July 2, 2014

Re: Himle RPT Review

Dear Reviewer,

Attached please find my research statement and 3 manuscripts representing samples of my work on Tourette syndrome. As you will see from my summary below, my research focuses on three primary areas: understanding TS from a behavioral perspective, examining the mechanisms by which behavioral treatments are effective for reducing tics, and treatment dissemination. In addition, my research employs a variety of designs and research methodologies, including small-N methods (i.e., multiple baseline, reversal, and changing criterion designs), quasi-experimental and survey research, and randomized controlled treatment outcome designs/methods. The work samples I have selected demonstrate my work in each of my three primary areas of interest as well as a sample of the research designs that I employ. I’ve included an older article as Work Sample A (Himle et al., 2007) because that paper serves as the foundation of much of the work I have continued to do over the past 6 years. In addition to highlighting the value of small-N designs in answering important mechanistic questions, that paper was instrumental to the field’s current thinking about the urge-reduction model of TS. I have also provided a more recent review article that summarizes current research as well as my own formulation of the urge reduction model (Work Sample D).

Overview of My Current and Future Research:

Tic disorders (including Tourette syndrome, TS) are a class of complex neurodevelopmental disorders characterized by involuntary motor and vocal tics. Although the exact cause of TS is unknown, it has historically been conceptualized as a purely biological condition resulting from structural and functional abnormalities within cortico-stiato-thalamo-cortical brain circuitry. However recent research, including my own, has demonstrated that environmental and psychosocial factors (which I conceptualize through a behavior analytic framework) influence the frequency, intensity, and complexity of tics and play an important role in the overall progression and course of TS symptoms. The overarching goal of my research program is to better understand TS from a biobehavioral model, which will lead to a better understanding of the clinical course of TS and will inform the development and testing of efficacious nonpharmacological interventions.

There is increasing data showing that although tics are involuntary, they are impacted by a variety of environmental variables. Historically, research in this area has focused on variables that were thought to have a direct biological influence (stress, anxiety). However research from my lab and others has shown that environmental influences are much more dynamic and are often socially mediated. My research focuses on understanding how operant and respondent-conditioning principles can be applied to explain how/why contextual stimuli and social consequences shape and facilitate tic suppression, even though the symptoms are involuntary. Much of my early work used carefully controlled small-N methods to demonstrate that tic suppression/expression can be facilitated by operant reinforcement and tics (i.e., frequency) can be brought under contextual control (see Woods & Himle, 2004; Himle et al., 2007b, Woods et al., 2008, see Work Sample A). Several research laboratories across the country are now using my operant tic-suppression paradigm to better understand the role of reinforcement on response inhibition in TS, including the underlying brain mechanisms. Although I continue this line of experimental research, I am also interested in it’s clinical application. For example, using
a function-based assessment protocol I examined common antecedent and consequence variables associated with tic exacerbation in a large sample of children with TS and found that that specific functional patterns were common (especially attention and escape functions) and predicted tic severity (Himle et al., in press, see Work Sample B). The next logical steps in this line of research, which are currently ongoing in my lab, are to (1) validate the functional assessment protocol (i.e., using functional analysis), (2) examine whether functional variables (e.g., social reactions in families) predict the immediate and long-term course of tic expression and (3) to formally test whether function-based intervention strategies can help reduce tics.

I am also interested in understanding the role of cognitive/neurocognitive variables in tic suppression/expression. Although the exact mechanism is unclear, suppression appears to rely upon frontal-subcortical networks that subserve executive functioning (EF; See Woods, Himle, et al., 2008). Initial results from ongoing research in my lab suggest that highly effortful or prolonged efforts to suppress tics might interfere with concurrent cognitive demands (e.g., learning of new information and new skills, Hayes et al., in prep). We are also currently examining whether suppression results in lasting depletion of EF resources after suppression has ceased. These findings could potentially explain why some children are better/less able to control their tics. Over the next several years, I will extend this line of research in several ways. In 2014, I applied for and was awarded a TSA Center of Excellence Designation (for which I am the Co-PI/Co-Director along with Dr. David Shprecher in the department of Neurology). Funding from this initiative will allow us to begin collecting data on all children who receive treatment at the U, including neurocognitive (and other) predictors of treatment response. Parallel with this study, I plan to begin collecting functional, developmental, and neurocognitive data on children at risk for TS prior to symptom onset and will follow these children longitudinally through the critical onset period (ages 5-9). I hope to identify environmental, social/developmental, and neurocognitive markers that predict the onset/severity of tics and associated symptoms (e.g., cognitive and emotional dysregulation). This information will shed light on factors related symptom course and will lead to new advancements in the assessment and treatment of tics and associated problems (e.g., early identification, predicting the course of the disorder, development of preventative interventions to reduce the most problematic symptoms and impairment).

A second major focus of my research is on understanding the mechanisms by which nonpharmacological treatments are effective for reducing tics. Although current treatments (e.g., habit reversal training, HRT, and suppression treatments) have shown to be effective for reducing tics, there is considerable variability in treatment response both within and between individuals. In addition, little is known about how these treatments work or whether they share common mechanisms. The hypothesis with the most empirical support is the urge-reduction model (preventing the tic results in habituation to premonitory urges thereby extinguishing the negative reinforcement cycle; Himle et al., 2007a, Himle et al., 2008, see Work Sample A). While this hypothesis may explain why seemingly different psychosocial treatments show similar levels of efficacy, group studies have cast doubt on whether pre-tic urges indeed habituate during suppression (Specht et al., under review). However we recently examined the effects of awareness training and competing response training on pre-tic urges using a more systematic and sensitive test of urge habituation (Ramanjam & Himle, in prep) and have found that (a) urges indeed do not habituate during suppression, (b) urges ratings do show a pattern consistent with habituation during HRT (suggesting HRT operates differently from suppression), and (c) it appears that different tics serve different functions and the function changes over time, possibly as a result of the aforementioned social contingencies. This is consistent with some of my previous research showing that pre-tic sensations are described differently (and are likely not functional) early in the course of the disorder (Chang et al., 2009) but the stimulus function
of the "urge" changes over time. This suggests that future research may need to examine treatment based on mechanisms of change (i.e., targeting the specific function of specific tics).

My third primary area of research interest involves empirical approaches to treatment dissemination. Both Chronic Tic Disorders and OCD have been shown to be responsive to psychosocial treatments (HRT for TS, see Himle et al., 2006; Exposure and Response Prevention for OCD, see Freeman et al., 2008). Despite data supporting their efficacy, these treatments are not widely available (Woods, Conelea, & Himle, 2010a). Developing and evaluating effective dissemination strategies for psychosocial treatments has become a primary focus of mental health research. In my view, dissemination needs to follow two data-driven steps. First, barriers must be systematically identified, and second, barriers must be systematically addressed. My research (see Woods, Conelea, & Himle, 2010) has identified that practical barriers (travel, time, lack of providers) are the most commonly cited barriers inhibiting the use of psychosocial interventions for TS. One way to address these dissemination barriers is the use of technology. For example, I recently completed a pilot investigation examining the efficacy, acceptability, and feasibility of HRT delivered via videoconference (see Himle et al., 2010b), completed a multi-site randomized pilot trial comparing video-conference delivered HRT to face-to-face delivery (Himle et al., 2012), and am a co-advisor on a student’s NRSA examining the delivery of behavior therapy using a voice over internet (VoIP) protocol (Ricketts et al., under review). Results of each of these studies has shown telehealth to be effective for delivering HRT. Another way to utilize technology to address practical barriers is to deliver the intervention online. Along these lines, I have partnered with the company Psych Tech, Ltd. to develop and test an individualized, adaptive online program for delivering behavior therapy to individuals with tics (called TicHelper). Together with PsychTech, we were recently awarded and completed an NIMH Phase I R43 (SBIR) during which we developed and tested a prototype of the tic helper program (with very positive results) and were recently awarded a Phase II (R44) application to finalize development and test the TicHelper program in a randomized controlled trial. A few of the most exciting aspects of the TicHelper program are that it is designed to be adaptive and has built in program evaluation tools. These features will allow us to continually update and evaluate that program as new research on behavior therapy for tics emerges.