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INDIVIDUAL & FAMILY PSYCHOPHARMACOLOGIC TREATMENT OF:
- MOOD AND ANXIETY DISORDERS • OBSESSIVE-COMPULSIVE DISORDER
- PERVASIVE DEVELOPMENTAL DISORDERS/AUTISM
- ATTENTION DEFICIT DISORDER • MENTAL RETARDATION • TOURETTE'S DISORDER
- TRAUMATIC PSYCHIATRY • TRAUMATIC BRAIN INJURY
- POST-TRAUMATIC STRESS DISORDER • CHRONIC PAIN MANAGEMENT

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NEUROPSYCHIATRIC ASPECTS OF MOOD AND AFFECTIVE DISORDERS

The most recent and authoritative textbook in the world in the area of neuropsychiatry is The Textbook of Neuropsychiatry, edited by Stuart Yudofsky, M.D. and Robert E. Hales, M.D., (American Psychiatric Association Press, June 1997). For an excellent discussion of this topic, see the chapter therein entitled *Neuropsychiatric Aspect of Mood and Affective Disorders* by Helen S. Mayberg, M.D., Roderick K. Mahurin, Ph.D. and Stephen K. Brannan, M.D.

The term "Mood and Affective Disorders" is the current psychiatric terminology for depressive disorders. Regarding depressed patients, there are theories implicating specific abnormalities in neurochemical and neuropeptide focal lesions in specific brain regions and selective dysfunction of known neural pathways have been proposed. Many are supported by a growing number of clinical and basic studies demonstrating anatomic, neurochemical, genetic, endocrine, sleep and selective cognitive abnormalities. The clinical, biochemical, neuropsychological and imaging markers of depression will be reviewed herein.

DEPRESSION: CLINICAL PRESENTATION

The diagnosis of primary major depression is based on the presence of a persistent negative mood state in association with disturbances in attention, motivation, motor and mental speed, sleep, appetite, and libido, as well as anhedonia, anxiety, excessive or inappropriate guilt, recurrent thoughts of death with suicidal ideation, and in some cases suicide attempts as in Table 32-1, next page.[1]

[1] Diagnostic criteria and further discussion of the clinical aspects of all depressive disorders is described in the Diagnostic and Statistical Manual (DSM-IV) (The American Psychiatric Association Press, 1994, pages 317-391).

TABLE 32-1: *CLINICAL FEATURES OF DEPRESSION*

Mood (Work-Disabling) Symptoms	
	Dysthymia
	Anhedonia
	Pessimism/Hopelessness
	Excessive/Inappropriate guilt
	Low self-esteem
	Crying spells
	Suicidality
	Anxiety
Motor	**Motor slowing**
	Restlessness/Agitation
Somatic	**Sleep disturbance**
	Abnormal appetite
	Weight change
	Decreased libido
	Easy fatigability/Low energy
	Apathy decreased drive
Cognitive (Work-Disabling) Symptoms	
	Impaired attention/short-term memory
	Poor executive functioning
	Psychomotor retardation
	Poor motivation
	Rumination

COGNITIVE DEFICITS IN DEPRESSION - SOCIAL/OCCUPATIONAL DISABLING DEFICITS

Cognitive deficits in depression consist of difficulty thinking, concentrating, decreased mental speed, lack of motivation, and apathy. These deficits are a common and potentially debilitating feature of major depression and impairment is most often encountered in the cognitive domains of attention, memory and psychomotor speed.

Cognitive deficits are usually of moderate intensity but can become severe in prolonged or intractable depression, adding to disability in everyday functioning. Additionally, clinically significant anxiety also occurs in many patients with depression, further impairing cognitive efficiency.[2]

[2] Rathus and Reber, 1994.

COGNITIVE MECHANISMS OF DECREASED MENTAL FUNCTIONING IN DEPRESSION

Depression-related cognitive deficits are based on reduced cognitive capacity or impaired ability to efficiently allocate cognitive resources to meet specific task demands.

Support for this hypothesis comes from studies showing a differential impression in effortful versus automatic cognitive tasks in depressed patients, as well as from findings of disproportionate cognitive impairment in depressed versus normal subjects when presented with concurrent tasks and competing for limited attentional resources.[3] Depressed subjects, when compared with non-depressed subjects, perform disproportionately worse on recall of unstructured verbal material than on structured material, the former presumably requiring more effortful cognitive processing.[4] In addition, depression-related cognitive dysfunction has been found to increase in accord with increased complexity and degree of encoding required by task material.[5] Other explanations for nonspecific impairment in patients with depression include: Decreased task motivation, intrusion of depressive thought content, and secondary effects of fatigue or restlessness.

In summary, these cognitive deficits produce significant work-related disability.

BIOLOGIC MARKERS OF MOOD DISTURBANCE

1. Neurochemical Abnormalities in Depression

Alterations in many neurotransmitters which include changes in norepinephrine, serotonin, dopamine, acetylcholine, opiates, and y-aminobuytric acid. Neurotransmitters are chemicals secreted by one nerve cell which communicates and activates the adjacent nerve cell resulting in normal central nervous system functioning.

2. Endocrine Changes in Depression

Studies of endocrine function in patients with depression have identified dysregulation of the hypothalamic-pituitary-adrenal axis and thyroid dysfunction

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[3] Hertel and Milan, 1994; Roy-Byrne et al., 1986.

[4] Watts et al., 1990.

[5] Weingartner, 1984.

POSITRON EMISSION TOMOGRAPHY (PET) SCAN FINDINGS IN DEPRESSION

The PET Scan is a test which measures the physiologic alterations in the brain. In contrast, Magnetic Resonance Imaging (MRI) examines anatomical structural alterations. The PET Scan measures the metabolism of glucose, which is the "fuel for the brain." In depression, there are a number of significant studies noting decreased glucose metabolism resulting in diminished cerebral functioning.

Attached after the last page, is a sheet showing two PET Scans, one of the brain of a person who is depressed and one of a person who is not depressed. On the left side, imagine that the upper part of the picture of the brain is the frontal lobe of the brain. Imagine that you are looking down on the patient's head. The frontal area, which is the area in front of one's head, is labeled "FR." On the sides of the skull are the temporal areas (near the temples) which are labeled "T"). The back of the skull is the occipital area.

In the depressed patient (the PET Scan upper left column labeled "DEP"), note that the color is primarily blue. This color corresponds to significantly diminished brain functioning. On the right side of the diagram is an approximately **c** -inch-wide vertical line. The red upper part of the line indicates high glucose metabolism. In contrast, the blue lower part of the line (.60) indicates significantly diminished glucose metabolism.

In the non-depressed patient, which is the PET Scan in the lower left column (labeled "NON-DEP" for non-depressed), note that in the upper part of this image there are significant areas of red in contrast to the depressed image where the frontal area is primarily blue. Since the fuel of the brain is glucose, and the metabolism in the frontal area is significantly diminished in depression, this accounts for what is called Frontal Lobe Syndrome which is manifest when a patient is apathetic and lacks motivation. Changes in the temporal lobe may also result in the patient having diminished memory.

The primary PET Scan findings indicate that in depression, global cognitive/mental impairment that is correlated with medical prefrontal hypoperfusion, is correlated with decreased frontal lobe brain dysfunction.[6]

In summary, abnormalities shown in a PET Scan are objective measures of decreased brain metabolism. The PET Scan is used primarily as a research tool, since it costs approximately $2,500.00. However, it is sometimes used in litigation in evaluating brain-injured patients who have had normal structural MRI scans, yet manifest severe frontal lobe symptomatology such as personality disturbance, which would be visible only on a PET Scan and not on an MRI. The most consistent findings have been decreases in frontal cortex metabolism and blood flow.[7] Specific anatomic location of these frontal changes involve both dorsolateral prefrontal cortex and the vertebral prefrontal and orbital frontal

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[6] Dolan, et al., 1992.

[7] Baxter, et al. 1989; Buchsbaum, et al., 1986; Lesser, et al., 1994; Mayberg, et al., 1994.

cortex.

Recent positive emission tomography findings indicate decreased frontal and temporal lobe glucose metabolism. This finding, in addition to associated multiple neurotransmitter/neuroendocrine dysfunction, results in social and occupational disabling cognitive depressive symptoms including lack of motivation, apathy, mental slowing, and difficulty thinking/concentrating which significantly impairs an individual's ability to function.

Clinical Comparisons

The pattern of memory deficits seen in patients with major depression has been found to be statistically similar to that in clinical groups with prefrontal-subcortical involvement (i.e., Parkinson's disease and Huntington's disease) in contrast to a "cortical" pattern of memory performance seen in patients with Alzheimer's disease.[8] Other studies comparing patients with primary depression with patients with neurologic depression (involving fronto-subcortical structures) have also demonstrated similarities in patterns of cognitive impairment, including deficits in concentration and memory.

DEPRESSION: TREATMENT CONSIDERATIONS IN MOOD DISTURBANCE

An untreated major depressive episode generally lasts 6-13 months, and treatment can significantly reduce this time-period since antidepressants and/or psychotherapy are generally effective in ameliorating depressive symptoms.

In summary, I feel this information will be helpful to both the clinician in evaluation, and to the attorney in litigation, as an aid to understanding the significant cognitive disability which occurs in affective depressive disorders and the devastating effects such disability has on the patient who for the first time is experiencing significantly impaired ability to function both in the workplace and in their daily life.

BIBLIOGRAPHY:

Yudofsky & Hales, Textbook of Neuropsychiatry, American Psychiatric Association Press, June 1997;

Diagnostic and Statistical Manual (DSM-IV), American Psychiatric Association Press, 1994.

[SEE PET SCAN ILLUSTRATION FOLLOWING PAGE]

[8] Massman, et al., 1992.

PET SCAN ILLUSTRATION