Cognition Enhancers: Current Strategies and Future Perspectives
Shubhada R. Ingole, Satyendra K. Rajput and S.S. Sharma*

Department of Pharmacology & Toxicology
National Institute of Pharmaceutical Education and Research
Sector 67, S.A.S. Nagar, Punjab, India-160062
*Corresponding Author: e-mail: sssharma@niper.ac.in

Cognitive impairment is the major health problem in normal aged life as well as in some disease conditions. Cognition enhancers can be used to facilitate attention abilities and acquisition, storage and retrieval of information, and to attenuate the impairment of cognitive functions associated with age and age-related pathologies. In course of time, numbers of neurotransmitters and signaling molecules have been identified which have been considered as therapeutic targets. Conventional as well newer molecules have been tried against these targets. Moreover, ongoing research progress have validated some of the newer targets such as nicotinic receptors, PDE4, 5HT6, calcium channel blockers which can be of therapeutic importance. In this review, some conventional as well as newer strategies have been discussed.

Introduction

Cognition is the physiological process of knowing, including awareness, perception, reasoning, and judgment. Cognitive functions mainly categorized into memory, attention, creativity and intelligence. It is subjective in nature and can be affected by number of factors including ageing, stress, hypertension, various pathological conditions such as dementia related to Parkinson’s disease (PD), Alzheimer’s disease (AD), schizophrenia, cancer and HIV1, 2. Cognitive enhancement may be defined as the amplification or extension of core capacities of the mind through improvement or augmentation of internal or external information processing systems. The enhancement aspects of cognition, such as learning and memory, now seems possible for people with normal age-related decline and in healthy people, although so far the effects of these cognition enhancers are modest.

Process of memory formation

During the process of learning and memory formation, brain undergoes a physical and chemical change which is called as synaptic plasticity. It shows involvement of various signal transduction pathways, induction of gene expression which results in formation of new synapses between nerve cells3. This process undergoes a continuous remodeling with time and new experiences4. Memory can be divided into mainly three types, namely, short-term memory (lasts for seconds or at the most minutes), intermediate long-term memory (lasts for days to weeks) and long-term memory (once stored, can be recalled up to years or even a lifetime later). The process of memory formation involves the binding of neurotransmitter to the receptor (NMDA, AMPA) which triggers the cascade of molecular events including activation of CREB and PKC pathways, results in the formation of new proteins i.e. receptors and some structural proteins that cement the synaptic connection between two repeatedly communicating neurons which ultimately results in development of long-term memory2-4. This process is depicted in figure.1. Certain evidences reveal the involvement of the NF-kb/Rel pathway in the regulation of synaptic plasticity. It is also shown that the inhibition of NF-kb action in neurons leads to enhanced cognitive functions5.

Cognitive dysfunction

Cognitive dysfunction, a major health problem in 21st century, one of the most functionally debilitating aspect of many neuropsychiatric disorders and neurodegenerative disorders, such as schizophrenia, depression, AD dementia, cerebrovascular impairment, seizure disorders, head injury and Parkinsonism6. Ageing play an important role in development of cognitive dysfunction such as age associated memory impairment (AAMI) by causing impairment in Long Term Potentiation (LTP) induction and synaptic plasticity7.

Enhancement of cognition

Many different strategies are proposed to enhance cognition. Most interventions target either disease pathologies or the processes underlying normal cognition, particularly synaptic plasticity. Many act via more than one pathway or target. Strategies and treatments for cognition enhancement are given as follows:

- Environmental enrichment and exercise
- Nutrients
- Herbal medicines
- Pharmaceutical drugs
- Advanced techniques and medical devices
Environmental enrichment and exercise

Environmental enrichment improves learning and memory, apparently by changes in gene expression related to structure of neuron, synaptic plasticity and transmission. Such changes might be prompted via neurotrophin expression (e.g., BDNF). Similar findings in elderly people are that leisure activities and physical exercise are linked with lower risks of dementia and cognitive decline respectively.

Nutrients

Micronutrient status can affect cognitive function at all ages. Many dietary supplements are recommended by various...
sources to improve cognition, including ‘nutraceuticals’ dietary components or similar that act like drugs. These agents are widely available in market. Such agents are usually well tolerated and no abuse potential is reported. It mainly includes vitamins, neutralteroids and fatty acids. Vitamin E is found to have antioxidant and free radical scavenging property. Also some findings showed that deficiency of vitamin B6, B12 and folate might contribute to age-associated cognitive impairment. Other includes Acetyl-L-carnitine, Alpha-lipoic acid, Lecithin, Thiamine, but there is no significant evidence of their efficiency in clinical trials. Melatonin is a hormone with clock-setting properties that is secreted at night from the pineal gland, at levels that decrease with ageing. Positive effects of melatonin have been reported on sleep and cognition in elderly people.

Herbal medicines

In traditional practices of medicine, numerous plants have been used to treat cognitive disorders, including neurodegenerative diseases such as Alzheimer’s disease (AD) and other memory related disorders. Various studies have been undergone to identifying potential new drugs from plant sources, including those for memory disorders. There are numerous drugs available in market that have been isolated from plants, e.g. alkaloids from plant sources have been investigated for their potential in AD therapy, and are now in clinical use. Usually herbal preparations are well tolerated but they may have harmful side-effects, including interactions with pharmaceuticals. Herbal medicines, such as, Ginkgo Biloba, Bacopa moniera (Bramhi), Shankhpushpi etc. has been found to increase memory power. Some of the herbal medicinal plants with potential cognitive enhancement activity are listed in table 1.

Pharmaceutical Drugs

A number of pharmaceutical compounds are in the market which has been used for their cognition enhancing property. Drugs to improve memory generally work by altering the balance of particular chemicals (neurotransmitters) in the brain that are involved in the initial learning of a memory or its subsequent reinforcement. Some of them along with their mechanism are listed in table 2. Some acts by selective enhancement of cerebral blood flow and metabolism, including enhanced glucose uptake, which may protect against the effects of hypoxia and ischemia. Reports from literature reveal that some medications currently available to patients with memory disorders may also increase performances in healthy people. Drugs designed for psychiatric disorders can also be used to enhance certain mental functions. However, the long-term effects of these drugs are unknown.

Drugs which act as cognition enhancer increase synaptic plasticity by, regulating release of neurotransmitter from the pre-synaptic terminal and increasing sensitivity and specificity of receptors and ion channels in the membranes of synapse to neurotransmitter signaling. Some of the agents also modulate the process at the transcriptional and translational level.

A. Drugs or substances acting on neurotransmitter level

Acetylcholine: In the pharmacological data, there are thousands of evidences which prove the involvement of both muscarinic and nicotinic acetylcholine receptors in encoding of new memories. Local infusions of cholinergic antagonists into specific anatomical structure demonstrate the importance of cholinergic receptors for particular aspect of memory task. A substantial decline on cognitive functions characterizes AD which further demonstrates the use of acetyl cholinesterase inhibitors (AChEIs) in AD treatment. Various AChEIs, including rivastigmine, donepezil and galanthamine, have been used for the treatment of mild to moderate AD. All of these compounds have also been proved efficacious in healthy aged people to enhance learning and memory.

Nicotine: Nicotine stimulates nicotinic cholinergic receptors and have been proposed to be act through modulation of signaling pathways, i.e. increased extracellular-signal regulated kinase 1/2 (ERK1/2) and cAMP response element-binding protein (CREB) phosphorylation. Two types of nicotinic receptors α7 nAChR and α4β2 known to be involved in cognitive function. Various results clearly support the concept that nAChRα7 agonists might provide a novel pharmacotherapy for neurological and psychiatric disorders while lacking the addictive potential of nicotine. JN403 is the selective and potent nAChRα7 partial agonist which enhances learning and memory performance in the social recognition test in mice. AZD 3480 (TC-1734) / Ispronicline, a α4β2 nicotine acetylcholine receptor partial agonist, is under clinical trials for study of its effect in AD and age-associated memory impairment.

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**Table 1. Some putative cognitive enhancing plants**

<table>
<thead>
<tr>
<th>Plant Name</th>
<th>Medicinal Plant Name</th>
<th>Medicinal Plant Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acorus calamus</td>
<td>Embelia ribes</td>
<td>Nicotiana tabacum</td>
</tr>
<tr>
<td>Angelica archangelica</td>
<td>Embelia officinalis</td>
<td>Paonia emodi</td>
</tr>
<tr>
<td>Asparagus racemosus</td>
<td>Eugenia caryophyllus</td>
<td>Panax ginseng</td>
</tr>
<tr>
<td>Bacopa monniera</td>
<td>Evodia rutaecarpa</td>
<td>Piper longum</td>
</tr>
<tr>
<td>Biota orientalis</td>
<td>Galanthus nivalis</td>
<td>Polygonum multiflorum</td>
</tr>
<tr>
<td>Boerhavia diffusa</td>
<td>Ginkgo biloba</td>
<td>Polypala tenuifolia</td>
</tr>
<tr>
<td>Celastrus paniculatus</td>
<td>Glycyrrhiza glabra</td>
<td>Pongamia pinnata</td>
</tr>
<tr>
<td>Centella asiatica</td>
<td>Huperzia serrata</td>
<td>Rosmarinus officinalis</td>
</tr>
<tr>
<td>Clitoria ternatea</td>
<td>Hydrocotyl asiatica</td>
<td>Salvia lavandulifolia</td>
</tr>
<tr>
<td>Codonopsis pilosula</td>
<td>Lawsonia inermis</td>
<td>Salvia miillormiza</td>
</tr>
<tr>
<td>Convolvulus pluricaulis</td>
<td>Lycoris radiate</td>
<td>Schizandra chinensis</td>
</tr>
<tr>
<td>Coptis chinensis</td>
<td>Magnolia officinalis</td>
<td>Terminalia chebula</td>
</tr>
<tr>
<td>Crocus sativus</td>
<td>Melissa cordifolia</td>
<td>Tinospora cordifolia</td>
</tr>
<tr>
<td>Curcuma longa</td>
<td>Nardostachys jatamansi</td>
<td>Withania somnifera</td>
</tr>
</tbody>
</table>

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**Excitatory amino acid:** It is well known that NMDA and AMPA receptor are mainly involved in induction of LTP. The antituberculosis antibiotic, D-cycloserine acts as a partial agonist at the glycine-binding site on NMDA receptors to enhance glutamate signaling but it is not found to be beneficial for AD. Memantine is a reversible glutamate NMDA receptor antagonist which might be modulating excessive background activity of this cation channel–glutamate receptor complex associated with age or pathology. Memantine has shown to improve memory in preclinical and clinical trials. Ampakines are also another group which has been shown positive effects on models of cognitive dysfunction. Ampakines bind to a site on the AMPA receptor but have no agonist or antagonist effects; instead, they stabilize the receptor in its channel-open state following the binding of released transmitter (glutamate). This prolongs current flow through the receptor and thus enhances synaptic responses. This group had moderate to large improvements on attention and memory in clinical trials.

**Monoamines:** Number of studies has proved the importance of monoamine neurotransmitters – dopamine, serotonin, and noradrenalin on cognition. The interaction of dopamine and glutamate can promote LTP and LTD in various brain regions. Dopamine neurotransmission, which is important for motor function and cognition, declines with age and this age-related decrease, may contribute to impaired attention and mental flexibility plus other neurological deficits. Serotonin appears to modulate the impact of dopamine upon spatial working memory and attention. Drugs that act via noradrenaline can have cognition-impairing or enhancing effects, indirectly by increasing cortical dopamine. Methylphenidate (Ritalin), a stimulant drug, is widely used to treat the Attention Deficit Hyperactivity Disorder (ADHD). Its mechanism of action is poorly understood; however, methylphenidate has been postulated to have an amphetamine-like effect in releasing amines such as dopamine and noradrenaline. One NS2359, a mixed monoamine reuptake blocker acts by equipotent reuptake blockade across the noradrenaline, dopamine and serotonin transporters is used in treatment of Attention Deficit Hyperactivity Syndrome (ADHD). Atomoxetine, a highly selective inhibitor of the presynaptic noradrenalin transporter with little or no affinity for other neurotransmitter transporters and receptors has shown good results in clinical trials in ADHD patient. Methylphenidate, another stimulant, also showed to improve the cognition in adult ADHD patients. Its mechanism is still poorly understood but it is postulated to exhibit effects on catecholamine, serotonin, glutamate, gamma amino-butryic acid (GABA) and histamine systems in the brain. At present, many compounds that alter the function of various neurotransmitters are being developed with AD as a target indication. Of these, the 5-HT6 receptor antagonists appear to hold much potential as new therapies, because in preclinical studies they have shown promising results by modulating multiple neurotransmitter systems. SB-742457, a 5-HT6 receptor antagonist is found to be very much efficacious in AD patients. Other compounds which are under development are SAM-531, SGS-518, PRX-07034, SYN-114, SB-399885 and SUVN-502 which are eagerly awaited.

**Adenosine:** Cyclic AMP (cAMP) plays a very important role

<table>
<thead>
<tr>
<th>SN</th>
<th>Category</th>
<th>Name</th>
<th>Mechanism</th>
<th>Comment</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Cholinergic agents</td>
<td>Donepezil</td>
<td>Acetylcholinesterase inhibitor</td>
<td>Symptomatic treatment of AD, Vascular dementia and dementia associated with PD</td>
<td>18</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Galantamine</td>
<td>Acetylcholinesterase inhibitor; also possible cholinergic agonist</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Rivastigmine</td>
<td>Acetyl cholinesterase and butrylcholinesterase inhibitor</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Glutaminergic agents</td>
<td>D-cycloserine</td>
<td>Partial NMDA agonist enhances glutamate signalling</td>
<td>Significant broad benefits in moderate-to-severe AD, Vascular dementia and combined of non-specified dementia</td>
<td>2-4</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Ampakine</td>
<td>Memantine</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Nicotinic agonist</td>
<td>Nicotine</td>
<td>Acetylcholine agonist and releaser</td>
<td>Facilitates learning/memory performance</td>
<td>20</td>
</tr>
<tr>
<td>4</td>
<td>Monoamines and agents acting on them</td>
<td>Methylphenidate</td>
<td>Modafinil</td>
<td>Effects on catecholamines, serotonin, glutamate, gamma amino-butryic acid, orexin, and histamine systems</td>
<td>Improve cognition in children and adults with ADHD</td>
</tr>
<tr>
<td>5</td>
<td>Adenosine and phosphodiesterase</td>
<td>Rolipram</td>
<td>Selective type-4 phosphodiesterase inhibitor</td>
<td>Improve LTP</td>
<td>25</td>
</tr>
</tbody>
</table>
in cell signaling by various types of LTP. Antagonism at adenosine receptors acts indirectly to inhibit phosphodiesterase which may be important in treatment of AD pathology. Thus, cognition is potentially enhanced by adenosine antagonists such as caffeine, and by phosphodiesterase inhibitors, both non-specific (e.g. papaverine and propentofylline) and specific (e.g. rolipram). Rolipram is selective phosphodiesterase type-4 inhibitor enhances long-term retention by increasing cAMP levels\textsuperscript{25}. It is also found that sub-chronic rolipram treatment leads to a persistent improvement in long-term object memory in rats.\textsuperscript{32}

B. Drugs increasing blood flow and enhance brain metabolism

Increase in cerebral metabolism and blood flow can be beneficial for memory improvement. Vasodilator agents like naftidrofuryl have been proposed to enhance cognition. Vascular dementia was thought to be the main condition that might respond to cerebral vasodilators, but impaired blood flow may occur in other disorders. Several other cognition enhancers have at least partial actions on these diffuse processes, including phosphodiesterase inhibitors and calcium-channel blockers (e.g. nimodipine). Other agents include the pyrrolidinones (racetams), ergot alkaloids, and vinpocetine, although these have some additional mechanisms. Many pyrrolidinone derivatives are available worldwide, including piracetam, oxiracetam, aniracetam, nefiracetam and levetiracetam\textsuperscript{33}. Actions of piracetam include enhancement of brain metabolism. Ergot alkaloids have marked effects on blood flow, which were originally thought to be the main mechanism of action. However, more complex actions, including neurotransmitter changes, are reported. Nicergoline has therapeutic potential in number disease conditions including mild to moderate dementia, Alzheimer-type dementia and vascular dementia\textsuperscript{34}. Vinpocetine, an alkaloid obtains from \textit{Vinca minor} is a highly potent vasodilator. Clinical studies of vinpocetine reports selective enhancement of cerebral blood flow and metabolism, including enhanced glucose uptake, which may protect against the effects of hypoxia and ischaemia\textsuperscript{35}. The list of compounds active on cerebral blood flow or able to enhance brain metabolism is obviously long. It can be speculated that rather than substances acting on blood flow it may be more interesting to study drugs improving the glucose/oxygen extraction from blood.

C. Drugs directed at transduction mechanisms

Signal transduction process involved in the cognition can be targeted for the development of better cognitive enhancing drugs. Most processes of signal transduction involve ordered sequences of biochemical reactions inside the cell, which are carried out by enzymes, activated by second messengers, resulting in a signal transduction mechanism. The main pathway which can be targeted by cognitive enhancers is the CREB pathway\textsuperscript{3}. Various compounds which act by inhibiting different forms of phosphodiesterase enzyme are under development. The novel selective PDE9 inhibitor BAY 73 6691 improves learning and memory in rodents which act possibly through modulation of the NO/cGMP-PKG/CREB pathway\textsuperscript{36}. Other phosphodiesterase inhibitors (PDEIs) such as PDE4 (e.g. Rolipram), PDE5 (e.g. vardenafil) PDE2 (e.g. BAY 60-7550) and PDE10 inhibitor are under development\textsuperscript{37}. Protein kinases including PKA, the Calcium–calmodulin-activated kinase are also interesting targets which are worth exploring\textsuperscript{38}.

D. Drugs acting via neuroprotection and neural growth

Production of neurotrophic factors is an important process that stimulates nerve growth and increases the complexity of neural connections, such as nerve growth factor (NGF) and brain-derived neurotrophic factor (BDNF). Several cognition enhancers are thought to work by protecting the brain from oxidative damage, free radical damage or neurotoxicity. Agents that act through such mechanisms include memantine, melatonin, idebenone, cerebrolysin, some endogenous neuropeptides and analogues. PDEIs also show the secondary release of neurotrophic factors, such as NGF and BDNF\textsuperscript{39}. Numerous small proteins are found in the brain, these neuropeptides have complex and multiple actions, and may act as hormones, neurotransmitters and local messengers. A role in cognition, including neuroprotective effects, has been proposed for vasopressin, somatostatin, growth hormone, insulin-like growth factor-1, (IGP-1) neuropeptide Y, orexins, vasoactive intestinal polypeptide, glucagon-like peptides, galanin, nociceptin/orphanin FQ, pro-opiomelanocortin derivatives, Thyrotropin-Releasing Hormone (TRH) and others\textsuperscript{40}.

E. Advanced techniques and Medical devices

Various non-invasive techniques and invasive medical devices are used to improve cognitive function. Non-invasive techniques include behavioral techniques or assistive software that provides new strategies to restoring memory and planning. Electromagnetic stimulation and biofeedback that modulate activity in a patient’s brain as part of a rehabilitation program is one of the non-invasive technique\textsuperscript{41}. Invasive approaches may improve cognition by using implantable medical devices that are able to record and stimulate specific brain region to restore cognition\textsuperscript{41}. Chronic bilateral deep brain stimulation (DBS) of the subthalamic nucleus (STN) or globus pallidus interna are effective neurosurgical procedures for treatment of motor symptoms in patients with advanced PD who cannot be satisfactorily treated with pharmacological treatments\textsuperscript{42}.

Future perspectives

The past few years have seen major breakthroughs in cognitive research, leading to an increased understanding of the pathophysiology. New tractable targets have been
identified in key disease pathways, improving the prospects for development of disease-modifying drugs for some devastating disorders causing memory impairment. The process of synaptogenesis and neurogenesis provides possible targets for cognition enhancement while processes important in disease-associated cognitive decline are important targets for early therapeutic intervention. Some possible interventions that might enhance or repair brain function would be surgical rather than pharmaceutical. These include the possible use of stem cells to encourage the growth of new brain cells to replace dead ones. Victims of strokes and of Parkinson’s disease have been early targets for experimental versions of this approach. At the other extreme, physical and mental exercise and diet regimes, which might enhance mental performance, are likely to be increasingly popular.

The future study will be mainly related for the development of therapeutic strategies that target the genome, use cell replacement, or both. Various strategies are under study to use stem cells to replace dead neurons in neurodegenerative disease. Nerve growth factor (NGF) has been shown to improve damage in spatial cognition following aging, whereas epidermal growth factor (EGF) is important in brain cell proliferation. Another approach of treating cognitive dysfunction with erythropoietin (EPO) in order to achieve neuroprotection and/or neuroregeneration represents a totally new approach. EPO nonspecifically influences components of the “final common pathway” that determine disease severity and progression in a number of entirely different brain diseases. EPO acts in an antiapoptotic, anti-inflammatory, antioxidant, neurotrophic, angiogenic, stem cell–modulatory fashion. Importantly, it appears to influence neural plasticity. Most likely due to these properties, EPO has been found by many investigators to be protective or regenerative and to improve cognitive performance in various rodent models of neurological and psychiatric disease. Experimental EPO treatment to improve cognitive function in patients with schizophrenia represents a novel neuroregenerative strategy for a chronic brain disease.

Various newer compounds are under preclinical and clinical developments targeting different pathways or targets such as nicotinic receptor, PDE4 inhibitors, 5HT6 antagonists and L-Type calcium channel modulator (Table 3).

Some genetic, neurochemical and imaging tests and computational models are in development to distinguish potential signs of early disease. Development of such biomarkers could allow early intervention with disease-modifying drugs.

**Conclusions**

Despite of several years of scientific efforts, still there is no satisfactory therapeutic strategy to cure cognitive impairment. A recent breakthrough in scientific and technical field has allowed researchers to understand the basic pathophysiology of the progression of diseases such as Parkinson’s disease, Alzheimer’s disease, schizophrenia and Attention Deficit Hyperactivity Syndrome (ADHD). Researchers have unveiled many of the new key players of the pathological cascades which lead to cognitive impairment. Many of newer

### Table 3. List of potential cognitive enhancers in pipeline of drug discovery and development

<table>
<thead>
<tr>
<th>Category</th>
<th>Drug</th>
<th>Indication</th>
<th>Status</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nicotinic alpha-7 Agonists</td>
<td>DMXBA, JN403, R3487/MEM 3454</td>
<td>Alzheimer’s</td>
<td>Preclinical</td>
<td>43</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Schizophrenia</td>
<td>Phase Ia completed</td>
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<tr>
<td></td>
<td></td>
<td>Alzheimer’s</td>
<td>Phase Ia</td>
<td></td>
</tr>
<tr>
<td></td>
<td>R4996/MEM 63908</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>α4β2 nicotine acetylcholine receptor partial agonist</td>
<td>AZD 3480 (TC 1734)</td>
<td>Age associated memory impairment mild cognitive impairment (MCI)</td>
<td>Phase II completed</td>
<td>23</td>
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<tr>
<td></td>
<td></td>
<td>Alzheimer’s</td>
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<tr>
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<td></td>
<td>Schizophrenia</td>
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<tr>
<td>PDE4 Inhibitors</td>
<td>MEM 1414</td>
<td>Alzheimer’s</td>
<td>Phase I completed</td>
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<td></td>
<td>MEM 1917</td>
<td>Alzheimer’s</td>
<td>Preclinical</td>
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<tr>
<td>5HT6 Antagonists</td>
<td>MEM 68626</td>
<td>Alzheimer’s</td>
<td>Preclinical</td>
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<td>SB-742457</td>
<td>Alzheimer’s</td>
<td>Phase Ii</td>
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<td></td>
<td>SAM - 531</td>
<td>Alzheimer’s</td>
<td>Phase Ii</td>
<td></td>
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<td></td>
<td>SGS-518</td>
<td>Schizophrenia</td>
<td>Phase I</td>
<td></td>
</tr>
<tr>
<td></td>
<td>PRX-07034</td>
<td>Alzheimer’s</td>
<td>Phase I</td>
<td></td>
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<tr>
<td></td>
<td>SYN-114</td>
<td>Alzheimer’s</td>
<td>Phase I</td>
<td></td>
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<tr>
<td></td>
<td>SUVN-502</td>
<td>Alzheimer’s</td>
<td>Phase I</td>
<td></td>
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<tr>
<td>L-Type Calcium Channel Modulator</td>
<td>MEM 1003</td>
<td>Alzheimer’s Vascular dementia</td>
<td>Phase 2a completed</td>
<td>44</td>
</tr>
<tr>
<td></td>
<td></td>
<td>MCI</td>
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</table>
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compounds targeting these pathways are under preclinical and clinical investigation and can be promising therapies for cognitive impairment. Apart from the pharmacological approaches, other approaches such as dietary supplementation and encouragement of healthy lifestyle which is physically and mentally stimulating are going to have a big impact on cognitive research in future.

Reference


Dear Readers,

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Letters should be addressed to:

CRIPS Editorial Office,
National Institute of Pharmaceutical Education and Research (NIPER)
Sector 67, S.A.S. Nagar - 160 062, Punjab
E-mail : crips@niper.ac.in, ss Sharma@niper.ac.in