Learning in the Normal and Abnormal Brain

**Outcome:** According to preliminary results of an NSF-funded experiment from the CELEST Science of Learning Center at Boston University, neuroscientists found that treating normal rats with a drug that blocked a certain type of receptor (the D1 receptor) in a part of the brain called the dorsal striatum could cause their habits to be broken. Treating the dorsal striatum with a D1 receptor blocker did not change the ability of normal rats to pay attention. Attention is a process controlled by a different part of the brain called the prefrontal cortex. Although these two brain sites are connected to one another, these results show that these sites do not influence one another in normal rats. Rats that are ADHD-like also were tested. These rats were not able to form habits and they had a hard time paying attention, whether or not the dorsal striatum was treated with the D1 receptor blocker. These findings show that ADHD-like rats behave as if their D1 receptor in the dorsal striatum is not functioning properly. ADHD-like rats also show that they have problems with their prefrontal cortex.

**Impact/benefits:** Current medications for ADHD focus on changing the prefrontal cortex while ignoring the dorsal striatum. These new findings suggest that ADHD may be more successfully treated if both prefrontal cortex and dorsal striatum are targeted by the treatment medication because these brain sites may not influence each others learning functions.

**Explanation/background:** D1 receptors in parts of the brain called the dorsal striatum and prefrontal cortex are very important for learning to take place. Because these brain sites are connected to one another, we wanted to know if blocking D1 receptors in the dorsal striatum would change how rats performed in certain learning tasks. We first looked at responses in a reward devaluation task, that is, a task in which food pellets were made less valuable by pre-feeding rats until they were full. If the rats made lever responses for food pellets despite being full, then their responses were made out of habit and under control of the dorsal striatum. Compared to a control treatment, treatment of the dorsal striatum with a D1 receptor blocker would be expected to disrupt their learned response habits and cause responses to be goal directed, that is, to make responses only when hungry. The second task examined the ability of rats to pay attention. Hungry rats first had to figure out which lever (left or right) produced a food pellet when pressed. Which lever was correct was based on the rat’s natural inclination to prefer pressing the right or left lever. In this case, the clue to earning food pellets was to press the lever they naturally preferred not to press. Once this problem was solved, rats had to solve a new problem that used a new clue. To solve this new problem, hungry rats had to ignore the old clue and pay attention to the new clue to earn food pellets. It was then asked if compared to a control treatment, would treatment of the dorsal striatum with a D1 receptor blocker disrupt the ability of rats to pay attention when the clue was changed. Paying attention is under control of the prefrontal cortex. These questions were investigated in a normal rat strain (WIS) and an ADHD-like rat strain (SHR).