Attention Deficit Hyperactivity Disorder (ADHD) is a behavioral disorder that disrupts neurocognitive functioning of frontal lobe and striatal brain circuits throughout the lifespan. Medial temporal lobe functioning is generally intact. With support from the NSF Center of Excellence for Learning in Education, Science, and Technology (CELEST), research led by Kathleen Kantak, in collaboration with Teghpal Singh, Kerry Kerstetter, Kimberly Dembro, Michael Mutebi, Roxann Harvey, Christian Deschepper, Linda Dwoskin and Audrey Wells, used a rat strain exhibiting an ADHD phenotype (the Spontaneously Hypertensive Rat – SHR) to evaluate memory system functioning associated with this disorder. As the SHR exhibit both hyperactivity and hypertension, two additional rat strains were evaluated to control for these characteristics: the WKY (non-hyperactive and non-hypertensive) and the WKHT (non-hyperactive but exhibiting hypertension). Relative to WKY and WKHT, the SHR made more working memory and set-shift errors (frontal lobe functions) and more habit learning errors (dorsal striatal function), but did not have deficits in amygdala-related stimulus-reward learning and in the use of a hippocampal place learning strategy (medial temporal lobe functions). Furthermore, a clinically relevant dose (1.5 mg/kg) and route (oral) of methylphenidate administration (the most often prescribed medication for ADHD) eliminated strain differences in frontostriatal neurocognitive functioning. The current approach meets the criteria necessary in a model that is appropriate for targeting neurocognitive deficits relevant to ADHD. These findings suggest that a model in which rats show naturally occurring frontostriatal deficits, such as observed in SHR, would have greater predictive and face validity for studying ADHD. An appropriate animal model of ADHD allows investigators to study the neurobiological basis of this disorder in ways impossible in human participants and in animals not displaying an ADHD phenotype. Findings were published in the journal Behavioral Neuroscience in 2008 and submitted for publication in early 2009.

**Figure 1.** Attentional Set-Shifting behavior in WKY and SHR either untreated during initial discrimination learning or treated with vehicle or methylphenidate during extradimensional set-shift testing (frontal lobe function). Values are the mean ± SEM number of trials to criterion. *p ≤ 0.05 compared to the WKY control groups and #p ≤ 0.05 compared to the vehicle- and methylphenidate-treated WKY and the methylphenidate-treated SHR. From Kantak et al. (2008).

**Figure 2.** Stimulus-Reward learning in WKY, SHR and WKHT strains during the Conditioned Cue Preference task (medial temporal lobe function). Values are the mean ± SEM preference ratios. * Significant conditioning (p<0.05) was observed in each strain with no differences between strains. From Wells et al. submitted (2009).