

CHAPTER 22 LIMBIC SYSTEM

Temporal Lobe: Stimulation. Seizures involving the temporal lobe are frequent and produce a variety of symptoms:

- autonomic phenomena –
- fear
- simple auditory sensations , and simple auditory and visual distortions
- vestibular sensations (dizziness)
- alterations in perception
- arrest of speech
- hallucinations in the auditory, visual or olfactory spheres
- repetitive movements of a complex type (automatisms)
- complex emotional behavior
- confusion with defects in memory recording.

Correlations of symptoms in simple and complex partial epilepsy with temporal structures: The correlations to be presented here represent the preferential effects of limited stimulation. Seizure discharges however spread rapidly with in a system that has been viewed as a widely distributed neuronal matrix. It is also important to take into consideration that the stimulation is performed in patients who are already subject to simple and complex partial seizures of temporal lobe origin. The brain being stimulated has already been the subject of various pathological processes. When limited symptoms occur with full awareness and without amnesia ,confusion or automatisms, the seizure is termed simple partial . When consciousness is altered in the sense that confusion ,amnesia and automatisms occur, the seizure is termed complex partial. Obviously ,a seizure of temporal lobe origin may begin as a simple partial seizure and then evolve into a complex partial seizure. Secondary generalization into a generalized tonic/clonic seizure may occur in both instances.

1. **Autonomic phenomena** result most commonly from stimulation of the amygdala. As discussed above ,autonomic phenomena may also occur on stimulation of cingulate or orbital frontal areas.
2. **Fear**, the most common emotion , occurring during a temporal lobe seizure is most readily reproduced by stimulation of the amygdala. Less often fear is produced by stimulation of the hippocampus. Less often other emotions such as anger may occur on stimulation of the amygdala in the human patient.
3. **Auditory and visual illusions**, the distortion or alteration in the quality of perception in these modalities is most readily produced by stimulation in the higher order auditory and visual association cortex. Note that the tertiary visual association cortex (V 5) is actually located in the temporal lobe. Crude auditory sensation, such as tinnitus (a tone, buzzing, or knocking in the ear), is best produced by stimulation of the primary auditory projection area, Heschl's (anterior) transverse gyrus (**Fig. 22-13**). At times, an auditory sensation is produced by stimulating the adjacent superior temporal gyrus, but this is considered to represent an alteration in the interpretation of sound rather than an actual auditory sensation. In Penfield's studies, auditory illusions (sounds seem louder, fainter, more distant, or nearer) occurred on stimulation of the superior temporal gyrus in either hemisphere. In contrast ,visual illusions (objects seem nearer, farther, larger, or smaller) occurred predominantly but not exclusively on stimulation in the nondominant temporal lobe. (**Fig. 22-15**).
4. **Vestibular sensations (vertigo, or dizziness)** can sometimes be produced by stimulation of the superior temporal gyrus adjacent and posterior to the auditory cortex (**Fig. 22-14**). The studies of Friberg and coworkers (1985) indicate a focal increase in cerebral blood flow in this region with contralateral vestibular caloric stimulation.
5. **Arrest of speech** is produced by stimulation of area 22 of the superior and adjacent middle temporal gyri of the dominant hemisphere (Wernicke's receptive aphasia area). In addition, arrest of speech also occurs on stimulation of the posterior temporal region of the dominant region, which extends into the angular and supramarginal inferior parietal areas. Arrest of speech is not specific to these areas, since it also occurs on stimulation of Broca's area (the inferior frontal gyrus) and of the supplementary motor areas of the dominant hemisphere (**Fig. 24-2**).
6. **Experiential Phenomena/Dreamy States: More complex visual and auditory illusions, déjà vu, déjà vécu ,jamais vu and other illusions of recognition, visual and auditory hallucinations :**
The localization of these several phenomena has been the subject of considerable controversy. Complex illusions consist of an alteration in perception the sensation that time or one's own thinking is slowing down or speeding up or that a visual scene or voices have become distant. Also in this category are illusions of recognition. **Jamais vu** is the sensation that the perception or scene is dream like. **Déjà vu** is the sensation of reminiscence, that perceptions have a familiarity. **Déjà vécu** is the sensation of a strangeness associated with the perception.

Visual and auditory hallucinations represent in this context the sensation, that a scene from memory has been reproduced.

It should be evident that all of these phenomena are interrelated and therefore will be discussed together.

Jackson & Beevor (1889) Jackson & Coleman in 1898 observed that the dreamy state characterized by vivid memory like hallucinations and /or the sensation of having previously lived through the same experience (déjà vu) was associated with pathology involving the mesial temporal structures.

However Penfield and Perot(1963) reproduced the phenomena by stimulation of the neocortex of the lateral temporal lobe,-particularly the superior temporal gyrus. In general deeper mesial temporal structures were not stimulated .**Auditory hallucinations** (hearing a familiar voice or music) occurred predominantly in relation to stimulation of the superior temporal gyrus of either hemisphere. **Visual hallucinations** (seeing a familiar scene or people, such as a parent) occurred predominantly but not exclusively when stimulating the superior temporal gyrus on the lateral surface of the nondominant temporal lobe. There was some tendency for the visual phenomena to be produced from the posterior temporal areas extending into the bordering area 19 of the occipital cortex. (**Fig. 22-16**). For all of these phenomena, the patient often uses the descriptive term “dream like”. In the studies of Penfield and Perot (1963) the illusions of recognition occurred predominantly when the nondominant temporal lobe was stimulated. Usually, both the auditory and visual hallucinations were identified by the patient as past experiences. As Gloor and colleagues (1982) demonstrated, often the patient may be describing an inner or past experience within an emotional context that the patient relates in visual terms.

Halgren et al (1978) reproduced these same phenomena by stimulation of mesial temporal structures (hippocampus and amygdala)-however a wide spread evoked response or afterdischarge was required. The content of the mental phenomena evoked was variable and related to the personality and past experience of the individual patient. The subsequent studies of Gloor et al (1982)[38]suggested that mesial temporal discharge was critical for the occurrence of the mental phenomena-with stimulation of the amygdala being most effective.. Less often stimulation of hippocampus or parahippocampal gyrus which resulted in an afterdischarge involving limbic and neocortical structures also produced the phenomena. The trajectories of the depth electrodes employed in these studies ,however did not sample adequately the neocortex of the superior temporal gyrus ,that area found to be critical in the earlier studies of Penfield and Perot. The studies of Bancaud et al (1994) resolved many of the issues of the stimulation studies. In 85%of dreamy states evoked by mesial temporal stimulation,the discharges spread to the temporal neocortex. In 53% of dreamy states evoked by stimulation of lateral neocortex, the discharge spread to mesial temporal structures. However in every spontaneous seizure in which a dreamy state was observed ,the amygdala, anterior hippocampus and the temporal neocortex were all involved.This suggests a network with the anterior hippocampus ,the amygdala and the superior temporal gyrus having privileged access to this system. (see also Burgerman et al –1995 and Walczak – 1995)

More definitive are the reports of Blume et al (1993) and Mullan &Penfield (1959) in which ictal experiential illusions or hallucinations were abolished by ablations limited to the lateral temporal neocortex but ictal automatisms, autonomic phenomena and ictal fear persisted until the previously spared amygdala and hippocampus were ablated.

In interpreting all of this data, from the standpoint of the localization of memory traces a certain degree of caution is essential. One should not jump to the conclusion that specific memory traces are localized to the areas stimulated during surgery. Certain points should be kept in mind:

1. The memory remains after ablation of the area that has been stimulated.
2. Moreover, these experiential responses are not obtained on stimulation of the "normal" temporal lobe during surgery directed at disease of the temporal lobe. However, in the studies of Sem-Jacobson and Torkildsen (1960) and Ishihashi (1964), experiential responses were obtained on stimulation of the temporal lobe in patients with schizophrenia (see below).
3. Although some of the patients with temporal-lobe seizures have disease involving the neocortex on the lateral surface, most have pathology involving the mesial temporal areas, that is, the amygdala, hippocampus, and parahippocampal gyri.

As we will see in the chapter on memory the hippocampal areas are involved in the recording of new memories.

7.Olfactory hallucinations . The olfactory hallucination is usually termed an unfamiliar , unpleasant odor. Rarely, during surgery, these olfactory hallucinations are produced by direct stimulation in or near the

cortex of the uncus. (Note that the lateral olfactory stria projects to the uncus.) In the early reports of Jackson & Beevor, and of Penfield, olfactory hallucinations were related to pathology involving the uncus (uncinate seizures). The more recent studies of Bancaud (1987)[42] suggest that this symptom also follows stimulation of the posterior orbital frontal cortex, as would be predicted from **Figure 28**. Gloor[33] reviews studies indicating elicitation of this symptom at times on stimulation of the amygdala.

8. Pure amnestic seizure with anterograde memory deficit but without confusion or unresponsiveness has been related by Gloor (1997) to selective bilateral functional inactivation of the mesial temporal structures but without involvement of the neocortical structures. Gloor suggests that when unresponsiveness and confusion occur in the temporal lobe seizure, spread to neocortical areas has occurred. A stronger alternative explanation, when seizures arise in the lateral temporal neocortex is that spread to the mesial temporal structures has occurred. Confusion with amnesia reflects then the interference effect of hippocampal stimulation on the capacity for recording new memories. During this time, relatively complex but familiar activities, such as the driving of an automobile, may be continued. The problem of memory recording will be discussed further in Chapter 30. For perhaps the best illustration of the phenomenon, refer to the case reports of Hughlings Jackson concerning "dreamy states" (in Taylor, 1931). For example, a physician with temporal-lobe seizures was able to perform a relatively complete physical examination and to begin appropriate treatment during such an episode but had no memory of anything he did.

9. Automatism-simple or complex stereotyped repetitive motor behavior occurs during a time when the patient is otherwise unresponsive to stimuli and confused. In general automatisms represent the primary or secondary bilateral involvement of the amygdaloid/hippocampal areas by seizure discharge. The automatisms are invariably accompanied by some degree of confusion; the patient is always amnestic for the behavior and other events. The testimony of witnesses must be obtained. The most common form are the repetitive oral movements involving mouth lips and throat such as chewing, licking swallowing. It is uncertain whether these oral automatisms represent the spread of discharge from amygdala to brain stem motor nuclei or the effects of release of the brain stem structures from higher control. Other automatisms consist of other repetitive complex movements, such as constantly rubbing an ear, or smoothing of bedding or clothing. Ictal automatisms otherwise represent the effects by the discharge of a wide spread interference in function of the mesial temporal and the temporal and frontal neocortical association areas. Similar automatisms may also occur in the absence seizure as a result of the interference effects of a wide spread discharge. Automatisms may also occur during the post ictal stage of a seizure, when neocortical and mesial temporal functions are also depressed in a widespread manner. Although automatisms are usually defined as occurring without reference to prevailing circumstances, it is often evident that environmental stimuli may trigger some of the more complex automatisms. Thus automatisms are often modified by or appropriate to a specific stimulus that has been introduced into the environment. Thus, patients may continue actions that were being performed at the onset of the seizure but in an imperfect, repetitive manner. If an object touches the back of the neck or ear, patients may brush this away repetitively. If attempts are made to restrain, patients may resist, assault those attempting to restrain them, or attempt to flee. Sometimes automatisms have a strong emotional flavor, such as those accompanied by laughter, crying, or anger. Automatisms or perseveration of speech may occur particularly in response to questions.

NEUROLOGICAL ASPECTS OF PSYCHIATRIC DISORDERS

It is not possible to discuss the full range of psychiatric disorders. What follows is an outline with emphasis on major neurological and neuropathological aspects. (An excellent review of psychiatric disorders is provided by Adams et al 1997. A more detailed neurobiologic perspective is provided by Kandel (2000a and 2000b). DSM III and DSM IV of the American Psychiatric Association provide a detailed monographic approach to definitions and classification).

Psychiatric disorders are essentially divided into those disorders characterized by psychotic disturbances of mental function and emotion (or to use the legal term - insanity) and the non-psychotic disturbances of mental function and emotion: the anxiety disorders/neurosis and the personality disorders. A psychotic disorder is defined (DSMIII) by "a gross impairment in reality testing. The individual incorrectly evaluates the accuracy of his or her perceptions and thought and makes incorrect inferences about external reality." "Direct evidence of psychotic behavior would be the presence of either delusions or hallucinations without insight into their pathological nature." "Behavior is grossly disoriented."

Psychotic Disorders: In terms of the traditional classification of psychotic disorders the following major categories may be listed:

1) Those disorders secondary to a general medical condition ,or diffuse neurological disorder or focal neurological disorder. These were formally called “organic”. A better term would be secondary psychosis .The disorders would include a. The acute confusional /delirious states associated with fever, or various metabolic disorders or the psychosis which may occur in severe disorders of the thyroid . b. Focal or multifocal disorders of cortical function particularly involving the frontal and temporal areas such as tumors or Pick’s disease c. more diffuse neurological disorders – of an acute nature as in encephalitis or of a more chronic nature as in general paresis of neurosyphilis or Huntington's, or Alzheimer's diseases.

2) Those disorders in which no underlying neurological or medical condition could be established. The term formerly employed was “functional psychosis” .Using the terminology usually employed in medicine and neurology, better labels would be primary or idiopathic or essential. As will be discussed below, it is now evident that modern research suggests that there is an underlying genetic, structural or biochemical neurologic basis .

Essentially two disorders are considered within this category :the schizophrenias and the major affective or mood disorders.

The modern classification of the "functional disorders" should be attributed to Kraepelin, who made the clear-cut separation of "dementia praecox (now called schizophrenia¹) and the affective disorders. He recognized that "dementia praecox" (schizophrenia) began in adolescence and early adult life, progressed as a chronic disorder and almost always ended with a marked deterioration of personality. It was recognized that exacerbations and remissions occurred but that the individual never returned to the pre-morbid level of personality and function. In contrast affective disorders were not characterized by this deterioration. One could hypothesize that a structural basis probably would be found in schizophrenia but not in affective disorders.

SCHIZOPHRENIA:

The diagnosis of schizophrenia is based on the following criteria: (1) there are psychotic features during the active phase .(2) There is a deterioration from previous level of function (3) there are characteristic symptoms and signs that involve multiple psychological processes that have been present for at least 1 month but with some symptoms of a premorbid or residual nature present for at least 6 months .These are as follows:

- a. content of thought: delusions (of persecution and reference) and hallucinations (predominantly auditory or somatic less often olfactory or visual)
- b. form of thought: loosening of associations
- c. affect: blunting, flattening, and inappropriate
- d. sense of self: loss of ego boundaries (depersonalization and derealization)
- e. volition: disturbance in self-initiated goal directed activity. This impacts work and academic performance
- f. relation to external world: is restricted .This impacts interpersonal relations.
- g. psychomotor behavior: reduced: (catatonia - waxy flexibility) or excessive stereotyped movements.

Overall symptoms are often described as positive (thought disorders, delusions and hallucinations)or negative (poverty of speech, decreased movements, poverty of affect and withdrawal). In a sense ,many of the positive symptoms are suggestive of temporal lobe dysfunction as in seizures of temporal lobe origin .Heath (1982) did find electrical seizure discharges on depth electrode recordings from the septal region ,hippocampus and amygdala. Many of the negative symptoms suggest the syndromes produced by prefrontal pathology (Mesulum –1990).

Various subtypes are defined by the predominant symptomatology at the time of evaluation : (1)**Paranoid** (the least severe) with prominence of delusions and auditory hallucinations but with relative preservation of cognitive function and affect .(2)**Disorganized** (the most severe) with disorganized speech and behavior and flat or inappropriate affect.(3) **Catatonic**(also in the most severe category) .This type was once seen frequently in chronic hospitals but is now rare.The characteristic features are motor immobility with retention of postures which have been set by the examiner (cataplexy) or stupor or excessive motor activity which is unrelated to external stimuli. Extreme negativism ,mutism and gegenhalten similar to frontal lobe disease may be present. Posturing ,mannerisms and grimacing may be present suggesting dystonia, or dyskinesias of basal ganglia disease.(4) **Undifferentiated** which does not clearly fall into the more specific subtypes noted above. (5) **Residual** in which positive symptoms are attenuated but negative symptoms are still present

Etiology of schizophrenia:

¹ The term schizophrenia was proposed by Bleuler to describe not the splitting of personality (into multiple personalities) but rather the divorce of one's self from reality (Autism) and the dissociation of thought processes, emotion and perception from the reality of the external world.

Neuropathology and Neuroimaging Studies: Many of these studies have been reviewed by Roberts et al (1997). The study of the underlying cellular neuropathology of schizophrenia involved those early leaders in the study of the cytoarchitecture of the cerebral cortex such as Alzheimer, Oscar Vogt, Spielmeyer and Schotz. Essentially, early findings as regards frontal cortex, could not be confirmed when quantitative studies with age matched controls were utilized. More recent careful morphometric studies have demonstrated reductions in volume of medial temporal limbic structures and abnormalities in the pattern of the temporal lobe gyri. See Shenton, et al, 1992.

The development of modern neuroimaging techniques has allowed a fresh approach to the problem, in vivo changes can be clearly delineated. CT scans demonstrated enlarged ventricles and widened sulci. More specific findings have been noted in MRI studies. Suddath et al, 1990, studied monozygotic twins who were discordant for schizophrenia - the hippocampus was smaller bilaterally with secondary enlargement of the ventricles in the twin affected by the schizophrenia, as opposed to the normal twin. Sets of twins without schizophrenia did not manifest such differences. The very careful quantitative MRI studies of Shenton, et al, 1992; demonstrated reductions of volume of gray matter in the left anterior hippocampus - amygdala - by 19%, the left parahippocampal gyrus by 13%, and the left superior temporal gyrus by 15%. The reduction in volume of the left posterior superior temporal gyrus, correlated with the degree of thought disorder. In other studies, these MRI findings have been noted early in the disease, prior to the introduction of any neuroleptic agents and prior to any process of deterioration. Other MRI studies reviewed by Foong et al (2001) have reported regional reductions in grey matter of the frontal or temporal lobes or hippocampus or amygdala, with the frontal lobe findings particularly associated with a predominance of negative symptoms. The specialized quantitative MRI studies by Foong et al (2001) indicated diffuse bilateral cortical abnormalities most prominent in the frontal and temporal areas. In patients with severe negative symptoms, there was as well significant reduction in the left parietal and bilateral temporal - occipital cortex and the genu of the corpus callosum. Studies of regional cerebral blood flow (RCBF) reviewed by Friston, et al, 1992 - suggested correlated decreases in RCBF in prefrontal and left parietal association areas when psychomotor poverty was present. Reality distortion was associated with increased RCBF in the left parahippocampal regions.

Dopamine hypothesis: The significant improvement in the symptoms of schizophrenia following the administration of dopamine receptor antagonists has led to the dopamine hypothesis regarding the underlying etiology of schizophrenia which suggests abnormal function in the dopaminergic meso frontal and mesolimbic circuits (refer to Kandel -2000)

Epidemiology - The overall prevalence of schizophrenia in the population is at least 0.5 cases per 100. Some estimates suggest overall cases, at home, in hospitals, in remission, or exacerbation may be close to 1.0 per 100. In terms of the population in mental hospitals prior to the introduction of the neuroleptics, patients with the diagnosis of schizophrenia, constituted 20-30% of admission and occupied 50% of the beds.

Genetics - The studies of Kallman in the 1940's indicated incidence in parents or siblings or fraternal twins to each be 11%. Monozygotic twins of an affected twin demonstrated a 68% incidence of schizophrenia. If both parents were affected, the incidence in the offspring was 50%. Other studies have reported statistics for identical twin pairs which were less than those found by Kallman, but still greater (e.g., 25-50%) than the 11% of siblings and fraternal twins affected.

Children of schizophrenic parents, removed from the home at an early age, into homes of normal adoptive parents, also developed schizophrenia at the same rate. Similar studies in monozygotic twins separated at any early age also confirmed these genetic factors. These studies suggest the importance of nature (genetics) over nurture. (cultural and learned factors). The precise type of inheritance remains uncertain. An autosomal dominant pattern with variable penetrance has been suggested.

AFFECTIVE OR MOOD DISORDERS

This large group of patients includes not only those patients with a psychosis but the much larger category of non psychotic mood disorders particularly depression. Depression is common occurring frequently not only among psychiatric admissions but also among general medical admissions. Depression is the most common reason for psychiatric liaison consultation for patients on a medical service. The major categories of depressive illness include (1) grief reaction (2) reactive or secondary depression in medical and neurological disorders (3) endogenous or primary depression +/- anxiety and agitation, and bipolar manic depressive disorder (4) depression as part of a neurosis or personality disorder.

Among the endogenous affective disorders, the following subcategories are recognized (1) Unipolar disorders, usually referring to a depression of mood and less often to a manic (severe) or hypomanic (less severe) state. (2) bipolar disorder in which both manic and depressive episodes occur.

Neurological basis (Brumback-1993) : In patients with cerebral infarcts , depression is most likely in those with infarcts of the left hemisphere involving the lateral frontal cortex or basal ganglia. Other studies ,however have implicated the right frontal area in patients with traumatic penetrating injuries particularly as regards the affective aspects of language (prosody) and gesture .Psychotic depression with hallucinations and delusions have been reported in patients with right temporal parietal infarcts.

As regards patients with endogenous depression ,no clear cut neuropathological findings have been reported .However Tebartz van Elst et al(1999, 2000) have reported an increased volume of the amygdala on quantitative MRI studies in patients with depression or bipolar disorder . Moreover PET scan and functional MRI studies by Drevets et al (1997) have demonstrated an area of decreased activity in the medial inferior prefrontal cortex (and anterior cingulate gyrus) below the genu of the corpus callosum during depression. During the manic phase of manic depressive disorder activity in this area is increased.

Epidemiology and genetic basis of affective disorders : Manic - depressive disease may be seen at any age. Depression is common in the elderly and often accompanies loss of spouse, ,many of the degenerative diseases of the nervous system and the various chronic medical disorders. The overall lifetime risk for a major depression is 8-12 % in males and 16-24 % in females. Patients with affective disorder have a high frequency of relatives with the same disorder .Among first degree relatives, 14-25% will be affected.. Adoptees have the same risk as the original biologic family as opposed to the adoptive family.

Bipolar disorder constitutes 10 % of all affective disorders and has a characteristic onset in younger/ middle aged adults with some cases already evident in adolescence. The overall frequency of bipolar disorder in the general population is 1-2 % . In contrast first degree relatives have a 15 % risk for bipolar disorder. Among twins 72 % of monozygotic twins are concordant for bipolar disease compared to 14 % of same sex dizygotic twins. In contrast , in monozygotic twins with unipolar endogenous disorder the concordance rate is 40% whereas the rate for dizygotic same sex twins is 11%.

Biochemical correlates : In patients with endogenous depression, metabolites of norepinephrine and serotonin are decreased in the CSF. In patients with endogenous mania ,metabolites of norepinephrine .are increased in the CSF. The tricyclic antidepressants (general nonspecific reuptake inhibitors of biogenic amines)and the monoamine oxidase inhibitors which are effective in treating depression increase norepinephrine and serotonin at selective receptor sites in the hypothalamus and limbic system. The tricyclic antidepressants also have anticholinergic side effects. The selective serotonin reuptake inhibitors (SSRI's) which have greater action on serotonin receptors than on norepinephrine sites ,overall are less effective than the tricyclic antidepressants in severe cases but also have less anticholinergic side effects .

In patients with depression, a hypothalamic dysfunction also occurs with increased secretion of ACTH and a secondary increase in secretion of cortisol from the adrenal cortex.

Patients with manic symptoms are treated with lithium carbonate ,but since time is required to achieve a therapeutic effect, neuroleptics (dopamine antagonists) are employed to decrease agitation . Electroconvulsive therapy may be used for severe episodes of severe endogenous depression or of mania. Suicide is a major risk in all types of affective disorders . If suspected to any degree immediate psychiatric consultation must be obtained , and immediate hospitalization arranged.

ANXIETY DISORDERS (NEUROSES)

A variety of syndromes are include under this category of disease (1) generalized anxiety (2) acute panic attacks (or acute anxiety attacks and hyperventilation syndrome),(3) post traumatic stress disorder ,(4)phobic disorders,(5)obsessive compulsive disorder,(6)Hysteria with conversion symptoms and (7) Hypochondriasis. In general , there are no clear cut structural abnormalities in these disorders ,although obsessive compulsive disorder (OCD) may also be seen in diseases of the basal ganglia .

Panic attacks : The autonomic activation that occurs with acute panic attacks is similar to that which occurs with fear .Attacks can be induced by intravenous administration of or inhalation of carbon dioxide .The adrenergic locus ceruleus and the serotonergic centers have been implicated in anxiety. In addition in patients with panic attacks , blood flow to the right limbic system and parahippocampal gyrus are increased between attacks .Attacks may be

decreased with the use of the antidepressants described above or with the use of benzodiazepines (the latter however have possible substance abuse potential).

Note that anxiety and hyperventilation may certainly occur in a number of systemic metabolic disorders such as hypoglycemia, hyperthyroidism, pulmonary disease, etc.

Hysteria: Patients with the conversion symptoms of hysteria are usually referred for neurological consultation prior to any psychiatric referral because the patient presents with apparent paralysis, or sensory deficits or blindness, or amnesia (dissociative state). Related disorders include dissociative reaction, fugue state, multiple personality (dissociative identity disorder) and compensation neurosis. This diagnosis accounts for 1-3% of all general hospital admissions. The term hysteria refers to the ancient concept among the classical Greek physicians that the symptoms represented the effects of a wandering uterus. The term conversion refers to the psychoanalytic concept that ego defense mechanisms in response to unconscious psychological conflicts convert the anxiety generated into physical symptoms. Most patients are female although conversion symptoms may occur in males. It is of importance to recognize that the initial modern studies on hysteria were undertaken by physicians who dealt with neurological disorders such as Charcot, Janet, Breuer and Freud (see Breuer & Freud –1957). In hysteria, the symptoms are not feigned, they are not the result of malingering. Vuilleumier et al, (2001) have recently reported that in patients with unilateral motor +/-sensory hysterical symptoms, there are significant focal contralateral deficits on SPECT scan during passive vibratory stimulation of both hands. These decreases in regional cerebral blood flow occurred in the contralateral thalamus, caudate and putamen. These focal deficits resolved on recovery from the focal neurological deficits. The authors suggest that limbic inputs from the amygdala and orbital frontal areas as a result of emotional stresses might modulate the activity of specific basal ganglia and thalamo cortical circuits. In addition, actual lesions in these areas may result in akinesia and motor/sensory neglect syndromes. Thalamic lesions may result in the useless limb which the patient fails to move despite an absence of motor lesion. They also hypothesize that the failure to move the limb might derive from the more primitive reaction seen in some animals such as the rabbit etc of instinctive freezing or immobilization in response to perceived life threatening stimuli (the appearance of a dog).

Obsessive/compulsive disorder: obsessions are thoughts which keep recurring despite the patient's desire to get rid of the idea for example the constant preoccupation that one is going to be contaminated by dirt or germs. The compulsions are the motor acts (rituals) that are performed to deal with the obsession, for example a constant hand washing routine. On PET scans, patients with this disorder are found to have increased metabolic activity in the dorsolateral prefrontal, and anterior cingulate cortex and the caudate nuclei (Buchsbaum et al 1997). Treatment with tricyclic antidepressants or SSRI'S produces a significant improvement in symptoms and a return to normal levels of metabolic activity in the caudate.

PERSONALITY DISORDERS

A variety of disorders are included within this category. Unfortunately, the terminology overlaps with some of the anxiety disorders listed above. In order of frequency in a large series (Winokur & Crowe-1976) the more common may be listed as follows: (1) hysterical or histrionic, (2) passive aggressive, (3) antisocial which overlaps with criminal behavior, (4) passive dependent, (5) schizoid –possibly a premorbid or less marked variant of schizophrenia (6) obsessive –compulsive personality –perfectionistic with excessive concern with details, standards and with a possible predisposition to OCD, (7) inadequate personality, (8) paranoid personality –possibly premorbid condition predisposition for paranoid schizophrenia.

We have already discussed above the effects of prefrontal lesions in producing alterations in personality, in some cases resulting in a loss of inhibitions and antisocial behavior. The “pseudopsychopathic” syndrome may follow damage to the prefrontal areas. Psychopathic is a term formerly employed instead of the more recent terms of antisocial or sociopathic personality disorder. Prefrontal damage early in life may result in antisocial behavior with problems in the control of anger and aggression. Studies of violent antisocial individuals have indicated smaller prefrontal areas. As discussed above, the orbital prefrontal areas are involved in a circuit that includes the amygdala and the anterior cingulate cortex and violent behavior may reflect dysfunction in other parts of this circuit (Davidson et al –2000).

DEVELOPMENTAL DISORDERS WITH ALTERATION IN SOCIAL BEHAVIOR

Autism and Asperger's syndrome are the two entities included here. We have already defined the term autism in relation to schizophrenia (the divorce of one's self from reality) and have discussed the role of the amygdala in the recognition of the emotional facial expression of others. In children with autism there is a discrepancy between (a) the development of motor skills (which are not entirely normal with findings relevant to gait and coordination)

and at times types of retentive memory and (b) the poor development of social /emotional interactions. Eye contact is avoided. Stereotyped motor automatisms may develop. Some patients can achieve a high level of intellectual function (Grandin-1997) although 78% are classified as mentally deficient. In some cases, the child appears to develop normally until 18-24 months of age and then regression occurs. In other cases, abnormalities of behavior are noted earlier in life and no speech develops. The overall incidence is 4.5–20 per 10,000 with a 4 or 5: 1 male predominance. There is an increased risk of the disease in siblings and identical twins. MRI studies have demonstrated cerebellar hypoplasia, which may affect some aspects of motor learning and cognitive function and attention shifting capacity (refer to cerebellar chapter). The careful neuropathologic studies of Kemper & Bauman (1993) have found alterations in hippocampus, amygdala, entorhinal cortex, septal nuclei, mammillary bodies as well as the cerebellum.

Some authors have considered Asperger's disorder a less severe form of autism. However the location and type of pathology differ from the findings in autism (Aronowitz et al ,1997). Neocortical abnormalities are present with areas of polymicrogyria and other aspects of a neuronal migration disorder. This has suggested etiologic events prior to the end of the fifth prenatal month. Verbal IQ is usually higher than performance IQ. Recognition of emotion in the facial expression of others is usually normal.