Mechanism of action of guanfacine: a postsynaptic differential approach to the treatment of attention deficit hyperactivity disorder (adhd).

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Abstract

The treatment of ADHD has focused on the use of psychostimulants drugs such as methylphenidate or amphetamine and derivatives, or not stimulants agents, such as atomoxetine. These agents act mainly on catecholaminergic presynaptic mechanisms. Recently the European Medicines Agency (EMA) has approved another not psychostimulant drug, guanfacine extended release (ER), as a new option to the treatment of ADHD, which acts at postsynaptic level. Guanfacine stimulates postsynaptic alfa-2A adrenergic receptors so it inhibits the production of cAMP and closes HCN channels enhancing the effectiveness of the signal of the pyramidal neurons of the prefrontal cortex (PFC), thus improving working memory and attention. In addition, stimulation of the alpha-2A receptors promotes growth and maturation of the dendritic spines of pyramidal neurons of the medial PFC, that are associated with brain function such as learning and memory. In contrast with psychostimulants or atomoxetine, guanfacine mimics noradrenaline stimulation of postsynaptic receptors alfa-2A on the PFC.