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Editorial : Calcium Channel Blockers in Mental Health and Neuro Sciences

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Calcium is a familiar ion; first year medical students learn of its physiological importance in a host of situations, such as in nutrition, in enzymatic reactions, in muscle contraction, and in the structure of bone.

Calcium has long been known to also play an important role in the physiology of the nervous system, for example, it is well recognised that calcium is a co-factor in several enzymatic processes in the central nervous system (CNS), that release of neurotransmitters from synaptic vesicles is calcium-dependent, that the stability of the neuronal membrane is partly regulated by calcium, that calcium is involved in neurotoxic processes etc. [1].

Several cognitive functions have been associated with calcium mechanisms. For example, the involvement of calcium is learning and memory processes is widely documented [2], [3]; most of the work to-date concerns calcium influx through receptors for excitatory amino acids [4]; compounds that block inonotropic glutamate receptors and inhibit calcium inflow, such as MK 801, are reported to impair memory [5], [6].

Voltage-dependent calcium channels, of which the best characterized are those that contain dihydropyridine binding sites, form a second mechanism controlling calcium inflow into the cells [7]. In recent years, these calcium channels in the neuron have assumed substantial importance; treatments affecting these channels have been shown to affect a number of functions related to the CNS. For example, repeated electroconvulsive shocks upregulate voltage dependent calcium channels, which effect appears to increase sensitivity to pain, enhance responsiveness to dopaminergic agonists etc [8], [9], [10].

Drugs that block calcium channels were initially introduced for their role in the control of the cardiovascular response in conditions such as hypertension. Such drugs are now documented to have several important roles in neurospychiatry. For example, verapamil has been suggested to have mild anxiolytic and antipanic activity [11]. Nimodipine has been suggested to enhance cerebral blood flow and increase cholinergic tone, and thereby benefit memory functioning in animal models [12]. as well as in clinical populations such as Alzheimer's disease [13], [14].

Verapamil and felodipine have been suggested to attenuate retrograde amnesia induced by electroconvulsive therapy [15]. Nifedipine has been found effective in the treatment of tardive dyskinesia; substantial clinical benefit is observed, within 2 weeks of treatment, and this benefit persists at 1-year follow up as well, with continued treatment [16]. Several other potential (experimental) applications of calcium channel blockers have been suggested; these include the treatment of mania and schizophrenia and are listed by Kaplan and Sadock [17], [18].

It must however be realized that negative findings have also been obtained. For example, Clincke and Wauquier [19] found that several calcium channel blockers were ineffective in reducing amnesia induced by hypoxia. Pickar et al [20] found that verapamil was ineffective in attenuating schizophrenic symptoms. Reiter et al [21] observed that verapamil increased anxiety and depression ratings in schizophrenic patients. Lee and Lin [22] found that nefedipine and verapamil can impair memory processes Loonen et al found no benefit with diltiazem in patients with tardive dyskinesia; Popik et al [7] found no electroconvulsive shocks.

Calcium channel blockers need to be further investigated for potential therapeutic roles in neuropsychiatric disorders. It is unlikely that open trials will convey additional useful information; double-blind, placebo-controlled trials are necessary. Besides the important clinical gains potentially accruing therein, further light will be shed on the pathophysiology of neuropsychiatric disorders.

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