Introduction

Stroke is a distressing event and in the western world it ranks the second leading cause of death in adults worldwide ***(Chemerinski et al, 2006).*** However the number of stroke survivors is increasing (around 2/3rd of 700.000 stroke patients each year survive in the United States alone, according to the national institute of neurological disorders and stroke (NINDS) because of the improvement in the management of acute stroke. This has resulted in a larger group of patients with important residual physical and psychological disabilities.

There are 2 main theories have been suggested to declare the association between stroke and its psychiatric sequelae. The first theory claims that the psychiatric sequelae are psychological reactions to the subsequent post-stroke disability, the second theory postulates that post-stroke psychiatric symptoms are specifically due to direct brain damage and according to the damaged area the symptoms may vary ***(Starkstein et al,1992)***.

Many people who survive a stroke feel fear, anxiety, frustration, anger, sadness, and a sense of grief for their physical and mental losses. These feelings are a natural response to the psychological trauma of stroke. Some emotional disturbances and personality changes are caused by the physical effects of brain damage ***(Bourgeois et al,2004).***

Mood disorders mainly Clinical depression or post-stroke depression (PSD) which is a sense of hopelessness that disrupts an individual's ability to function, appears to be the emotional disorder most commonly experienced by stroke survivors. Donald M. Hilty, who is director of mood disorders and health services research at the University of California at Davis, said the prevalence of major depression after a stroke could range from 10% to 40% and minor depression from 12% to 29%, depending on when it is detected.

The need for better detection and periodic testing was particularly important for PSD. The depression may not initially be present. Instead, it may show up in a month, three months or six months. So, if clinicians screen for depression in the months after a stroke, they would likely identify several more cases. Patients with post-stroke depression often differ from those with primary depression in that they have more cognitive impairment (memory and concentration problems), irritability, more psychomotor retardation (or slowing) and more mood lability ***(Bourgeois et al,2004).***

Other post-stroke neuropsychiatric illnesses, including anxiety disorders, apathy, delusional disorders, personality disorders, sexual dysfunction and cognitive impairment are also common. Clinicians need to be on the lookout for psychiatric symptoms not only immediately post-stroke, but up to six months after the event ***(Angelelli et al, 2004).***

Anxiety has been associated with stroke, The Prevalence of Post-stroke anxiety is about 23% ***(Angelelli et al, 2004)***, with a majority of PSA patients also having PSD.

Emotional lability is a common complication of stroke patients. It is characterized by sudden, easily provoked episodes of crying that generally occur in appropriate situations and are accompanied by a congruent mood change. Pathological laughing and crying is a more severe form of emotional lability and is characterized by episodes of laughing and/or crying that are not appropriate to the contex ***(Robinson and Starkstein, 2002).***

The clinical presentation in a given individual may depend on the localization of the pathologic process. Strokes that preferentially affect frontal lobes or subcortical structures are more likely to manifest with prominent personality change. Duffy and Campbell (2001) identify three distinct prefrontal syndromes – dysexecutive type, disinhibited type, and apathetic type.

Right hemisphere strokes have been shown to evoke personality changes in association with unilateral spatial neglect, anosognosia, motor impersistence, and other neurological deficits ***(American Psychiatric Association, 2000)***.

Patients with left hemisphere lesions may become paranoid ***(Benson, 1973)***, while injury to the right hemisphere

occurring early in life may lead to a personality pattern characterized by shyness, depression, isolation and schizoid behaviour ***(Eslinger and Geder, 2000).***

The cognitive impairment can be a short-term problem marked by poor attention, poor memory, and a waxing and waning ability to be present. When the cognitive impairment continues, it may indicate the presence of vascular dementia ***(Hilty et al, 2005).***

The relative risk of dementia after stroke is five-fold compared with that in age-matched controls, and lasting longer than 4 years, although it is highest in the first 6 months ***(Tatemichi et al, 1994).*** After excluding approximately 15% of patients, who have prior dementia, the cumulative risk over 3 years is 30% ***(Hénon et al, 2001).***

Madureira et al, (2001) have recently reported rates of post-stroke cognitive impairment of approximately 40-55% and reported also that 55% of 220 patients had evidence of cognitive impairment insufficient for diagnosis of dementia in the following 3 months post stroke onset, 6% of them only had dementia**.**

Psychosis may take several forms following stroke. The most common types are the transient psychotic symptoms, Patients with severe mood disorder, either depression or mania, also experience psychotic episodes after stroke. The overall rate of psychotic symptoms gradually reduces to roughly 10% at 1

year. In elderly patients, occult cerebrovascular disease may cause a diathesis for psychotic forms of depression. Case reports of schizophrenia like psychosis have been reported after stroke, but rare ***(Alex et al, 2004).***

Sexual dysfunction and dissatisfaction with sexual life are common in both male and female stroke patients and in their spouses. Psychological and social factors seem to exert a strong impact on sexual functioning and the quality of sexual life after stroke ***(Korpelainen et al,1999).***

Aim of the Work

1. To review the literature of post-stroke psychiatric manifestations.
2. To correlate the psychiatric manifestations with the anatomical sites of the lesions.
3. To Review the recent update investigations for early detection of the most common post-stroke psychiatric disorders and management for better outcome

Brain Organization and Cerebral Basis of Emotion

As early as the 19th century Hughlings-Jackson (1875) recognized that symptoms associated with brain lesions may produce both loss of normal function as well as emergence of new, sometimes abnormal symptoms. These new symptoms may arise from the effect of injury on distant uninjured brain areas leading to the release of normally "inhibited" functions or the loss of normally "activated" functions. Thus, we will review brain anatomy, particularly the limbic region, to help understanding the basis of emotional disorders following brain ischemia.

Language is usually mediated predominantly by the left or dominant hemisphere. Language, however, includes a broad range of function such as reading, writing, comprehension, expression and repetition of language, naming objects, appropriate syntax, grammatical use of language, and virtually any reasoning task that requires words. The non-dominant right hemisphere, on the other hand, mediates functions such as recognition of shapes, appreciation of the relative position of objects in space, musical ability, and facial recognition. Thus, the brain is both anatomically and functionally lateralized. In trying to understand the brain structures which subserve emotion, differences in hemispheric structure as well as

localization of function must be taken into account for their possible effect on the nature and type of emotion ***(Robinson et al, 2006).***

The anterior regions of the frontal lobes appear to be important in drive, attention, motivation, inhibition of socially inappropriate behavior, temporal (time) organization as well as sequencing, and recognition of organizational themes. There are three general regions of the frontal lobe that are recognized as having different functional roles: the medial portion (including the anterior cingulate), the lateral area, and the orbitofrontal region. Injury to the dorso- and ventrolateral prefrontal cortex is characterized by cognitive executive function deficits as well as depressive disorder. Orbitofrontal injury is characterized by marked personality change with disinhibition, irritability, and unconcern. Medial-frontal injury is characterized by lack of drive and motivation ***(Robinson et al, 2006).***

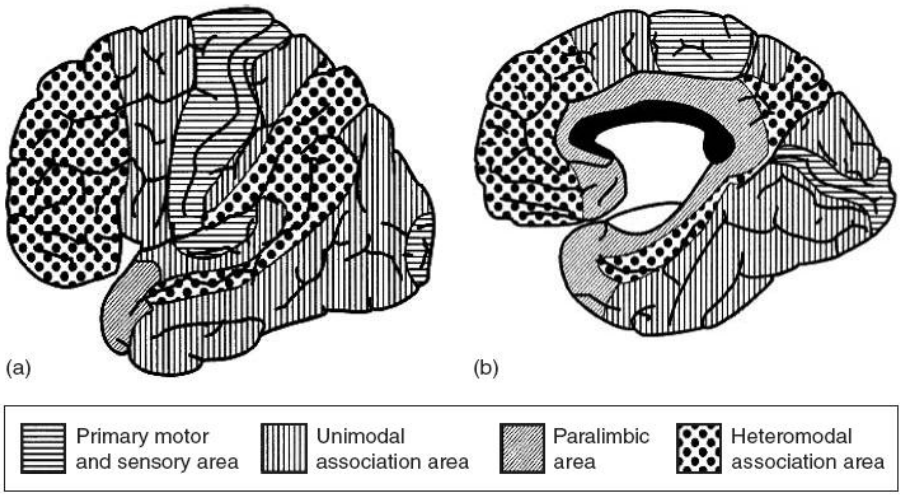

Figure (1): Distribution of primary and association cortex on lateral (a) medial and (b) view of the brain ***(Modified from Coffey and Cummings, 1994).***

The neocortex is differentiated into primary motor and sensory areas as well as unimodal and heteromodal association areas. The distribution of these regions is shown in Fig. (1). Primary sensory areas subserve vision, hearing, and somatic sensations and are located in the parietal, temporal, and occipital cortex. Primary motor cortex subserves movement and is located in the posterior portion of the frontal lobe. The association cortex is the largest functional brain region occupying more than three-quarters of the neocortex ***(Mesulam, 1985).*** The unimodal association areas subserve a second level of information processing after primary sensory cortex. These areas serve modality specific information processing and are located in the temporal, parietal, and occipital cortices (Fig.1). The unimodal auditory area, for example, is located in the posterior and superior parietotemporal junction. Lesions produce a modality specific loss of language and comprehension (i.e., fluent aphasia). The heteromodal association cortex mediates the highest level of information processing. In humans, there is general agreement that the inferior parietal lobule and prefrontal cortex are heteromodal association areas. Lesions of these areas produce complex behavioral or cognitive deficits which transcend unimodal sensory impairments. Prefrontal lesions, for example, produce deficits in motor programming, memory retrieval, set shifting, abstraction, and judgment.

Thus, the cognitive and behavioral processes of the human brain can be divided into a regional neuroanatomy of the cerebral

cortex. Processing of sensory information proceeds from primary to association to integrative regions. Cerebral infarctions, depending upon their location, produce characteristic syndromes of behavioral, cognitive, and emotional deficits ***(Robinson et al, 2006).***

Papez (1937) proposed that several of these limbic structures are particularly important in emotion. These limbic structures which compose the "Papez circuit" form a tight circular pathway, starting in the hippocampus (a structure which plays an important role in memory), extending through the fornix to the mamillary bodies (also important in memory), and to the anterior nucleus of the thalamus (important in sensory processing), with radiation to the cingulate cortex and back to the hippocampus (Fig. 2). This circuit has connections to both memory and sensory areas of the brain.

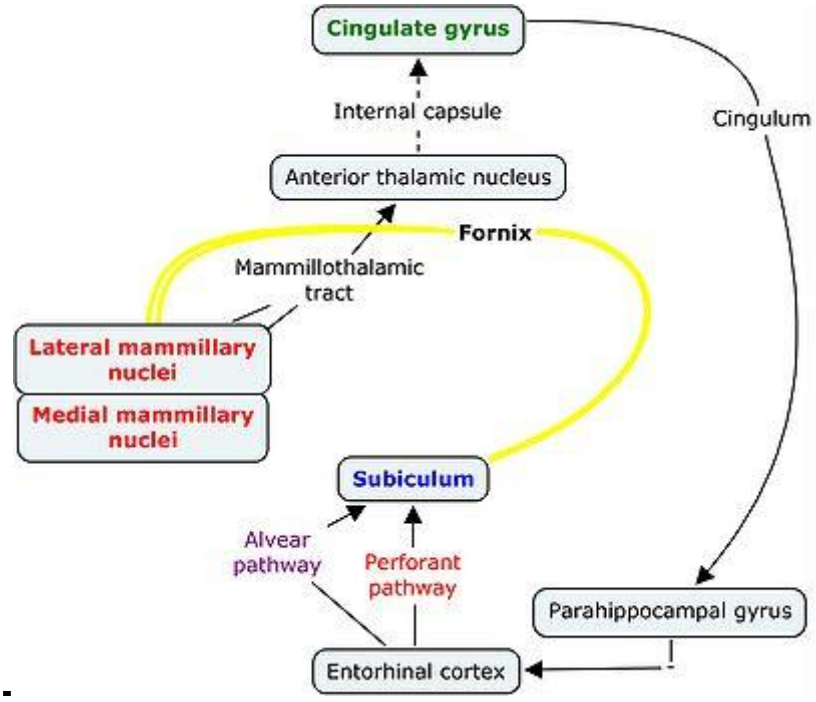

Figure (2): Papez circuit ***(Described by James Papez in 1937).***

Cortical limbic structures are three-layered as opposed to the six-layered neocortex. All of the limbic structures are connected to the hypothalamus and through indirect connection with the amygdala and hippocampus. The hippocampus, as indicated previously, plays a major role in memory while the amygdala is related to control of aggression and affective response to incoming sensations. The amygdale also modulates anxiety, associations between stimuli and reinforcement, and formation of emotional memory. The parahippocampal gyrus (which includes the entorhinal cortex) is a meeting point where sensory information integrates with brain activity in higher cortical regions. Thus, sensory information first reaches the cortex at unimodal primary sensory areas. It is then projected to secondary sensory areas and then to multi-modal association cortex. These cortical regions project to the parahippocampal gyrus providing integrated sensory information. This integrated information goes to the hippocampus and amygdala which receive inputs from the hypothalamus and other limbic structures. The cingulate gyrus appears to be involved in highly complex mammalian functions including maternal behavior, play, pain, and attention. This structure has been surgically interrupted as a treatment for obsessive compulsive disorder, pain, and depression. The basal ganglia includes the caudate nucleus, putamen, and globus pallidus. The striatum refers to the caudate and the putamen. The caudate is a large nucleus that

runs along the length of the lateral ventricles and is continuous anteriorly with the putamen. Medially, within the head of the caudate nucleus, is the nucleus accumbens.Nucleus accumbens and some adjacent dopamine rich nuclei are often termed the ventral or limbic striatum. The extended amygdala outputs to the ventral striatum are thought to influence emotional motor behavior ***(Robinson et al, 2006).***

The basal ganglia mediate cognitive and language functions as well as emotion and motor processes. Five cortical subcortical circuits have been described ***(Alexander et al, 1986)*** that link specific cortical regions with basal ganglia and thalamus. The five loops originate in the supplementary motor cortex, the frontal eye fields, dorsal lateral prefrontal cortex, the orbital frontal cortex, and the anterior cingulated cortex, respectively. The three behaviorally and emotionally relevant circuits involve the dorsal lateral prefrontal cortex, the orbital frontal cortex, and the anterior cingulate cortex and are schematically shown in Fig. (3). Each circuit has sequential connections between the frontal and/or temporal lobes, caudate or putamen, globus pallidus, and substania nigra and thalamus with connections back to the frontal lobes. There are also indirect pathways connecting the subthalamic nucleus, the globus pallidus externa, and the globus pallidus interna. The ventral striatum flows to the ventral pallidum and to the thalamus. The ventral pallidum is also called the substantia innominata, an area rich in acetyl choline containing neurons.

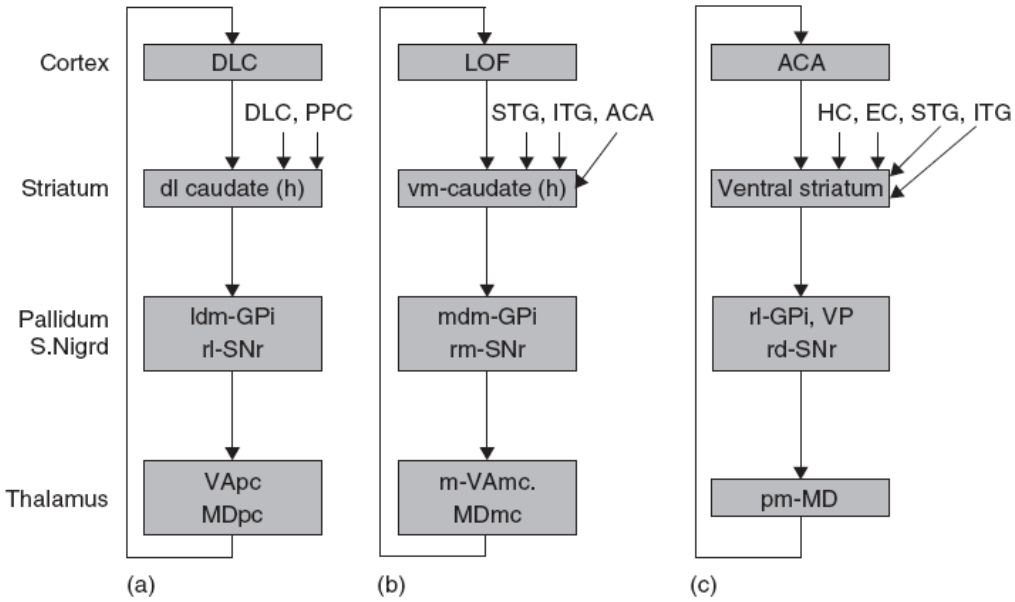

Figure (3): The three (a–c) circuits relevant to behavior are shown. Injury to the dorsolateral prefrontal circuit produces executive dysfunction, damage to the orbitofrontal circuit causes disinhibition, and dysfunction of the medial frontal circuit produces apathy. VA: ventral anterior nucleus; MD: medial dorsal nucleus; DLC: dorsolateral prefrontal cortex; PPC: posterior parietal cortex; STG: superior temporal gyrus; ITG: inferior temporal gyrus; ACA: anterior cingulate area; HC: hippocampal cortex; EC: entorhinal cortex; Gpi: internal segment of globus pallidus; Vapc: ventralis anterior pars parvocellularis; MDpc: medialis dorsalis pars parvocellularis; pm: posteromedial; LOF: lateral orbital frontal

The open afferent and efferent connections to the frontal-subcortical circuits mediate coordination between functionally similar areas of the brain. Specific chemoarchitecture and multiple neurotransmitter interactions modulate the functional activity of each circuit. Dorsolateral prefrontal circuit lesions cause executive dysfunction, orbitofrontal circuit lesions lead to

personality changes characterized by disinhibition and anterior cingulate circuit lesions present with apathy. The neurobiological correlates of neuropsychiatric disorders including depression, obsessive-compulsive disorder, schizophrenia and substance abuse, imply involvement of frontal-subcortical circuits ***(Tekin and Cummings, 2002).***

In summary, the cerebral basis of emotion appears to involve both limbic and paralimbic structures. A great deal of interest has been focused on the dorsal lateral, orbital frontal, and cingulate circuits involving the striatum and the thalamus, and how they may mediate depression and other emotional syndromes. Future research may identify how these structures as well as neuronal response to injury may lead to post-stroke emotional disorders and their natural course of recovery ***(Robinson et al, 2006).***