The Effects of Norepinephrine and Dopamine in Remediating Selective Attention Deficits  

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**Introduction**

As humans we are constantly bombarded with more stimuli than we can process. Fortunately, we possess a filtering mechanism known as selective attention that allows a person to attend to one stimulus and ignore others. However, when environmental conditions change it may be necessary to redirect attention to the previously ignored (ground stimuli, attentional shift). Converging evidence suggests these attentional shifts may be mediated by two neurotransmitters in the frontal cortex, dopamine (DA) and norepinephrine (NE). It is hypothesized that malfunctions in these systems may underlie cognitive deficits found in people with attention deficit disorder (ADD). Additionally, drug treatments for ADD alter functioning in both DA and NE. As rodents have evolved similar abilities to shift attention and these are mediated by comparably neurotransmitter and neuromodulatory pathways as humans, experiments may be done with rodents to test hypotheses regarding what dysfunctions the brain may underlie disorders in which attentional shifts are impaired.

Previous work in our lab has shown that when the frontal cortical NE system of a rat is compromised it causes deficits in attentional shifts similar to those found in patients with frontal lobe damage or ADD. It is hypothesized that drugs with actions identical to those used to treat patients with ADD may reverse these impairments. Currently, we tested drugs that act to supplement DA (apomorphine) or NE (tomoxetine) in rats with depletions of the NE system while they performed in a task of attentional shifts.

**Materials & Methods**

- 60 Male Long Evans hooded rats (200-275g)
- Initially rats were trained to focus on one attribute (e.g. texture of the complex stimulus, a colored, textured pot filled with digging media. Subjects were to attend to this dimension despite changes in the other dimensions (e.g. texture).
- Animals were then given a task of selective attention, the extradimensional test (ED). In this test rats were given a new set of complex stimuli and were rewarded for attending to the same dimension (e.g. texture) as in prior test while ignoring another dimension (e.g. digging medium).
- Performance in the ED was compared to performance in the extradimensional test (ED) test. During the ED, when subjects were presented with novel stimuli, they had to shift attention to a previously irrelevant dimension (e.g. digging medium) and disregard the formerly relevant dimension (e.g. texture). Rats were given intraperitoneal injections of either tomoxetine (0.5 or 0.9 mg/kg), apomorphine (0.3 or 1.0 mg/kg), or a placebo prior to the ED.
- In addition to the ED and ED test, subjects underwent tests to ensure that changes in performance during the ED were not due to impairments in stimulus reward learning or reversal of stimulus-reward rules. These reversal tests occurred after the initial test of selective attention, the ID, and the ED.

**Results**

![Figure 1: The actions of Tomoxetine on the NE system of a rat by inhibiting the reuptake of NE in the prefrontal cortex.

![Figure 2: The actions of apomorphine on the DA system by increasing the release of DA in the prefrontal cortex.

![Figure 3: The actions of apomorphine on the DA system of a rat by increasing the release of DA in the prefrontal cortex.

![Figure 4: The changes in performance of rats on the ID test with different doses of NE or DA or a placebo.](image)

**Conclusions**

1. The current work failed to replicate previous findings and found no impairment in attentional shifts after NE lesion. Two explanations exist for this finding. First, these lesions may have been smaller than in the previous study due to variability in the potency of the neurotoxin. An alternative hypothesis is that the stress of intraperitoneal injections increased activity in the NE system of the prefrontal cortex to alleviate the effects of the lesions. Further analyses and experiments will be done to assess these possibilities.

2. Despite the failure of NE lesions to impair attentional shifts, the critical role of NE was confirmed in these studies by finding that tomoxetine but not apomorphine affected ED tests. Administration of tomoxetine to SHAM rats impaired attentional shifts.

3. Additionally, a DA agonist, facilitated learning of new stimulus reward rules (reversal performance) regardless of lesion condition. This finding confirms previous reports that DA is involved in learning new reinforcement contingencies.

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