

Center for Studies of Addiction Newsletter



HIGHLIGHTING DR. REAGAN WETHERILL'S RESEARCH GROUP

Reagan Wetherill, Ph.D., a clinical psychologist and Assistant Professor of Psychiatry, conducts research that integrates neuroimaging, genetics, pharmacology, and a clinical perspective to: 1) identify neural features that contribute to alcohol and drug use, 2) examine the effects of acute and chronic alcohol and drug use on the brain and behavior, with a specific focus on memory processes and alcohol-induced blackouts, and 3) develop more effective approaches to intervention and prevention. She is currently conducting two major projects: one evaluating a promising medication for reducing heavy drinking and the other examining the influence of the natural hormonal milieu on the brain and behavior of naturally cycling female cigarette smokers.

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Dr. Wetherill's NIAAA-funded K23 research project is an integrative study designed to examine the effects of topiramate on neural activity, heavy drinking, and the moderating effect of genetic variation in individuals with alcohol use disorder. In a previous study, topiramate robustly decreased heavy drinking, an effect that was moderated by allelic variation in rs2832407, a polymorphism in the gene encoding a kainate receptor subunit, which binds glutamate. Although the mechanism underlying topiramate's effects on alcohol use remains unclear, it both facilitates GABA function and inhibits glutamate activity, potentially suppressing mesocorticolimbic dopamine release. This, in turn, decreases the reinforcing effects of alcohol and devalues the previously rewarding properties of alcohol-related cues over time. To advance our understanding of topiramate's effects and the effort to personalize pharmacotherapy in patients with alcohol use disorder, Dr. Wetherill is recruiting patients from Dr. Henry Kranzler's 12-week, parallel-groups, placebo-controlled study of topiramate in heavy drinkers with DSM-5 alcohol use disorder. That study is stratifying the random assignment using rs2832407 genotype. To achieve Dr. Wetherill's study aims, patients from the clinical trial are asked to complete two neuroimaging scan sessions, one prior to randomization and one following six weeks of study medication (topiramate or placebo). Data collection is ongoing and findings from this study could improve our understanding of how topiramate exerts its beneficial effects in treating alcohol use disorder, which could contribute substantially to the personalized treatment of heavy drinkers.

Recently, Dr. Wetherill, together with Dr. Franklin, started a new NIDA-funded study examining the influence of the natural hormonal milieu on the brain and behavior. Cigarette smoking remains the leading preventable cause of death in the United States and women who smoke are at higher risk of developing tobacco-related diseases, experience more severe tobacco-related health consequences, and have lower odds of successfully quitting smoking than men. Further, animal studies have shown that the ovarian hormones, estrogen and progesterone, which fluctuate over the course of the menstrual cycle, modulate addictive behavior. The animal literature indicates that during the pre-ovulatory or follicular phase of the menstrual cycle, when the ratio of progesterone-to-estrogen is low, females are more likely to engage in addictive behaviors. In contrast, during the pre-menstrual or luteal phase of the menstrual cycle, when the progesterone-to-estrogen ratio is high, addictive behaviors are attenuated, suggesting that progesterone could protect women from a relapse to smoking or other addictive behaviors. Thus, the research team is conducting a longitudinal neuroimaging study of naturally cycling females who smoke cigarettes. The women are followed and assessed across three to four natural menstrual cycles, during which time they complete three MRI scans at specific points in the menstrual cycle based on their hormone levels. Participants also complete a neurobehavioral battery and daily web-based surveys. Data collection for this study is underway. The results from this study could help to identify optimal times during the month for women to attempt to quit smoking and times when they are at greatest risk for relapse.

The work described above is supported by the Penn Center for Studies of Addiction; the National Institute on Drug Abuse; the National Institute on Alcohol Abuse and Alcoholism; and an outstanding staff that includes Melanie Maron, Timothy Pond, Nathan Hager, Sarah Moskat, Danielle Romer, Danielle Pelosi, Chaela Nutor, Stefanie Darnley, Gail Kaempff, Laurie Downing, Remona Gray, and the staff at the Penn Center for Functional Neuroimaging.

EMPLOYEE PROFILE: ANDREA ALBELDA, BS

Andrea Albelda is the Grants Manager for the Center for Studies of Addiction. Prior to joining the CSA, Andrea was a Grants Coordinator in the Division of Endocrinology, Diabetes, and Metabolism in the Perelman School of Medicine. She found her way to grants management through her work at the Philadelphia Department of Public Health in the Communities Putting Prevention to Work (CPPW) effort, which was funded by the American Recovery and Reinvestment Act of 2009. In that role, Andrea assisted the Director with proposal design and review and department-wide grant submissions.



Andrea is a graduate of Penn State University, where she received a Bachelor's of Science in Spanish, with a background in Education. Although her current career path is not directly related to her college degree, she hopes eventually to return to school to pursue a degree in Special Education. It was through mutual Penn State friends that Andrea met her husband, Ben, who also works in the Department of Psychiatry (in the Center for Interdisciplinary Research on Nicotine Addiction). Together they enjoy watching football and Game of Thrones, and they are huge Philly sports fans. They are

also the loving parents to two ferocious cats, Missy and Jax (you can follow Jax on his own Instagram account, just ask Andrea for his handle). Andrea also spends time on the weekends volunteering in the Animal Care and Control Team off-site adoption center at the Petco in Andorra, where she has helped to find new homes for many kitties.

Andrea has enjoyed her time at the CSA so far and looks forward to spending many more years helping to ensure that the CSA continues to be a well-funded and well-respected center in the field of addictions research!

WE MOVED

Thoughts of home(s)....

The Penn Center for Studies on Addiction (CSA) has now occupied newly-renovated space at 3535 Market Street for more than 8 months – reflecting the move of investigators and staff from 3900 Chestnut Street (in February 2017) and 3440 Market Street (in July 2017). The new space is on the 5th floor of 3535 Market Street, enabling easy convergence and collaboration with addictions researchers who have been working on the 4th Floor of the same building for many years. The new 5th floor space still “smells new” – and it provides plenty of room for the next chapter in addictions treatment research at Penn.

At the VA (1971-1988). It is worth remembering that good research can take place under considerably less comfortable conditions. The original “home” of what became the CSA was a (very) humble one story brick-building on the VA campus – a converted VA laundry facility offered to Dr. O’Brien when he and Dr. Woody established the first substance abuse services for opioid-addicted Veterans returning from the Vietnam War, in **1971**. This facility at the southern edge of the VA campus, aka “**Building 7**” (Federal Buildings are not generally known for their creative labels), offered medication-assisted treatment for opioid dependence, along with treatment for other addictions. The adjacent brick two-story “**Building 3**” became the location for much-needed alcohol treatment services, and “**Building 15**”, a few yards uphill, eventually housed Dr. O’Brien’s office and the early human laboratory space. For nearly two decades, this little cluster of buildings supported pioneering treatment-research in addiction. Early studies demonstrated the ability of learned drug cues to trigger drug desire, the ability of addicted patients to benefit from professional psychotherapy, the efficacy of opiate-substitution treatments, the efficacy of opiate antagonist treatments (for both opioid addiction and eventually for alcoholism), and the importance of treating psychiatric co-morbidities. The Addiction Severity Index, an instrument now used worldwide to measure addicted patients’ problems and response to treatment, came to life in these early buildings.

All of these findings occurred in interiors that were “rich in human interactions”: as the space was tight, it ensured the regular bumping together of impassioned investigators and research ideas – and the patients whose struggles inspired and shaped the research. These proximities forged close, long-lasting relationships among the early investigators and a strong commitment to research with clear translational benefit for the patients. Of course, when any of us stopped to notice it, the *physical* interiors themselves were uninspiring. The painted cinderblock walls were not easy on the eye, and the furnishings had been (for the most part) cast off by the main VA hospital. Heating and cooling was a recurrent challenge, and whenever the environmental problems were identified, we were solemnly reminded that the building was indeed a

converted laundry facility and was not intended for extended human occupancy!

Speedie's (1988-1990). By 1988, the rapidly-growing addictions group was “splitting the seams” of Building 7, and the building’s mounting physical problems led to the search for a new research home. Penn offered some “on-campus” space – in the upper floors of a three-story Victorian building on Chestnut, between 39th and 40th Streets. The lower floor was initially unoccupied, and the addictions investigators fondly hoped for a café, deli, or coffee shop. Instead, the University leased the first-floor space to [Speedie's Sports Pub](#). *This meant that our patients struggling with addictions had to navigate the foyer of Speedie's to enter or exit the clinical addictions research space!*

Chestnut Hall (1990-2017). Dr. O'Brien pointed out the problem with this geography (a pub within an addiction treatment center) to Penn, and the glaring incongruity led to new space: a massive, custom renovation of the long-vacant ballroom and kitchen area of the old [Chestnut Hall](#) hotel at [3900 Chestnut](#). The architects retained historical elements of the 1930's building (the arched exterior windows, 19 vertical feet of incoming light in each; the original columns of the ball-room) and planned interior transoms to pull light inward into the renovated spaces. The entry foyer was light-filled, two-stories high – a gently sweeping staircase linked the first floor to the mezzanine research offices. Beginning in September of 1990, the space at 3900 Chestnut became home to our growing group of addictions investigators, and to a number of center grants. We lived in this gracious space during the heady years of the “NIH Budget Doubling” (1998-2003). In 2011, we celebrated the 40th anniversary of the founding of the CSA – with a special acknowledgment of Dr. O'Brien's extraordinary contributions to the field.

Amidst all the positives during the 27+ years at Chestnut Hall, the physical space itself – despite its beautiful sweeping interior – also had its challenges. Floods from air-conditioner overflow trays (or more worrisome sources) were a common occurrence that caused ceiling tiles to crumbled and collapse. Mysterious wall leaks would soak our carpets. Pieces of pipe once crashed through the ceiling, causing an injury. Unexpectedly, bricks fell into the mezzanine bathroom (from construction) and through Dr. O'Brien's tall office windows (from intoxicated fraternity parties across the street).

3535 Market Street (2017-). Our expressions of concern about these events fueled the relocation and, in late 2014, Penn formally initiated the consolidation of the investigators and staff at 3900 Chestnut Street with those at 3440 Market Street. The new building at 3535 Market Street was already home to several other addictions investigators, and Penn's meta-plan was to consolidate most of Psychiatry in this site, including the Departmental administrative hub, formerly at Blockley Hall. From the planning stage to completed renovations of the 5th Floor took more than two years, with initial move-ins to the current space during a snowy week in [February 2017](#).

Some of us are still adjusting to the new “corporate high-rise” environment at 3535 Market. Though it clearly smells better, is less damp, and definitely less dangerous (!), than some of our previous locations – memories of the early research homes are still vivid for many of us. Like all memories of home, they take on a warmth and a glow because of the special people within the early spaces. They applauded our first steps, our first words, our first science. Their caring spirit, creative passion, and enduring humor have been a magic carpet lifting us across the decades – while always making us feel right at home, *wherever we are*. Magic, indeed.

Anna Rose Childress, Ph.D.

UPCOMING EVENTS AT THE CENTER

November 6, 2017

Kelly Cosgrove, PhD, Yale University
Imaging sex differences in tobacco smoking with PET

November 27, 2017

Ali Ely, PhD
Title to Be Announced

December 11, 2017

Teresa Patten, PhD candidate, University of Pennsylvania
Title to Be Announced

For a full listing of CSA seminars, please go to: <http://www.med.upenn.edu/csa/seminars.html>

Penn Behavioral Health



Treatment Research Center

Addiction Treatment
& Research



CONTACT US

Click below for a complete list of our clinical trials:

http://www.med.upenn.edu/csa/addiction_clinicaltrials.html

If you have any questions regarding one of our clinical trials,
please call 215-746-0222 or email: addicted@med.upenn.edu