**Overall Impact:**

The proposed research should provide useful information on the role of thalamic inhibition in well-developed and highly stereotyped motor skills. The proposed research will use keyboard typing as an exemplar of a highly stereotyped “automatized” motor behavior, then relate behavioral measures to thalamic GABA concentration, measured by magnetic resonance spectroscopy (MRS). Prior research has indicated a relationship between thalamic GABA concentration and bulk motor output, but the proposed research is innovative in that it will test whether higher GABA concentrations correlate with *decreased motor variability* and therefore increased motor automaticity. If it is found that thalamic GABA concentrations correlate to task performance, the project could make a significant impact on the understanding of thalamic involvement in motor automaticity, providing insight into both healthy and disordered human motor behavior.

**Significance:**

* **Strength**: Better understanding of the role of thalamic inhibition in motor behavior could have near-term implications for the treatment of motor disorders in humans.
* **Strength**: By using a naturalistic task and human subjects, the potential findings hold high promise for translational neuroscience.
* **Strength**: The proposed research may also hold useful results for basic neuroscience, and critically, findings that might be impossible to obtain from animal research because the motor skill level being studied would be prohibitively difficult to train in animals.
* **Weakness**: While the applicant made it clear that thalamic function is important to motor behavior, it was unclear what a low-resolution assay of thalamic GABA levels might be able to explain about the \*overall\* function of the thalamus in automatized motor control. Namely, it’s unclear what GABA levels might say about thalamic (excitatory) facilitation of motor signals. While this is out of the scope of the proposed research, the application did make mention of overall thalamic function without making a distinction between excitatory and inhibitory contributions.

**Investigators:**

* The applicant did a good job at foreshadowing the training portion of the application with specific mention of co-sponsors and training goals.
* Strategic mention of the Action Control Lab’s previous work did well to frame the techniques and methods being proposed in terms of prior success.

**Innovation:**

* **Strength**: The design of behavioral measures and analysis is rigorous and will produce a detailed and thorough behavioral dataset to test against MRS data and potentially link motor behavior to thalamic GABA concentration.
* **Strength**: The statistical methods proposed are straightforward and redundancy measures are considered.
* **Neutral**: Application-specific toolkits for MRS and kinematics analysis are relatively inscrutable, however the prior work of the Action Control Lab indicates that they are part of a sound methodology.
* **Strength**: The task (keyboard typing) and subjects (humans) bolster the significance of any findings. The proposed research relies on much less abstraction than typical motor neuroscience studies.
* **Weakness**: It is possible that the low spatial resolution of MRS will limit the impact of potential findings.

**Approach:**

* **Strength**: Working hypotheses were straightforward and clearly stated.
  + Hypothesis 1: Metrics of both temporal and spatial variability will reduce with increasing sequence automation.
  + Hypothesis 2a: Individuals with higher thalamic inhibition (ie. higher GABA concentrations) will display lower motor output variability during typing.
  + Hypothesis 2b: Thalamic GABA will correlate with metrics of motor variability related to increasing sequence automation.
* **Strength**: *Alternative outcomes were highly detailed, demonstrating excellent understanding of the experiments and expected data*.
* **Weakness**: While previous research was discussed with a good level of detail, many citations were missing*.* For the purposes of the class, I gave the applicant the benefit of the doubt on any uncited statements that were labelled “(CITE)” and did not score them negatively.

**Environment:**

* The facilities and equipment are of high quality, and the applicant shows a good understanding of how to use them.