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# Systemic administration of guanfacine improves food-motivated impulsive choice behavior primarily via direct stimulation of postsynaptic $\alpha_{2A}$-adrenergic receptors in rats

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## Highlights

- Guanfacine improved food-motivated impulsive choices in the delay discounting task.
- Stimulation of the $\alpha_{2A}$-adrenergic receptor was involved in the effect of guanfacine.
- A selective noradrenergic neurotoxin did not affect the effect of guanfacine.

## Abstract

Impulsive choice behavior, which can be assessed using the delay discounting task, is a characteristic of various psychiatric disorders, including attention-deficit/hyperactivity disorder (ADHD). Guanfacine is a selective $\alpha_{2A}$-adrenergic receptor agonist that is clinically effective in treating ADHD. However, there is no clear evidence that systemic guanfacine administration reduces impulsive choice behavior in the delay discounting task in rats.
In the present study, we examined the effect of systemic guanfacine administration on food-motivated impulsive choice behavior in rats and the neuronal mechanism underlying this effect. Repeated administration of either guanfacine, methylphenidate, or atomoxetine significantly enhanced impulse control, increasing the number of times the rats chose a large but delayed reward in a dose-dependent manner. The effect of guanfacine was significantly blocked by pretreatment with an $\alpha_{2A}$-adrenergic receptor antagonist. Furthermore, the effect of guanfacine remained unaffected in rats pretreated with a selective noradrenergic neurotoxin, consistent with a post-synaptic action. In contrast, the effect of atomoxetine on