

Pathological Display of Affect in Patients with Depression and Right Frontal Brain Damage

An Alternative Mechanism

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Two patients are reported with the acute onset of pathological crying following right inferior frontal brain damage. Both had severe endogenous depression and neither had pseudobulbar palsy. These and other cases argue that two organic brain diseases—one structural and the other “physiopharmacological”—may interact to produce pathological display of affect that cannot be accounted for by traditional neurological explanations. A pharmacological mechanism for the rapid amelioration of pathological affect by tricyclic medications and its possible relationship to the newly discovered descending motor systems of the brain that use norepinephrine and serotonin as neurotransmitters is offered. These cases also suggest that pathological affect is a valuable clinical indicator of an underlying major depression in some brain-injured patients.

Pathological display of affect is a well-described clinical phenomenon in which a patient will intermittently exhibit extreme affective behaviors, usually laughing, crying, or both, in response to trivial environmental stimuli that have little, if any, emotional valence (Black, 1982; Poeck, 1969; Wilson, 1924). The displays are realistic, involuntary and have an “all-or-none quality.” These outward affective displays do not usually reflect the actual internal feeling state (emotions) of the patients, who often complain bitterly of their inability to control these highly exaggerated affective behaviors.

Traditionally, two neurological mechanisms are thought to underlie pathological affect. The best known is pseudobulbar palsy following bilateral lesions in the neocortical upper motor neuron innervation of the bulbar motor nuclei (Benson, 1979; Lieberman and Benson, 1977). Pathological affect associated with pseudobulbar palsy is commonly called pseudobulbar affect. Clinical studies (Benson, 1979) have not yet resolved whether lesions causing pseudobulbar affect need only involve pyramidal motor cortex (area 4) or the pyramidal tract, which is composed of large myelinated fibers from area 4 and small myelinated and unmyelinated fibers from the premotor cortex (area 6) and primary sensory cortex (areas 1, 2, and 3) (Carpenter, 1976; Russell and DeMyer, 1961), or

whether the lesions also need to involve the premotor cortex or its descending pathways to the brainstem reticular formation and tectum (Kuypers and Lawrence, 1967).

The second mechanism, less well known, results from unilateral or occasionally bilateral lesions or, more rarely, epileptic activity involving the basal forebrain, medial temporal lobe, diencephalon, or tegmentum of the brainstem (Brown, 1967; Contu and Drew, 1966; Davison and Kelman, 1939; Gainotti, 1979; Ironside, 1956; Offen *et al.*, 1976; Sackheim *et al.*, 1982; Sethi and Rao, 1976; Wilson, 1924). In this instance pathological affect occurs without pseudobulbar palsy.

More recently, a third alternate mechanism has been proposed by Ross and Rush (1981, cases 2,3,4,5). They suggested that pathological affect could be triggered in patients by a unilateral brain lesion, involving predominantly the right frontal opercula, when combined with a major depressive disorder. Although these patients have left-sided upper motor neuron weakness of at least the face and hand, they have neither pseudobulbar palsy nor a *structural* lesion involving the basal forebrain, medial temporal lobe, hypothalamus, or tegmentum. In these patients, the pathological display of affect rapidly resolves with antidepressant medication well before the dysphoric mood responds.

We now report a new patient and review in detail a previously reported patient (Ross and Rush, 1981, case 3) to further clarify the potential neurological mechanisms involved in depression, motoric behaviors, and pathological affect. These cases also emphasize that in certain brain-damaged patients pathological affect may be a valuable clinical indicator of an underlying major depression complicating a neurological illness. Robinson *et al.* (1984) reported that major depression,

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The authors wish to thank Luis Gutierrez, M.D., for his help in the psychiatric evaluation of case 1, and John Rush, M.D., Frank Benson, M.D., and Bernard Carroll, M.D., Ph.D., for reviewing and commenting on the manuscript. The authors also express their appreciation to Sherry Kreager for her patient secretarial assistance.

defined by DSM-III criteria (American Psychiatric Association, 1980) but which cannot be ascribed to bereavement or reactive depression, occurs in at least 25% of stroke patients. Using criteria developed specifically for diagnosing depression in the presence of brain damage (Ross and Rush, 1981; Ross *et al.*, 1986), Gordon *et al.*² found in pilot studies that the prevalence of major depression complicating stroke may be closer to 65%. A slightly greater incidence of depression occurred following right- rather than left-brain damage, which is in keeping with a recent study of poststroke depression by Sinyor *et al.* (1986) and in contrast to a study by Robinson *et al.* (1984). Because depression is not a well-appreciated complication of brain damage, recognizing the significance of clinical clues (Ross and Rush, 1981). *e.g.*, "unexpected" pathological affect, should assist practitioners in managing the prominent psychiatric complications that commonly accompany brain injury (Lipsey *et al.*, 1984).

Case Reports

Case 1

A 68-year-old right-handed man presented to the Parkland Memorial Hospital emergency room because of a mild left facial droop and 3 weeks of persistent right frontal headache. One year earlier, his initial complaints of weight loss, a chronic cough, and hemoptysis led to a diagnosis of a squamous cell carcinoma of the right lung. The patient refused surgery but underwent radiation therapy. Three months before the onset of headaches he experienced brief "blackout" spells that lasted a few seconds, unaccompanied by tonicoclonic movements, complex motoric behaviors, affective displays, confusion, or experiential phenomena. His family noted intermittent gait difficulties and a change in mentation, characterized by increased forgetfulness and mild apathy several months before the onset of headaches.

On neurological examination, the patient was mildly inattentive and had some difficulty on recent memory testing, serial sevens, and proverb interpretation. His affect was *flat* but not depressed. There was blurring of his optic disc margins bilaterally. A mild left lower facial weakness was present. No overt weakness was found on motor testing other than a left upper extremity drift. Reflexes were 2+ and equal with bilateral down-going toes. Sensory examination was normal except for a slight decrease in position sense in the toes bilaterally. His gait was wide based and somewhat

unsteady. An emergency computed tomography (CT) scan (Figure 1) demonstrated an inferior right frontal mass with surrounding edema that showed ring enhancement with contrast. Tracking edema into the right parietal operculum and anterior temporal lobe was also present causing a slight midline shift to the left. He was admitted and started on dexamethasone 10 mg per day in divided doses.

Neurosurgical evaluation found him oriented, alert, and cooperative with a very mild left hemiparesis and a blunted affect. Radiation therapy to his head was started. Five days later he underwent resection of the tumor through a right frontal craniotomy with complete removal of the single metastasis from the right frontal operculum.

Immediately upon awakening in the recovery room, it was observed that he had numerous crying spells. In addition, he now had a severe left lower facial paralysis without clinical evidence of pseudobulbar palsy or sensory loss, thus substantiating that the surgery had caused an acute and significant injury to his right inferior frontal lobe. Specifically, he had no dysphagia for liquids or solids, he could volitionally cough with force and move his tongue rapidly, and he had a normal gag and jaw jerk. The crying spells persisted and markedly worsened over the next few days as he recovered from surgery. The nurses reported that his crying was almost continuous.

Psychiatric consultation uncovered history from patient and family of numerous prior episodes of major depression, which were associated with marked increases in alcohol consumption. His long history of alcohol abuse started as a teen and was associated with several hospital admissions during which he experienced delirium tremens. Despite his drinking, he maintained a steady job and supported his family.

His current depressive episode began 6 months before admission soon after his brother-in-law died from lung cancer. It was characterized by severe insomnia, anorexia with weight loss, psychomotor retardation, anhedonia, and death wishes. Before surgery the depression was not accompanied by any crying outbursts or agitated behaviors, according to the patient and his family. At the time of psychiatric evaluation, the patient admitted to feelings of helplessness, depression and hopelessness. He cried frequently even when trying to verbalize non-emotionally laden material. According to his family, this excessive crying had never occurred in the past, even during his previous bouts of depression. The patient himself was highly embarrassed by the crying spells because he was unable to control them, and they did not seem to be related necessarily to his internal feeling state or to the things he was talking about at the time. The crying spells, which made interviewing difficult, were con-

² Details of this work can be found in Grant NS 22471, National Institutes of Health, National Institute of Neurological and Communicative Disorders and Stroke, Washington, DC, entitled *Treatment of Affective Deficits in Stroke Rehabilitation*, Gordon WA (Principal Investigator), funded as of September 1985.

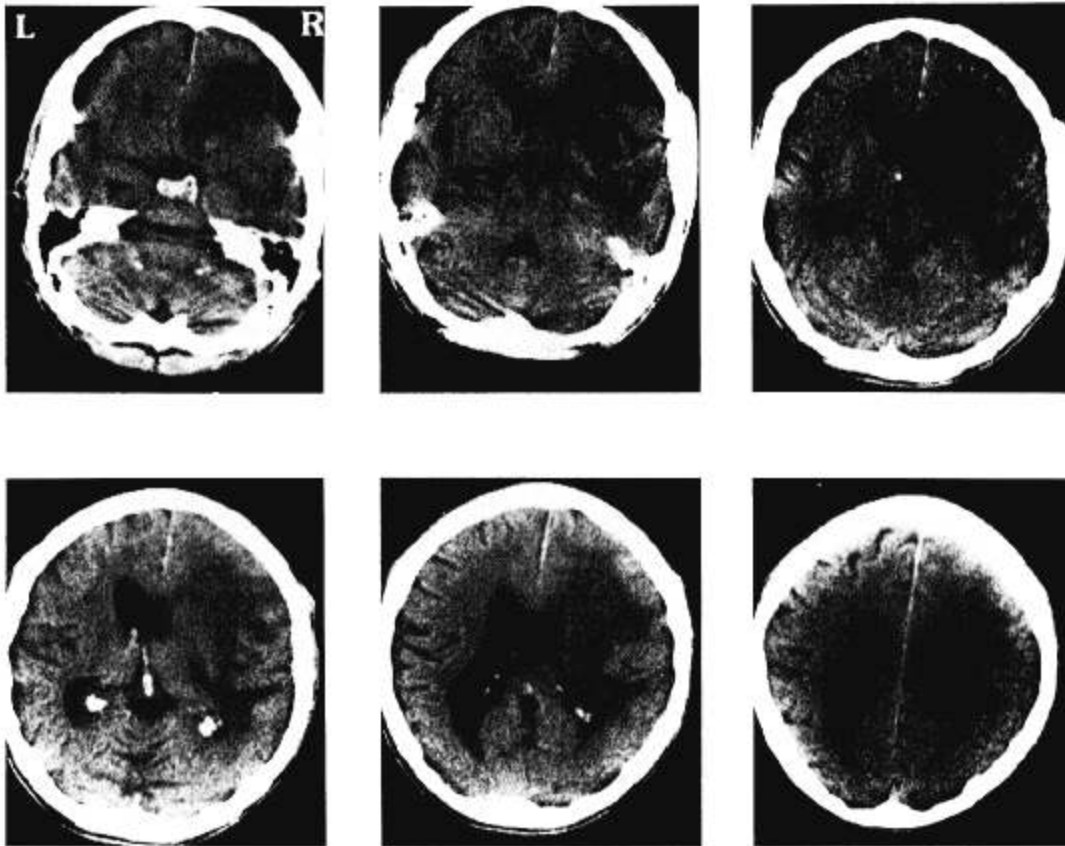


FIG. 1. Emergency CT scan of case 1. A ring-enhancing mass deep in the right inferior frontal lobe is evident with tracking edema involving the parietal and temporal lobes. There is compression of the right lateral ventricle and a midline shift to the left. Postoperative CT showed resolution of tracking edema with persistence of edema involving predominantly the inferior frontal lobe.

sistent with pathological crying and did not have any features associated with dacrystic epilepsy (Offen *et al.*, 1976). Between the spells he had a flat affect.

A diagnosis of major depressive disorder, melancholic type, was made. Doxepin hydrochloride was begun and increased over 4 days to 100 mg h.s. Within 2 days, the crying spells had abated to a point at which the nursing staff felt that he was no longer depressed. However, psychiatric reevaluation confirmed that he still had severe residual depression by reported symptoms. On repeat neurological examination 2 days later, he was alert and cooperative with normal left hemisphere-dependent cognitive and language functions. A moderately severe paralysis of the left lower face was present at rest and during volitional movements. There was no clinical evidence of pseudobulbar palsy. He had a flat affect with loss of spontaneous affective prosody and gesturing even when talking about emotionally charged experiences. Only one short crying spell was observed, during which the left facial weakness disappeared. His ability to repeat a sentence with affective variation was poor, but comprehension of affective prosody and gesturing was preserved. These findings are consistent with motor aprosodia, which

usually results from right frontal opercula damage (Ross, 1981).

Two weeks after surgery a repeat CT scan showed residual, nontracking edema of the right inferior frontal lobe most marked in the opercula region. Four weeks after surgery during an outpatient visit the patient reported that his crying spells had totally subsided. His mood was markedly improved but not completely normal even though his affect remained flat. The left lower facial weakness showed some improvement.

Case 2

A 70-year-old right-handed man was admitted to the Dallas Veterans Administration Hospital for evaluation of syncope. Two years previously he had suffered a stroke involving predominantly his right superior parietal lobe and resulting in a moderate left upper and lower extremity hemiparesis with sensory loss that spared his face. On admission, a grade 2/6 pansystolic murmur and atrial fibrillation were found. Only mild weakness of his left extremities was evident. While being evaluated for syncope, he sustained a second stroke involving his right frontal and anterior parietal opercula by CT (Figure 2). This resulted in a

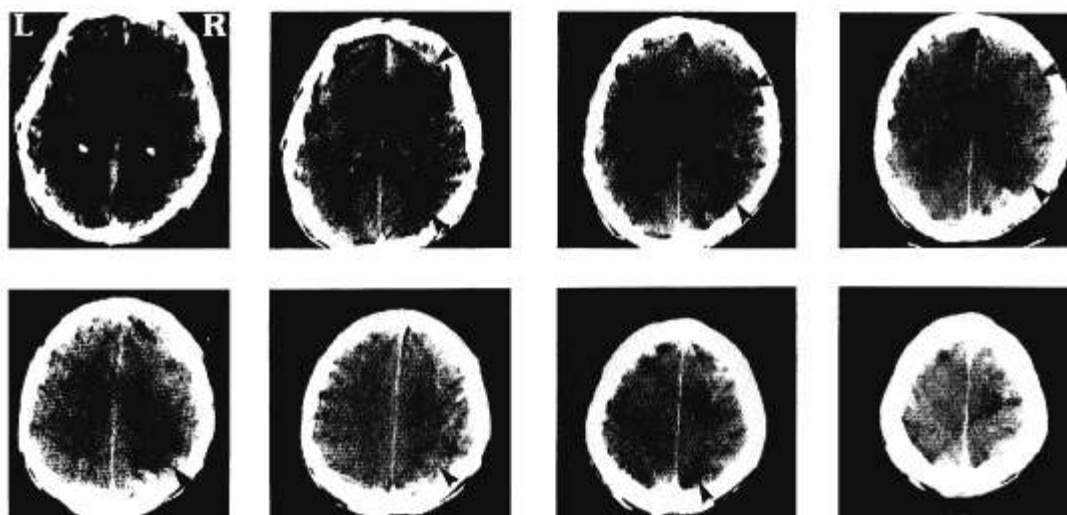


FIG. 2. CT scan of case 2. Lower arrowheads point to an old superolateral infarction of the right parietal lobe, and the upper arrowheads point to an acute right frontoparietal opercula infarction.

severe left hemiplegia, involving face, arm, and leg, with sensory loss. He initially became delirious and was observed to have severe, intermittent, and numerous crying episodes that began immediately after the stroke.

Neurological examination 1.5 weeks later demonstrated mild inattention with left-sided neglect and implicit denial of illness. Recent and remote memories, calculations, right/left orientation, reading, writing, and similarities were normal. He had a severe left spastic hemiplegia with sensory loss affecting face, arm, and leg equally with increased reflexes and a Babinski sign. There was no clinical evidence for pseudobulbar palsy. The patient could volitionally cough with force and move his tongue rapidly, he had no dysphagia for liquids and solids, and he had a normal jaw jerk and gag reflex. There was no aphasia; but his speech was affectively flat, and he did not gesture. His ability to repeat sentences with affective intonation was severely compromised, but comprehension of affect in speech and gestures was preserved. These findings are consistent with motor aprosodia (Ross, 1981), a result of his right opercula stroke.

In addition, the patient had innumerable crying spells that had an all-or-none quality and were not associated with any particular environmental stimuli. During the crying spells his left facial weakness *completely resolved*. He could not control these episodes and denied emotionally congruent internal feelings during the crying spells. Between the crying spells, however, his affect was flat. These crying spells had not been present before his second stroke and were consistent with the syndrome of pathological crying. They did not have any features associated with dacrystic epilepsy (Offen *et al.*, 1976).

Over the next few weeks, as his implicit denial of

illness improved, he gradually admitted to feeling "blue" and "sad." The nursing personnel also observed that he had severe anorexia and marked insomnia. Anhedonia and psychomotor retardation were also present. He then became preoccupied with his spouse's fidelity, a severe right eye injury that he "incurred during World War II," and harrowing war experiences.

However, on speaking with his wife, who visited him daily in the hospital, none of his preoccupations were substantiated. After World War II, he apparently suffered a severe endogenous depression during which he had delusions about an eye injury and war experiences that never occurred. He had done well, according to his wife, until 5 years before hospitalization, when after retirement he began to gradually lose interest in all previous hobbies and activities and incessantly watched television. He became insomniac and anorectic with weight loss. He sobbed frequently and talked about feeling worthless. However, his current crying episodes were totally unlike the ones his wife had observed over the previous 3 years. The poststroke episodes were very severe in quality, short in duration, inordinately numerous, and, for the most part, not accompanied by an emotionally congruent internal feeling state.

Based on past psychiatric history and his current symptoms, a major depressive disorder with melancholic and psychotic features was diagnosed. Unfortunately, treatment with antidepressants was precluded because of his subsequent clinical deterioration and ultimate death from two episodes of ventricular tachycardia with cardiac arrest and a third stroke involving his left hemisphere.

Discussion

These two cases underscore the additive effect on behavior of two separate organic brain diseases: a) a

structural lesion of the brain involving the right hemisphere, and b) a nonstructural, physiopharmacological disturbance of brain function causing a psychiatric condition. Based on clinical history both patients *before* their brain injuries were experiencing a major depression that met DSM-III and Research Diagnostic Criteria (Spitzer *et al.*, 1978). Yet neither patient exhibited pathological crying. Immediately following right inferior frontal brain damage, case 1 from surgery and case 2 after an ischemic stroke, both displayed pathological crying without clinical evidence of pseudobulbar palsy, seizure activity, or CT evidence of lesions in the basal forebrain, medial temporal lobe, diencephalon, or tegmentum. Thus, our patients' pathological crying cannot be accounted for by traditional neurological explanations. Furthermore, the precipitous onset of their pathological crying as opposed to the gradual onset in other patients who become depressed *following* right frontal brain lesions (Ross and Rush, 1981, cases 2, 4, 5) vividly illustrates how the interaction of psychiatric and neurological diseases produces behaviors not usually associated with either disease.

Before discussing the possible neurological basis for the precipitous onset of pathological affect in our patients, a brief review of the functional-anatomical organization of the various motor systems is necessary. Following lesions of either the right or left neocortical motor regions, which include area 6 (premotor cortex) and area 4 (pyramidal motor cortex) or their descending pathways, two levels of motoric deficits may occur (Figure 3). The first is loss of volitional control over the contralateral extremities and face—the classical hemiplegic deficit. Because this loss involves predominantly contralateral rather than bilateral motoric control, according to the concept of dominance developed by Denny-Brown and associates (1952; 1954), hemiplegia represents a “nondominant” functional loss. The second level of loss, however, involves “dominant” (Denny-Brown *et al.*, 1952; Denny-Brown and Banker, 1954) motoric function. For the left it is the modulation of speech and pantomime (Benson, 1979); and for the right it is the graded modulation of affective behaviors, other than extreme affective displays, through prosody and gestures (Ross, 1981, 1985; Ross and Mesulam, 1979; Ross *et al.*, 1981). In both instances, the loss of motor control causes a behavioral deficit that involves both sides of space including the “nonparalyzed,” ipsilateral face and limbs causing Broca aphasia (Benson, 1979) or motor aprosodia (Ross, 1981), respectively.

In addition, there are other motor systems that exist in the brain (Armand, 1982; Kuypers, 1973). Most important to this discussion, however, are those involved with the motoric control of extreme, nonvolitional, affective displays (Figure 3). Clinical and experimental studies suggest that these displays are probably organized by the basal forebrain and temporal limbic system through bilateral descending pathways via the diencephalon and brainstem tegmentum (Brown, 1967; Contu and Drew, 1966; Offen *et al.*, 1976; Wilson, 1924). Because graded affective behaviors, propositional language, and extreme affective displays are modulated by anatomically separate motor systems, a lesion involving one system but not the others will produce paradoxical motoric behaviors, first described in detail by Monrad-Krohn (1924, 1939). In fact, our patients clearly illustrate this point: both manifested the syndrome of motor aprosodia (Ross, 1981), causing a flat affect that involved their nonparalyzed right limbs and face; yet superimposed was pathological crying during which their volitionally paralyzed left lower facial muscles and nonparalyzed left upper and right facial muscles became activated. This occurred because the motoric systems organizing extreme affective display were intact, although the right neocortical motor system, which modulates graded affective behaviors bilaterally and volitional movement contralaterally, was injured by their right-sided brain lesions.

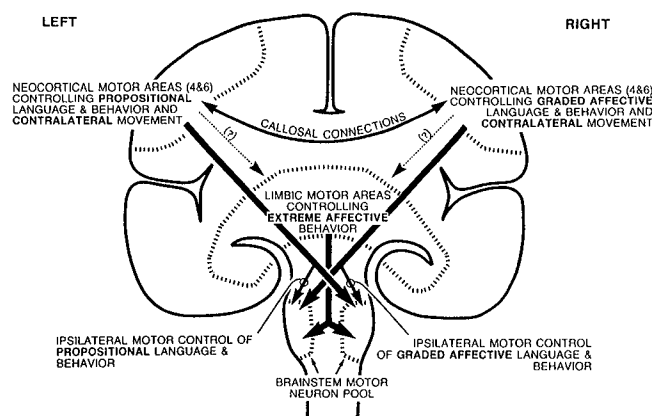


FIG. 3. Highly schematized drawing of the neocortical and limbic descending motor systems. Note that the nondominant neocortical control of volitional movement by each hemisphere is predominantly contralateral whereas the “dominant” neocortical control by each hemisphere for certain volitional motoric behaviors, speech, and pantomime for the left, and affective prosody and gestures for the right, is organized bilaterally. The limbic motor areas organize extreme affective displays, such as laughing and crying. Whether the neocortical motor systems have direct anatomical influence over the limbic motor system is not known. Because each motor system and its descending pathway to the lower motor neuron pools are separated anatomically in the brain, paradoxical motoric behaviors may result if one system is disrupted by a lesion leaving the others intact.

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In most normal situations, one exercises volitional control over displaying extreme affective behaviors (Wilson, 1924). This control is gained through the normal maturation of brain and the learning of societal rules and regulations. Humans who consistently

show poor control of extreme affective displays are newborns and young children. Because there is strong clinical evidence that the right neocortical motor system is dominantly involved in the graded modulation of affective behaviors through voice and gesture (Ross, 1985), one might conclude that it is the influence of this motor system on temporal limbic and limbic-related structures that allows voluntary control over extreme affective displays. If this were the case, however, one would expect pathological affect to occur whenever a lesion involved the right neocortical motor system or its descending pathways. As this does not happen with any regularity, one must surmise that other motor or nonmotor systems in the brain also help control the display of extreme affect, even though the right frontal neocortex may be particularly influential in controlling these behaviors. For instance, pathological display of affect commonly occurs following bilateral lesions causing pseudobulbar palsy (Benson, 1979; Lieberman and Benson, 1977), thus implying that the left neocortical motor system also has some regulating influence on extreme affective displays. Therefore, to explain the occurrence of pathological crying in the patients reported in this communication and previously (Ross and Rush, 1981, cases 2, 3, 4, 5), a second factor must be operative—depression.

Considerable evidence gathered through discrete electrical stimulation of the brain in awake patients suggests that internal feeling states, including dysphoric moods and other experiential phenomena such as déjà vu, hallucinations, paranoia, and delusions, are generated by the amygdala and hippocampus, which are part of the temporal limbic system (Gloor *et al.*, 1982; Halgren *et al.*, 1978; Ross, 1985). These are also the same structures intimately involved with the motoric organization of extreme, nonvolitional, affective displays. If the major affective disorders are viewed as organic, nonstructural diseases of the brain that are caused by physiopharmacological changes that involve at least the temporal limbic system and related structures (Ross and Rush, 1981), then a hypothetical neuroanatomical model to explain the phenomenon of pathological display of affect in patients with both endogenous depression and lesions of the right neocortical motor system is feasible.

Assume that depression causes state changes in the temporal limbic system so that the threshold for displaying mood congruent, extreme affective behaviors is lowered, accounting for the irritability, sobbing, and agitation that often accompany depression. If the lowered threshold is combined with a brain lesion that greatly reduces the neocortical control of limbic behaviors, then pathological display of affect would result. Treating the depression with tricyclic drugs re-

stores the brain to a more normal physiological state through pharmacological manipulation, which, in turn, raises the temporolimbic threshold for triggering extreme affective behavior, thereby ameliorating the pathological affect. Because this amelioration occurs well before the lifting of mood in all reported cases to date (Ross and Rush, 1981), a further refinement of the model is necessary to explain the rather immediate effect of tricyclic medications on pathological affect.

Recent anatomical studies of the descending pathways from brainstem have shown that there are two motor systems that use biogenic amines as neurotransmitters (Bowker *et al.*, 1981; Kuypers, 1982). One emanates from the nucleus coeruleus and subcoeruleus and the other, from the median raphe. The former uses norepinephrine as its neurotransmitter whereas the latter uses serotonin. These descending motor pathways synapse either directly on motor neurons or interneurons in the spinal cord and brainstem (McCall and Aghajanian, 1979), and they are not segmentally organized (Huisman *et al.*, 1981) so that graded and fractionated motoric control is very unlikely (Kuypers, 1982). It is thought that these motor systems either sensitize the motor neurons for action (Kuypers, 1982; White and Neuman, 1980) or are responsible for organizing primitive nonvolitional kinds of motor behaviors, such as extreme emotions (Kuypers, 1982). In addition, there are various descending influences (McCall and Aghajanian, 1979) on the coeruleus and raphe emanating from amygdala (coeruleus and subcoeruleus) (Baraban and Aghajanian, 1982; Hopkins and Holstege, 1978), rostral basal forebrain, hypothalamus and habenular nuclei (raphe) (Aghajanian and Wang, 1977), and periaqueductal gray (coeruleus and raphe) (Marchand and Hagino, 1983), which in turn are linked anatomically to hippocampus, hypothalamus, and other forebrain limbic structures.

Thus, extreme, nonvolitional, affective displays in patients, whether they are pathological or mood congruent, are probably organized by the temporal limbic system and basal forebrain via the diencephalic periaqueductal gray-habenular-biogenic amine descending motor systems. Part of this system has already been conceptualized anatomically as a "dorsal pathway" that might be responsible for relaying information from forebrain limbic structures to the "midbrain limbic areas" (Aghajanian and Wang, 1977). Because tricyclic drugs have powerful influences at aromatic amine synapses (Maas, 1975) and can modulate directly the norepinephrine and serotonin influences on motor neurons when administered systemically (Menkes *et al.*, 1980), pharmacological amelioration of pathological laughing and crying may follow from the direct alteration of synaptic activity of the "limbic" motor system at the level of the motor neuron or

interneuron. This hypothesis would account, therefore, for the immediate response of pathological display of affect to tricyclics in our patients well before the dysphoric mood and associated depressive symptoms resolve.

Additionally, the hypothesis may also explain a well-known clinical phenomenon that often occurs during tricyclic and monoamine oxidase inhibitor (MAOI) therapy of depression, namely, in the early phases of treatment patients often appear behaviorally improved well before their mood, with its inherent suicidal risk, responds to therapy (Stern *et al.*, 1980). Thus, the pharmacological basis for the antidepressant, *mood-altering* activity of the tricyclics and MAOIs must be distinctly different from their acute effects on the affective-motoric behaviors associated with depression, *e.g.*, psychomotor retardation, agitation, sobbing, anxiety. Furthermore, these affective behaviors seem to respond differentially to the institution of various types of tricyclic medications. For example, tricyclics such as desipramine, that are strongly noradrenergic (Maas, 1975) seem to be more effective in treating psychomotor retardation, whereas tricyclics such as trazadone (Feighner, 1980), that are strongly serotonergic, are best for controlling anxious behaviors. The initial behavioral response to tricyclics, however, does not appear to be predictive of overall treatment outcome (Stern *et al.*, 1980). There is also other evidence for pharmacologically dissociating the motoric behaviors and mood states associated with depression based on drugs (Ghose *et al.*, 1977; Menkes *et al.*, 1980) such as amphetamine and cocaine (Post *et al.*, 1974), which have powerful effects at aromatic amine synapses. These drugs have been shown to improve the outward affective-motoric behaviors of depressed patients but have little, if any, lasting effect on depressive mood or vegetative abnormalities.

Conclusion

The two patients reported give us further insight into the possible cerebral organization of mood, emotional experience, graded affective behaviors, and extreme affective displays and allow speculation about how these systems interact in patients with both structural and physiopharmacological (psychiatric) brain disturbances to produce abnormal behaviors. They also substantiate the clinical observation that pathological display of affect following damage to the right frontal opercula is an important sign that the patient may be suffering from an underlying major depressive disorder (Ross and Rush, 1981). Whether focal lesions of the left neocortical motor system in combination with major depression can trigger pathological affect

remains an open question, but to date the authors have not encountered such patients. In keeping with the ideas presented in the discussion regarding the possible role of biogenic amines in the modulation of extreme affective displays are the recent reports indicating that levodopa (Udaka *et al.*, 1984; Wolf *et al.*, 1979) and low-dose tricyclics (Schiffer *et al.*, 1983) are useful for controlling pathological laughing and crying in nondepressed patients with degenerative brain diseases associated with dementia or following closed-head trauma or focal brain lesions. Based on the rapid response of patients treated with low-dose tricyclics, Schiffer *et al.* (1983) have also surmised that the pharmacological mechanism for the antidepressant activity of tricyclics is probably different from their salutary effects on pathological display of affect.

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