosis are factors that are strongly associated with the development of poststroke depression. In contrast, an association with stroke site is much more controversial. As far as stroke site and location is concerned, we must quote the beautiful studies from Iowa City by Robinson and collaborators, who have tried to get around this controversy by showing that poststroke depression can occur in both left and right hemisphere stroke, but with an anterior to posterior gradient, which is different according to the hemisphere involved, being posterior to anterior with a left hemisphere lesion and anterior to posterior with a right hemisphere lesion. Comparison of studies is difficult because of inconsistencies due to methodological problems, and the relationship between poststroke depression and lesion location may be, in fact, more complex than suspected. In addition, lesion location may be only a small part of what is important in the development of poststroke depression. However, there is room to improve the details and quality of correlations studies, as shown by Robinson et al, who emphasized that strokes leading to major or minor depression may have different locations. The timing of assessment may also be critical. It is possible that, during the acute phase of stroke, depressive features may correlate with a lesion in the left frontal region, whereas, in the long term, they correlate with lesions closer to the occipital pole in the right hemisphere. In the Lausanne Emotion in Stroke Study, we have tried to assess, during the acute phase, abnormalities associated with subsequent depression during the chronic phase. One of the important findings is that the predictive value of early changes is rather poor, as the patients who will go on to develop depression during the chronic phase are not necessarily those who show the most important signs of behavioral depressive changes during the acute phase. Indeed, in the Lausanne Emotion in Stroke Study, only 10% of patients with depression at 1 year had shown severe sadness during the acute phase. Another important finding in terms of distinguishing between depression and poststroke dementia is that, in our experience, most cases of poststroke depression show a strong association with lesions in the subcortical white matter, thalamus, basal ganglia, and brain stem rather than cortical damage with specific cognitive disturbance. While therapeutic recommendations in poststroke depression currently do not differ from those for other forms of depression, clinical trials comparing available drug treatments are virtually nonexistent.

**Poststroke Fatigue**

I would like to close by emphasizing a very intriguing syndrome belonging to those abnormalities that I have classified under pseudodepressive syndromes after stroke, namely, poststroke fatigue. Fatigue itself is a feature of depression, and, in the *DSM-IV*, is listed as one of the criteria. However, the interesting aspect is that it can also occur without depression. Fatigue in neurological disease has been much more extensively studied in conditions other than stroke, such as multiple sclerosis or Parkinson’s disease. Of course, fatigue is something that is well known to everybody, but its definition is not always clear. We have
defined fatigue as a reversible decrease or loss of abilities associated with a heightened sensation of physical or mental strain, even without conspicuous effort, due to an overwhelming feeling of exhaustion, which leads to an inability to sustain, or a difficulty in sustaining, even routine activities. Preliminary data show that patients with fatigue can be depressed, but that a large cohort (20% to 50%) of patients are not. One important aspect is that patients with poststroke fatigue do not show either very severe neurological disturbance or functional impairment. In fact, these patients are often rather a challenge to the treating physician because they are not depressed and have recovered very well from their stroke without any subsequent hemiparesis or cognitive disturbance but are still unable to return to work because of severe fatigue in the absence of any concomitant disease, such as sleep apnea or endocrine dysfunction. Our preliminary findings emphasize that patients with so-called primary poststroke fatigue may have mainly brain stem lesions. We speculate that many cases of poststroke fatigue may correspond to subtle attentional dysfunction, although neuropsychological assessment shows no cognitive-executive disturbance. Ongoing research involves PET correlation studies to delineate secondary hemispheric changes in patients with poststroke fatigue and infratentorial lesions. Hopefully, the findings will prove useful in the understanding and potential differential treatment of fatigue and depression after stroke. They may also be helpful in the choice of treatment strategies (mainly sertraline and other serotonin reuptake inhibitors), which remains anecdotal in a field in which clinical trials are clearly needed.

References
