CORTICO-STRIATO-CEREBELLAR CIRCUIT DYSFUNCTION IN PSYCHOTIC (DELUSIONAL) DEPRESSION

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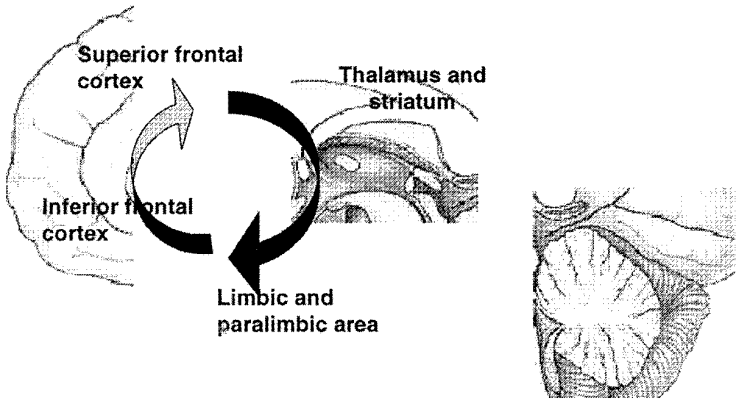
"Is emotion magic product or is it a physiologic process which depends on an anatomic mechanism?" In attempting to answer his question, ***Papez*** (1937) proposed that "the hypothalamus, the anterior thalamic nuclei, the gyrus cinguli, the hippocampus, and their interconnections constitute a harmonious mechanism which may elaborate the functions of central emotions, as well as participate in emotional expression." The limbic system as defined by Papez has been shown in clinical and experimental studies for over half a century to be critical for the experience and expression of emotion. Mayberg et al (1999) showed that with sadness, regional cerebral blood flow (rCBF) increases in limbic and paralimbic (subgenual cingulate, anterior insula) and decreases in neocortical areas (dorsolateral prefrontal and inferior parietal areas) in normal healthy subjects. Drevets (2000) reviewed the neuroimaging studies of mood disorder and concluded that two circuits are highly responsible from pathogenesis of major depression;

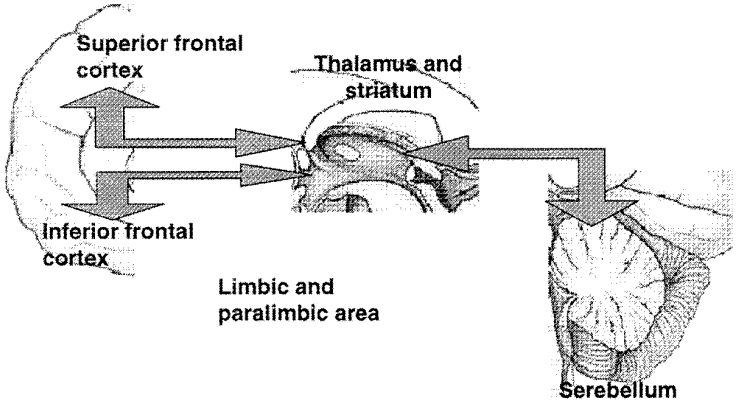
1. **limbic-thalamic-cortical circuits (LTC)**, involving the amygdala, medial thalamus, and orbital and medial prefrontal cortices
2. **limbic-cortical-striatal-pallidal-thalamic circuits (LCSPT),** involving the components of the LTC circuit along with parts of the striatum and pallidum.

Recently my colleagues and I (Gönül et al, 2002)

Figure 1: Circuits Playing role in the pathogenesis of major depression with psychotic and non-psychotic features.



limbic-cortical- striatal-pallidal-thalamic circuits (LCSPT), previously defined by Drevets



Cortico-striato-cerebellar circuit in psychotically depressed patients

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presented our SPECT data in psychotically depressed patients. Twenty-eight subjects with primary, familial pure depressive disorder were included in this neuroimaging study. Twelve had of them had mood congruent delusions. They were drug-free for at least four weeks prior to SPECT scan. Control group was consisted of 16 healthy subjects.

Repeated measures of ANOVA showed that rCBF patterns were significantly different between depressed groups and control group. Although depressive patients without psychotic symptoms had dysfunction in LCSPT circuit, psychotically depressed patients had abnormal rCBF in frontal lobe, striatum and cerebellum (figure 1).

The cerebellar projections to prefrontal cortex from cerebellum via thalamus and striatum had been studied extensively but the availability of transneuronal viral tracers that replicate in synaptic neurons and amplify the detectable signal at second order sites has provided new insights into this feedback circuitry (Middleton and Strick 1994). These data showed that a cortical association area such as Brodmann's area 46 (inferior cortical region in our study) sends efferents to the cerebellar cortex that in turn sends information back to area Brodmann's area 46. It is likely that this pattern is reproduced throughout the cerebrocerebellar system, such as that cortical areas projecting to cerebellum receive information back to cerebellum.

Fronto-cerebellar dysfunction has been previously proposed by Andreasen et al (1999) in schizophrenia as "cognitive dysmetria". The main idea is, there is an abnormality in a basic process that regulates the synchrony of both thought and action. If the synchrony is "off," much like sending signals at the incorrect baud rate between two nodes in a computer network, the signals become garbled. As a consequence, the individual with mistimed information transfer may incorrectly connect perceptions and associations and misinterpret both external and internal processes, leading in turn to delusions or hallucinations.

It is not known the exact mechanism is delusions in major depression. Recent SPECT findings in our lab give us an idea that there may be a common pathology for formation of delusions in schizophrenia and psychotic depression.

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KAYNAKLAR

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