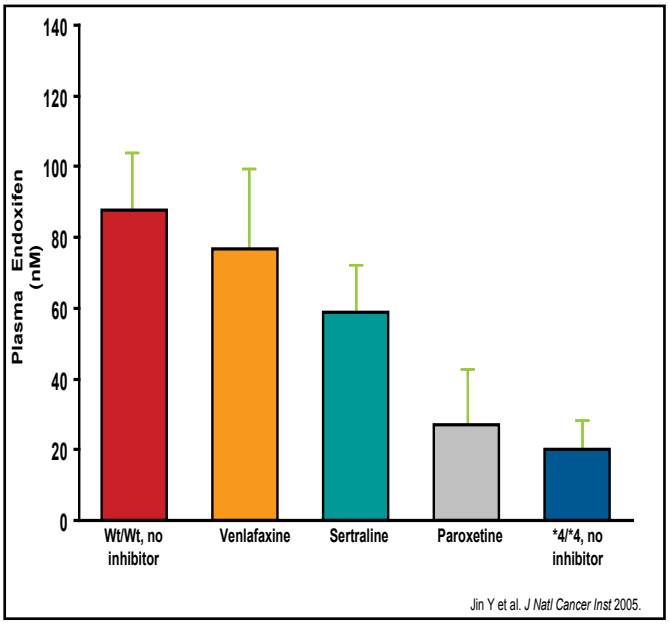
Commenting on these results, Dr. Flockhart noted that venlafaxine can be effectively used to treat tamoxifen-related hot flashes while retaining tamoxifen protection. "This can improve compliance with this very effective medication" and thereby have a direct impact on long-term survival. Other investigators have carried these observations forward, and there is now consensus that the following agents are potent inhibitors of CYP2D6 and should not be prescribed with tamoxifen: bupropion, fluoxetine, and paroxetine (Figures 1 and 2).

Figure 1. Partial List of Common CYP2D6 Inhibitors.

- **Strong (should be avoided in women taking tamoxifen)**
  - **Paroxetine (Paxil)**
  - **Fluoxetine (Prozac)**
  - **Bupropion (Wellbutrin)**
- **Moderate**
  - **Sertraline (Zoloft)**
  - **Duloxetine (Cymbalta)**
  - **Citalopram (Celexa)**
  - **Escitalopram (Lexapro)**
  - **Celecoxib**
  - **Diphenhydramine**
  - **Chlorpheniramine**
- **Weak Inhibitors**
  - **Venlafaxine (Effexor)**
  - **Desvenlalfaxine (Pristiq)**

Figure 2. Inhibition of CYP2D6 Affects Endoxifen Concentrations.



High-Tech Exposure Therapy for PTSD

Post-traumatic stress disorder (PTSD) first gained public awareness after the Vietnam War, as large numbers of returning veterans presented with depression and problems with substance abuse, which occur frequently with PTSD, and either a lack of or inappropriate emotional responses. As the Iraq War grinds into its fifth year, it's not surprising that PTSD has regained the headlines. Bringing a high-tech solution to this latest battlefield is Barbara Olasov Rothbaum, PhD, ABPP, Emory School of Medicine, Atlanta, GA.

Dr. Rothbaum first gained an understanding of the onset of PTSD. Plotting the course of PTSD after trauma exposure, Dr. Rothbaum assessed female rape victims on a weekly basis for a total of 12 weeks following their assault. Results showed that in the first week, 94% met symptomatic criteria for PTSD. "This indicates that this is the normal response to trauma," said Dr. Rothbaum. "What we wanted to figure out is when a normal response to trauma ends and when a pathopsychological response that requires diagnosis and treatment begins." While all subjects showed improvement after 4 weeks, a subset of patients stalled in their recovery. "We now see PTSD as a disorder of extinction. So, what you want to do is extinction training through exposure therapy—therapeutic exposure."

Therapeutic exposure can be imaginary, wherein the patient recalls the trauma in the present tense, or in vivo, where the site of the trauma is actually revisited; thanks to advances in technology, the trauma also can be virtually recreated. This technique, called virtual reality (VR), reasonably creates all the sensory inputs of sight, sound, vibration, and even smell of an actual traumatic setting. First used to treat Vietnam veterans, VR applications have expanded to include treatment for social disorders, fear of heights, and fear related to the events of 9/11.

VR is currently used in conjunction with relaxation techniques, education, and cognitive therapy, but Dr. Rothbaum is investigating the use of pharmacotherapy to enhance the efficacy of VR therapy. The investigative drug is D-cycloserine (DCS), an older antibiotic that has been shown to be a potential cognitive enhancer, facilitating extinction of the fear response in animal studies. Dr. Rothbaum first used DCS to help patients who had a fear of heights [*Arch Gen Psychiatry* 2004] and was eager to try it with veterans who were returning from Iraq.

Her current study randomizes PTSD patients to one of 3 treatments, alprazolam, placebo, or 50 mg DCS, given 30 minutes prior to VR trauma exposure. "Animal data indicate that it's best to have the drug on board during the consolidation as well as during the exposure." Though results on the first 27 patients are still blinded, all patients seem to be responding well to therapy with VR.

"But you have to ask yourself, 'What is the treatment ideal?" Dr. Rothbaum asks. "Well, that would be to prevent PTSD before it starts." To that end, she has proposed a study of emergency room trauma patients to be treated immediately for PTSD or observed for 12 weeks. The working hypothesis is that early disruption may change how the traumatic memory is consolidated. "It's like getting right back on the bike after you've fallen off."

For more information on virtual reality therapy, please visit www.virtuallybetter.com.

Trichotillomania and Skin Picking: Recognition and Clinical Management

Within the spectrum of obsessive-compulsive disorders (OCD), distinctive behaviors exist that do not respond to typical OCD treatments, including skin picking and trichotillomania (TRIC). Awareness of these disorders is not widespread, but Jon Grant, JD, MD, University of Minnesota, Minneapolis, MN, emphasized that their prevalence is not insignificant. He reported that 11.8% of adolescent inpatients he surveyed were identified as actively skin picking. "Importantly, this is not a behavior to be confused with body dysmorphic disorder: This is not picking to improve appearance. This is more like nail biting – most patients are not even aware that they're doing it." The number of individuals with TRIC also is higher than might be expected; a study of several thousand college students reported an incidence of 5% overall.

Onset for both disorders is early—10 to 15 years of age—and unlike the behaviors that are typical of OCD, these tend to involve pleasure or gratification. "Historically, people always thought of these as OCD problems, but they don't respond at all—or not as robustly—to the same treatments." To identify the TRIC patient, look for recurrent pulling of hair that results in noticeable hair loss, a sense of tension before pulling, pleasure or relief at the time of pulling, and often, with men, eating of the hair. TRIC also is often seen with comorbid nail biting.

Diagnostic criteria for skin picking include recurrent picking at or manipulating of the skin (anywhere on the body) that results in noticeable damage, picking of the skin using any tool (nails, tweezers, etc), many hours of picking, and additional picking at night. To emphasize the seriousness of this condition, consider that 45% of such patients have scarring, 30% experiences infections, and 3% actually requires grafts to restore skin integrity.

"From a treatment perspective, what has befuddled clinicians about these diagnoses is 'How do we characterize them?'" said Dr. Grant. "Are these really just variants of OCD?" Clinical studies say no. SSRIs that are effective in OCD have few responders among TRIC patients. On the other hand, TRIC may respond to naltrexone and other anti-addictive medications, while OCD does not. This last observation is suggestive of certain correlations; comorbid substance abuse is higher for TRIC than OCD, and rates are higher still for skin picking relative to TRIC. "Perhaps an addiction model might be useful to look at for these behaviors."

Dr. Grant reported an ongoing study using N-acetyl cysteine to treat TRIC. "We actually use this amino acid in gambling addiction." In his current blinded investigation, 50 patients were enrolled and randomized to 2400 mg of active agent or placebo. Though interim results are still blinded, some patients have reported having stopped picking for the first time in their lives, an outcome that is so profound that Dr. Grant doubts that it could be merely a placebo effect.

Dr. Grant also reported recent data for lamotrigine (median dose, 200 mg/day), which demonstrated a reduction in skin picking from an average of 2 hours a day to just one hour a day (n=24). Though there are no on-label therapies for either disorder, other treatment options that might be considered are naltrexone, acamprosate, baclofen, isradipine, or ondansetron. Dr. Grant stresses, however, that these interventions may have little or no effect for the patient who does not report pleasure or urges that are related to the dysfunctional activity. "You need to really take a close look at the family history and all of the comorbidities to get at what's really driving the behavior."

For more information on trichotillomania, please visit www.trich.org.