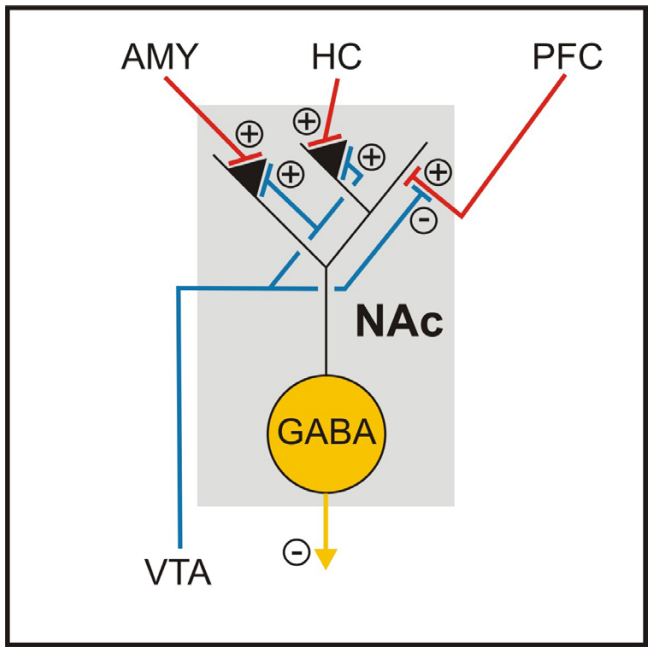

Figure 2
Neuronal connections of Nucleus Accumbens. Glutamatergic afferences from the prefrontal cortex, hippocampus and amygdala terminate on GABAergic medium spiny neurons and are modulated pre- and postsynaptically by dopamine. The glutamatergic input from the hippocampus and the amygdala drives the medium spiny neurons into a depolarized state and the input from the prefrontal cortex is capable of triggering action potentials [119]. AMY = amygdala; HC = hippocampus; PFC = prefrontal cortex; NAc = nucleus accumbens; VTA = ventral tegmental area.

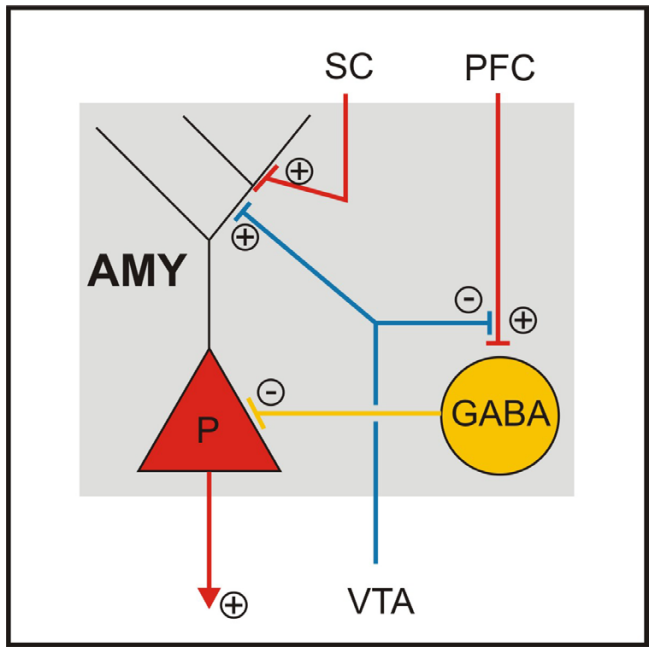

Figure 3
Neuronal connections of Amygdala. Glutamatergic afferents from the prefrontal cortex (PFC) contact GABAergic interneurons in the basolateral amygdala, which then inhibit the firing of pyramidal cells, while afferents from sensory cortices terminate mainly on glutamatergic pyramidal cells. The PFC input is suppressed presynaptically, whereas the sensory cortical input is enhanced postsynaptically by DA [67,120]. AMY = amygdala; P = pyramidal cell; PFC = prefrontal cortex; VTA = ventral tegmental area, SC = sensory cortices.

transmission seem to be supported by the available experimental evidence. The higher DAT density in ADHD patients, which should improve DA clearance from the synaptic cleft [28-30], the action of MPH as an indirect DA agonist, and imaging data demonstrating increased extracellular DA concentrations in the striata of healthy controls after MPH treatment [51], all argue for a reduced striatal DAergic transmission in ADHD. The opposing view assuming an accumbal DA hyperfunction in ADHD, in contrast, maintains that DAT density may be regarded as a measure of DA fibre density [31-34]. It further proposes the fact that there are two different kinds of DA transmission in the striatum [52]: Firing of DA neurons leads to a phasic release of DA in relatively high concentrations. The transmitter is cleared by the very effective DAT, so only very low concentrations of DA remain in the extracellular space. This tonic transmission is, however, still strong enough to activate autosynaptic D2 receptors which inhibit phasic DA firing. By blocking the DAT, MPH may increase the tonic extracellular DA concentrations and thus decrease the phasic transmission [53]. The observation that DA antagonists increase the positive effect of MPH on motor behaviour [54,55], but prevent its enhancement of cognitive capacities [56], further supports this hypothesis. In this view, the two impairments in PFC and NAc are probably even causally related, since alterations of DA metabolism in the PFC reciprocally change the DA activity in the striatum [57-62].

The DA projection to the amygdala matures in close coordination with that of the PFC, such that DA hypoinnervation of the PFC goes along with DA hyperinnervation of the amygdala (and entorhinal cortex) after early trauma [63]. Furthermore, the amygdala receives a strong projection from the PFC [64] which serves to put reflexive fear reactions under cognitive control (fig. 3) [65-67]. Although these neuronal effects after early trauma in gerbils should be considered only as a partial model of ADHD, it might be fruitful for further reasoning to remember that a high frequency of associated emotional problems has been reported in ADHD patients [9], but