IMPLICATION OF GABAERGIC AND SEROTONERGIC RECEPTORS IN NEUROPSYCHIATRIC DISORDERS

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ABSTRACT

BACKGROUND
Despite the numerous emerging antidepressant treatments selective serotonin reuptake inhibitors still remain the treatment of choice. There are some preclinical studies which have shown that low brain levels of Gamma aminobutyric acid are associated with depression. There is also evidence that some drugs that mimic GABA have potent antidepressant and mood stabilising properties.

KEYWORDS
GABA, Serotonin, PFC.

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GABA is primarily synthesised from glutamate by the enzyme L-glutamic acid–L-decarboxylase. It is subsequently metabolised by GABA transaminase to succinic semialdehyde and succinic acid.

Serotonin Receptors
These receptors belong to G protein-coupled receptors (GPCRs) and ligand-gated ion channels (LGICs), present in all the tissues as per their distribution. They mediate both excitatory and inhibitory neurotransmission. 5-HT is synthesised from amino acid tryptophan.

Role of GABAergic and Serotonergic Receptors in Psychiatric Disorders
Serotonin modulates the release of GABA in the pre and postsynaptic neurons. Animal studies showed that serotonin activation leads to increased presynaptic release of GABA and decrease in the postsynaptic response to GABA, which mainly occurs through intracellular mechanisms. The serotonin expression has been determined by various analytical techniques which showed that 5HT1A and 5HT2A are found in the pre-frontal cortex and produce multiple co-expression of 5HT receptors in the neurons. Apart from that 5HT2 receptor activity is modulated by GABAergic receptor through PKC mediated pathway. In vitro kinase assay it has been proven that increased PKC phosphorylation plays an important role in mediating the serotonergic modulation of GABA currents in the pre-frontal cortex neurons.

Buspirone, an anxiolytic drug has a selective partial agonistic action on 5HT1A receptors. By stimulating presynaptic 5HT1A receptors, it reduces the activity of dorsal raphe serotonergic neurons. Clinical trial studies have proved that its therapeutic efficacy is similar to that of first line antidepressant drugs. So it can be used as an antidepressant adjunct.

CONCLUSION
In depression, the pathophysiology is complex and the metabolic activity is decreased in the caudate nucleus and prefrontal cortex. Patients who have attempted suicide have significantly lower CSF levels of 5HT-metabolite 5-hydroxyindoleacetic acid. To have a good therapeutic
response, the GABAergic drugs may be combined to lessen anxiety in early stages of depression.  

REFERENCES