17th Annual Research Day

DEPARTMENT OF PSYCHIATRY

UNIVERSITY OF PITTSBURGH

SCHOOL OF MEDICINE

JUNE 8, 2017
17TH Annual Department of Psychiatry Research Day
University Club
Thursday, June 8, 2017, 8:00 am – 4:00 pm

8:00am-8:30am  Registration (Main Lobby)

8:30am-11:45pm  Poster Session

(Posters must be removed from Ballroom A by 11:45am)

11:45am-12:00pm  Remove posters and pick up lunch on 2nd and 3rd floors

12:00pm-1:00pm  Lunch

Roundtable Discussions (Registration and Confirmation Required)

<table>
<thead>
<tr>
<th>SESSION #</th>
<th>TOPIC</th>
<th>LOCATION</th>
</tr>
</thead>
</table>
| Roundtable 1 | Developing and Using Apps in Research  
Facilitator: Oliver J. Lindhiem, PhD | Conference Room A 3rd Floor |
| Roundtable 2 | Subject Recruitment and Retention  
Facilitator: Duncan B. Clark, MD, PhD | Conference Room A 3rd Floor |
| Roundtable 3 | Understanding the Department’s Grant Review Process  
Facilitator: Daniel J. Buysse, MD | Conference Room A 3rd Floor |
| Roundtable 4 | Neuromodulation as a Research Tool  
Facilitators: Mary L. Phillips, MD and Fabio Ferrarelli, MD, PhD | Conference Room A 3rd Floor |
| Roundtable 5 | Crafting a Research Career as a Clinical Psychologist  
Facilitator: Stephanie D. Stepp, PhD | Conference Room A 3rd Floor |
| Roundtable 6 | Reproducibility in Research  
Facilitator: Meredith Lotz Wallace, PhD | Conference Room A 3rd Floor |
| Roundtable 7 | Integrating Contextual Risk Factors in Research  
Facilitators: David A. Brent, MD and Nadine Melhem, PhD | Conference Room A 3rd Floor |
| Roundtable 8 | Mentorship 101  
Facilitator: Erika E. Forbes, PhD | Conference Room B 3rd Floor |
| Roundtable 9 | Managing Professional Relationships in Academia  
Facilitator: Hermi Woodward | Conference Room B 3rd Floor |
| Roundtable 10 | Strategies for Writing "Killer" Specific Aims  
Facilitator: Robert A. Sweet, MD | Ivy Room 2nd Floor |

General Seating for Research Day participants not registered for Roundtable discussions:
1st Floor: No seating is available on the 1st floor during lunch due to transition activities
2nd Floor: Gold Room
3rd Floor: Hallway Conversation Areas
4th Floor: Rooftop Terrace (weather permitting)

1:15pm-2:15pm  Keynote Address (Ballroom A)
Brooke Molina, PhD
Professor of Psychiatry, Psychology and Pediatrics
2:15pm-2:45pm Speed Dat(a)ing Session I (Ballroom A)
1. Zachary Freyberg, MD, PhD
2. Layla Banihashemi, PhD
3. Lauren Bylsma, PhD
4. Peter Franzen, PhD

2:45pm-3:00pm Break – Light refreshments will be served in Ballroom A

3:00pm-3:30pm Speed Dat(a)ing Session II (Ballroom A)
1. Leslie Horton, PhD
2. Meredith Lotz Wallace, PhD
3. Matthew MacDonald, PhD
4. Lori Scott, PhD

3:30pm-4:00pm Awards Ceremony (Ballroom A)
David A. Lewis, MD
Distinguished Professor of Psychiatry and Neuroscience
Thomas Detre Professor of Academic Psychiatry
Chairman, Department of Psychiatry

4:00pm Adjourn
Research Day
Poster Session
Maps
<table>
<thead>
<tr>
<th>Name</th>
<th>Poster Title</th>
<th>Poster Location</th>
<th>ID #</th>
<th>Poster Session Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acuff, Heather</td>
<td>Determining relationships between white matter structure and function in offspring at risk for bipolar disorder: The bipolar offspring study</td>
<td>Ballroom A</td>
<td>1</td>
<td>9:30am - 11:45am</td>
</tr>
<tr>
<td>Alarcón, Gabriela, PhD</td>
<td>Adolescents' gender and depressive symptoms are associated with amygdala functional connectivity during social reward</td>
<td>Ballroom A</td>
<td>2</td>
<td>8:30am - 9:30am, 10:30am - 11:45am</td>
</tr>
<tr>
<td>Alessi, Maria, BS</td>
<td>Obesity &amp; executive function in older adults: The moderating role of physical activity</td>
<td>Ballroom A</td>
<td>3</td>
<td>9:30am - 11:45am</td>
</tr>
<tr>
<td>Bachman, Peter, PhD</td>
<td>Toward a mechanistic biomarker of prodromal psychosis? The relationship between pre-attentive information processing and stress</td>
<td>Ballroom A</td>
<td>4</td>
<td>8:30am - 9:30am, 10:30am - 11:45am</td>
</tr>
<tr>
<td>Bachrach, Rachel, PhD</td>
<td>Drinking motives predict severity of binge drinking in underage drinkers</td>
<td>Ballroom A</td>
<td>5</td>
<td>9:30am - 11:45am</td>
</tr>
<tr>
<td>Benno, Maria Tina, BS</td>
<td>Relationships among pre-pregnancy weight and gestational weight gain early in pregnancy</td>
<td>Ballroom A</td>
<td>6</td>
<td>8:30am - 9:30am, 10:30am - 11:45am</td>
</tr>
<tr>
<td>Berholomey, Megan, PhD</td>
<td>Ketamine reduces yohimbine-cue-induced reinstatement of ethanol seeking and depressive-like behavior in female rats</td>
<td>Ballroom A</td>
<td>7</td>
<td>9:30am - 11:45am</td>
</tr>
<tr>
<td>Boccardi, Aleia</td>
<td>How brains are built: Community neuroscience education to improve child outcomes</td>
<td>Ballroom A</td>
<td>8</td>
<td>8:30am - 9:30am, 10:30am - 11:45am</td>
</tr>
<tr>
<td>Bridgwater, Miranda, BS</td>
<td>The relationship between premorbid adjustment and emotional intelligence in first-episode schizophrenia</td>
<td>Ballroom A</td>
<td>9</td>
<td>9:30am - 11:45am</td>
</tr>
<tr>
<td>Burns, Sarah, BS</td>
<td>A greater decline in physical activity appears to underlie the gain in body weight associated with mild hyperandrogenemia and consumption of a Western-Style Diet (WSD) in adolescent female monkeys</td>
<td>Ballroom A</td>
<td>10</td>
<td>8:30am - 9:30am, 10:30am - 11:45am</td>
</tr>
<tr>
<td>Byrd, Amy, PhD</td>
<td>Psychophysiological assessment of emotional reactivity during parent-child conflict as a predictor of reactive aggression in daily life</td>
<td>Ballroom A</td>
<td>11</td>
<td>9:30am - 11:45am</td>
</tr>
<tr>
<td>Chase, Henry, PhD</td>
<td>Examining a rule-based avoidance paradigm in individuals with Obsessive-Compulsive Disorder</td>
<td>Ballroom A</td>
<td>12</td>
<td>8:30am - 9:30am, 10:30am - 11:45am</td>
</tr>
<tr>
<td>Choukas-Bradley, Sophia, PhD</td>
<td>Symptoms of depression increase girls’ trajectories of sexual risk behavior from ages 14 to 18</td>
<td>Ballroom A</td>
<td>13</td>
<td>9:30am - 11:45am</td>
</tr>
<tr>
<td>Chung, Daniel Wonjae, PhD</td>
<td>Transdiagnostic comparison of dysregulated erbB4 splicing and parvalbumin expression across multiple psychiatric disorders</td>
<td>Ballroom A</td>
<td>14</td>
<td>8:30am - 9:30am, 10:30am - 11:45am</td>
</tr>
<tr>
<td>Conlon, Matthew, MD</td>
<td>Care transitions in the psychiatric hospital: Are older adults at greater risk?</td>
<td>Ballroom A</td>
<td>15</td>
<td>9:30am - 11:45am</td>
</tr>
<tr>
<td>Corbit, Victoria, BS</td>
<td>Dysregulation of cortical input to central striatum in the Sapap3-KO OCD mouse model</td>
<td>Ballroom A</td>
<td>16</td>
<td>8:30am - 9:30am, 10:30am - 11:45am</td>
</tr>
<tr>
<td>Cummings, Logan, BA</td>
<td>Sleep disturbance and emotion regulation dysfunction in depression: Self-report and neural evidence</td>
<td>Ballroom A</td>
<td>17</td>
<td>9:30am - 11:45am</td>
</tr>
<tr>
<td>D’Aiuto, Leonardo, PhD</td>
<td>Human three-dimensional neuronal platforms for drug screening</td>
<td>Ballroom A</td>
<td>18</td>
<td>8:30am - 9:30am, 10:30am - 11:45am</td>
</tr>
<tr>
<td>DePoy, Lauren, PhD</td>
<td>NPAS2 knockout increases intravenous cocaine self-administration</td>
<td>Ballroom A</td>
<td>19</td>
<td>9:30am - 11:45am</td>
</tr>
<tr>
<td>Dienel, Samuel</td>
<td>Development of transcripts regulating dendritic spines in layer 3 pyramidal cells of the monkey prefrontal cortex: Implications for the pathogenesis of schizophrenia</td>
<td>Ballroom A</td>
<td>20</td>
<td>8:30am - 9:30am, 10:30am - 11:45am</td>
</tr>
<tr>
<td>Drab, Douglas</td>
<td>Student pharmacists’ perceived competence and knowledge in conducting SBIRT</td>
<td>Ballroom A</td>
<td>21</td>
<td>9:30am - 11:45am</td>
</tr>
<tr>
<td>Eckstrand, Kristen, MD, PhD</td>
<td>Anterior cingulate connectivity during reward processing mediates the relationship between trauma exposure and depressive and anxiety states in young adults</td>
<td>Ballroom A</td>
<td>22</td>
<td>8:30am - 9:30am, 10:30am - 11:45am</td>
</tr>
<tr>
<td>Name</td>
<td>Poster Title</td>
<td>Poster Location</td>
<td>ID #</td>
<td>Poster Session Time</td>
</tr>
<tr>
<td>-----------------------</td>
<td>------------------------------------------------------------------------------</td>
<td>-----------------</td>
<td>--------</td>
<td>----------------------------------</td>
</tr>
<tr>
<td>Edmiston, E. Kale, PhD</td>
<td>Predicting quality of life in distressed young adults: Cortico-thalamic BOLD signal and reward processing</td>
<td>Ballroom A</td>
<td>23</td>
<td>9:30am - 11:45am</td>
</tr>
<tr>
<td>Emery, Rebecca, MS</td>
<td>The relationship between impulsivity and body mass index depends on how impulsivity is measured: Findings from a comprehensive meta-analysis</td>
<td>Ballroom A</td>
<td>24</td>
<td>8:30am - 9:30am 10:30am - 11:45am</td>
</tr>
<tr>
<td>Flores, Luis, PhD</td>
<td>Right posterior superior temporal sulcus and temporoparietal junction response to social reward moderates the relation between naturalistic emotional closeness and positive affect among adolescents</td>
<td>Ballroom A</td>
<td>25</td>
<td>9:30am - 11:45am</td>
</tr>
<tr>
<td>Flynn, Emily, BS</td>
<td>An analysis of eating disorders and reward processing in a high-risk female sample</td>
<td>Ballroom A</td>
<td>26</td>
<td>8:30am - 9:30am 10:30am - 11:45am</td>
</tr>
<tr>
<td>Freyberg, Robin, PhD</td>
<td>The postpartum stress scale and smoking relapse</td>
<td>Ballroom A</td>
<td>27</td>
<td>9:30am - 11:45am</td>
</tr>
<tr>
<td>Friibance, Sarah</td>
<td>Deficits in attentional modulation of auditory stimuli in first episode schizophrenia</td>
<td>Ballroom A</td>
<td>28</td>
<td>8:30am - 9:30am 10:30am - 11:45am</td>
</tr>
<tr>
<td>Garver, Megan, BS</td>
<td>Dysregulated phosphoproteome expression in the auditory cortex in schizophrenia</td>
<td>Ballroom A</td>
<td>29</td>
<td>9:30am - 11:45am</td>
</tr>
<tr>
<td>George-Milford, Brandie, MA</td>
<td>Approaches to recruitment in a pediatric community sample</td>
<td>Ballroom A</td>
<td>30</td>
<td>8:30am - 9:30am 10:30am - 11:45am</td>
</tr>
<tr>
<td>Germeroth, Lisa, PhD</td>
<td>Self-efficacy in smoking restraint, but not motivation, predicts postpartum smoking resumption among women</td>
<td>Ballroom A</td>
<td>31</td>
<td>9:30am - 11:45am</td>
</tr>
<tr>
<td>Goldschen, Lauren</td>
<td>Coping with eating disorders on a college campus: A qualitative study</td>
<td>Ballroom A</td>
<td>32</td>
<td>8:30am - 9:30am 10:30am - 11:45am</td>
</tr>
<tr>
<td>Golt, Joshua, BS</td>
<td>Emotion dysregulation in youth with autism, but not autism symptom severity, is associated with greater use of intensive care services</td>
<td>Ballroom A</td>
<td>33</td>
<td>9:30am - 11:45am</td>
</tr>
<tr>
<td>Graur, Simona, MSW, LCSW</td>
<td>Impulsive sensation seeking de-couples the putamen from the posterior cingulate cortex</td>
<td>Ballroom A</td>
<td>34</td>
<td>8:30am - 9:30am 10:30am - 11:45am</td>
</tr>
<tr>
<td>Green, Cathrin, BS</td>
<td>Sensitivity to the disinhibiting effects of alcohol for adults with and without a history of ADHD</td>
<td>Ballroom A</td>
<td>35</td>
<td>9:30am - 11:45am</td>
</tr>
<tr>
<td>Greenberg, Tsafrir, PhD</td>
<td>Anxiety mediates the relationship between amygdala activity during emotion processing and poor quality of life in young adults</td>
<td>Ballroom A</td>
<td>36</td>
<td>8:30am - 9:30am 10:30am - 11:45am</td>
</tr>
<tr>
<td>Grubisha, Melanie, MD, PhD</td>
<td>A schizophrenia-associated missense mutation in kalirin converges on multiple rhoA-dependent pathways involved in cytoskeletal morphology</td>
<td>Ballroom A</td>
<td>37</td>
<td>9:30am - 11:45am</td>
</tr>
<tr>
<td>Haigh, Sarah, PhD</td>
<td>Deficits in complex MMN to group size deviance in first-episode schizophrenia-spectrum psychosis</td>
<td>Ballroom A</td>
<td>38</td>
<td>8:30am - 9:30am 10:30am - 11:45am</td>
</tr>
<tr>
<td>Hamilton, Jessica, MA</td>
<td>Heart rate variability and depressive symptoms among high-risk late adolescents: The role of sleep</td>
<td>Ballroom A</td>
<td>39</td>
<td>9:30am - 11:45am</td>
</tr>
<tr>
<td>Hanford, Lindsay, PhD</td>
<td>Maternal caregiving moderates the association between emotionality and network topology in infants</td>
<td>Ballroom A</td>
<td>40</td>
<td>8:30am - 9:30am 10:30am - 11:45am</td>
</tr>
<tr>
<td>Haszto, Connor</td>
<td>Meta-analysis of membrane phospholipid metabolites in schizophrenia</td>
<td>Ballroom A</td>
<td>41</td>
<td>9:30am - 11:45am</td>
</tr>
<tr>
<td>Herb, Taylor, BS</td>
<td>Effects of nicotine versus placebo e-cigarette use on symptom relief during tobacco abstinence</td>
<td>Ballroom A</td>
<td>42</td>
<td>8:30am - 9:30am 10:30am - 11:45am</td>
</tr>
<tr>
<td>Herbstsomer, Robert Adam</td>
<td>Blinding of psychotherapy and pharmacology in clinical trials</td>
<td>Ballroom A</td>
<td>43</td>
<td>9:30am - 11:45am</td>
</tr>
<tr>
<td>Hildebrand, Mariah, BS</td>
<td>Circadian perturbation reveals susceptibility and resilience to reward-related behavior in adolescence</td>
<td>Ballroom A</td>
<td>44</td>
<td>8:30am - 9:30am 10:30am - 11:45am</td>
</tr>
<tr>
<td>Name</td>
<td>Poster Title</td>
<td>Poster Location</td>
<td>ID #</td>
<td>Poster Session Time</td>
</tr>
<tr>
<td>-----------------------------</td>
<td>------------------------------------------------------------------------------</td>
<td>-----------------</td>
<td>--------</td>
<td>-----------------------------------</td>
</tr>
<tr>
<td>Hildebrandt, Britny, MA</td>
<td>Exploring reward system responsivity in the nucleus accumbens across chronicity of binge eating in female rats</td>
<td>Ballroom A</td>
<td>45</td>
<td>9:30am - 11:45am</td>
</tr>
<tr>
<td>Hoffman, Gil, MD, PhD</td>
<td>Altered gradients of glutamate and GABA transcripts in the cortical visuospatial working memory network in schizophrenia</td>
<td>Ballroom A</td>
<td>46</td>
<td>8:30am - 9:30am 10:30am - 11:45am</td>
</tr>
<tr>
<td>Hunter, Daniesha, BS</td>
<td>Congruent parental report of child symptom severity: A study of fathers with a history of childhood ADHD and their preschool aged children</td>
<td>Ballroom A</td>
<td>47</td>
<td>9:30am - 11:45am</td>
</tr>
<tr>
<td>Hyde, James, PhD</td>
<td>Simultaneous <em>in vivo</em> calcium imaging and cortico-striatal hyperstimulation generated perseverative grooming in awake behaving mice</td>
<td>Ballroom A</td>
<td>48</td>
<td>8:30am - 9:30am 10:30am - 11:45am</td>
</tr>
<tr>
<td>Jakubowski, Karen, MS</td>
<td>Associations between cumulative adverse childhood experiences and cardiometabolic disease and mortality: A systematic review and meta-analysis</td>
<td>Ballroom A</td>
<td>49</td>
<td>9:30am - 11:45am</td>
</tr>
<tr>
<td>Kaplan, Gabrielle, BS</td>
<td>Mitochondrial complex I alterations in a mouse model of bipolar mania</td>
<td>Ballroom A</td>
<td>50</td>
<td>8:30am - 9:30am 10:30am - 11:45am</td>
</tr>
<tr>
<td>Karim, Helmet</td>
<td>Functional activation during emotion processing in late-life depression: Early markers of treatment response</td>
<td>Ballroom A</td>
<td>51</td>
<td>9:30am - 11:45am</td>
</tr>
<tr>
<td>Kennedy, Traci, PhD</td>
<td>Peer influences on alcohol use among young adults with ADHD histories</td>
<td>Ballroom A</td>
<td>52</td>
<td>8:30am - 9:30am 10:30am - 11:45am</td>
</tr>
<tr>
<td>Kincman, Joelle, PhD</td>
<td>OPTIMUM: Optimizing outcomes of treatment-resistant depression in older adults</td>
<td>Ballroom A</td>
<td>53</td>
<td>9:30am - 11:45am</td>
</tr>
<tr>
<td>Kolko, Rachel, PhD</td>
<td>Mothers' loss of control over eating during pregnancy in relation to their infants' appetitive traits</td>
<td>Ballroom A</td>
<td>54</td>
<td>8:30am - 9:30am 10:30am - 11:45am</td>
</tr>
<tr>
<td>Krivinko, Josh</td>
<td>Fingolimod treatment alters phospho-peptides with roles in dendritic morphology</td>
<td>Ballroom B</td>
<td>55</td>
<td>9:30am - 11:45am</td>
</tr>
<tr>
<td>Kuflewski, Jennifer</td>
<td>Measuring expression of candidate genes for Mediating reduced dendritic spine density in schizophrenia</td>
<td>Ballroom B</td>
<td>56</td>
<td>8:30am - 9:30am 10:30am - 11:45am</td>
</tr>
<tr>
<td>Kukich, Melanie, BS</td>
<td>Patterns of sensory rating due to the interaction of menthol status and nicotine content</td>
<td>Ballroom B</td>
<td>57</td>
<td>9:30am - 11:45am</td>
</tr>
<tr>
<td>Larsen, Bart, MS</td>
<td>Greater learning-dependent change in hippocampal circuitry relates to reward learning</td>
<td>Ballroom B</td>
<td>58</td>
<td>8:30am - 9:30am 10:30am - 11:45am</td>
</tr>
<tr>
<td>Levenson, Jessica, PhD</td>
<td>Longitudinal sleep phenotypes among offspring of bipolar parents and community controls</td>
<td>Ballroom B</td>
<td>59</td>
<td>9:30am - 11:45am</td>
</tr>
<tr>
<td>Manning, Elizabeth, PhD</td>
<td>OCD-relevant impairment in cognitive flexibility and altered cortico-striatal activity in SAPAP3 knockout mice</td>
<td>Ballroom B</td>
<td>60</td>
<td>8:30am - 9:30am 10:30am - 11:45am</td>
</tr>
<tr>
<td>Marek, Scott, PhD</td>
<td>Anterior cingulate theta band oscillations support adolescent maturations of cognitive flexibility</td>
<td>Ballroom B</td>
<td>61</td>
<td>9:30am - 11:45am</td>
</tr>
<tr>
<td>McCalley, Daniel</td>
<td>Long-term, cognitive consequences of adolescent cannabinoid self-administration in female Sprague-Dawley rats</td>
<td>Ballroom B</td>
<td>62</td>
<td>8:30am - 9:30am 10:30am - 11:45am</td>
</tr>
<tr>
<td>McFarland, Christine, BS, BA</td>
<td>Measuring the context of healing: Using PROMIS in chronic pain treatment</td>
<td>Ballroom B</td>
<td>63</td>
<td>9:30am - 11:45am</td>
</tr>
<tr>
<td>McKeon, Ashlee Brooke, PhD, CRC</td>
<td>Slow wave activity and sigma predict cognitive symptoms in combat-exposed military service members and veterans with posttraumatic stress disorder</td>
<td>Ballroom B</td>
<td>64</td>
<td>8:30am - 9:30am 10:30am - 11:45am</td>
</tr>
<tr>
<td>McKinney, Rachel</td>
<td>Verbal episodic memory deficits in first-episode psychosis</td>
<td>Ballroom B</td>
<td>65</td>
<td>9:30am - 11:45am</td>
</tr>
<tr>
<td>McKone, Kirsten</td>
<td>Social anxiety may not differentially explain ADHD-related early adult alcohol use</td>
<td>Ballroom B</td>
<td>66</td>
<td>8:30am - 9:30am 10:30am - 11:45am</td>
</tr>
<tr>
<td>Miragaia, Alex, MD</td>
<td>Facilitating sturdy brain development in adolescents in the juvenile justice system</td>
<td>Ballroom B</td>
<td>67</td>
<td>9:30am - 11:45am</td>
</tr>
<tr>
<td>Name</td>
<td>Poster Title</td>
<td>Poster Location</td>
<td>ID #</td>
<td>Poster Session Time</td>
</tr>
<tr>
<td>---------------------------</td>
<td>------------------------------------------------------------------------------</td>
<td>-----------------</td>
<td>------</td>
<td>----------------------------------</td>
</tr>
<tr>
<td>Mizuno, Akiko, PhD</td>
<td>An investigation for neural basis of subjective cognitive decline</td>
<td>Ballroom B</td>
<td>68</td>
<td>8:30am - 9:30am</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>10:30am - 11:45am</td>
</tr>
<tr>
<td>Montez, David, PhD</td>
<td>Developmental improvements in mean behavioral performance and behavioral variability are related to stabilizing gain signals</td>
<td>Ballroom B</td>
<td>69</td>
<td>9:30am - 11:45am</td>
</tr>
<tr>
<td>Montrenes, Joshua, BS</td>
<td>Clinical presentation of inpatient youth with ASD and Comorbid Psychotic Spectrum Disorders</td>
<td>Ballroom B</td>
<td>70</td>
<td>8:30am - 9:30am</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>10:30am - 11:45am</td>
</tr>
<tr>
<td>Murty, Vishnu, PhD</td>
<td>Context-dependent neurodevelopment of mesolimbic dopamine systems during adolescence</td>
<td>Ballroom B</td>
<td>71</td>
<td>9:30am - 11:45am</td>
</tr>
<tr>
<td>Ohm, David, MA</td>
<td>Mural creation to develop aesthetic empathy</td>
<td>Ballroom B</td>
<td>72</td>
<td>8:30am - 9:30am</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>10:30am - 11:45am</td>
</tr>
<tr>
<td>Pecina, Marta, MD, PhD</td>
<td>Inflammation, striatal dopamine receptor binding and anhedonia in depression</td>
<td>Ballroom B</td>
<td>73</td>
<td>9:30am - 11:45am</td>
</tr>
<tr>
<td>Pergi, Eliese</td>
<td>Investigating real-life stress reactivity in adolescence: A novel approach</td>
<td>Ballroom B</td>
<td>74</td>
<td>8:30am - 9:30am</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>10:30am - 11:45am</td>
</tr>
<tr>
<td>Piantadosi, Sean, BA</td>
<td>Identifying cellular mechanisms underlying the anti-compulsive properties of fluoxetine</td>
<td>Ballroom B</td>
<td>75</td>
<td>9:30am - 11:45am</td>
</tr>
<tr>
<td>Pongibove, Maria</td>
<td>Temporal learning dynamics of age-related reward processing</td>
<td>Ballroom B</td>
<td>76</td>
<td>8:30am - 9:30am</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>10:30am - 11:45am</td>
</tr>
<tr>
<td>Quach, Alina</td>
<td>Neurocognitive development of response inhibition and risk for substance use</td>
<td>Ballroom B</td>
<td>77</td>
<td>9:30am - 11:45am</td>
</tr>
<tr>
<td>Rengasamy, Manivel, MD</td>
<td>Pediatric inflammatory bowel disease and depressive symptomatology</td>
<td>Ballroom B</td>
<td>78</td>
<td>8:30am - 9:30am</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>10:30am - 11:45am</td>
</tr>
<tr>
<td>Rich, Matthew, MS</td>
<td>Calcineurin regulates cocaine-cue neuroplastic changes in the amygdala to alter relapse-like behavior</td>
<td>Ballroom B</td>
<td>79</td>
<td>9:30am - 11:45am</td>
</tr>
<tr>
<td>Salk, Rachel, PhD</td>
<td>The clinical utility of depression and weight-related subtypes among weight-concerned women smokers</td>
<td>Ballroom B</td>
<td>80</td>
<td>8:30am - 9:30am</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>10:30am - 11:45am</td>
</tr>
<tr>
<td>Sapra, Manish, MD, MMM</td>
<td>Introducing peer navigators: Improving patient engagement by embedding enhanced peer support services in acute care settings</td>
<td>Ballroom B</td>
<td>81</td>
<td>9:30am - 11:45am</td>
</tr>
<tr>
<td>Sarpal, Deepak, MD</td>
<td>Relationship between duration of untreated psychosis and intrinsic corticostriatal connectivity in patients with early phase schizophrenia</td>
<td>Ballroom B</td>
<td>82</td>
<td>8:30am - 9:30am</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>10:30am - 11:45am</td>
</tr>
<tr>
<td>Schreiber, Justin, DO, MPH</td>
<td>Mental health elective for pediatric residents</td>
<td>Ballroom B</td>
<td>83</td>
<td>9:30am - 11:45am</td>
</tr>
<tr>
<td>Scott, Lorraine, BS</td>
<td>Stuck on a feeling: Spontaneous recall of daily events among children at high vs. low familial risk for depression</td>
<td>Ballroom B</td>
<td>84</td>
<td>8:30am - 9:30am</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>10:30am - 11:45am</td>
</tr>
<tr>
<td>Sequeira, Gina, MD</td>
<td>Impact of gender expression on disordered eating, body dissatisfaction and BMI in a cohort of transgender youth</td>
<td>Ballroom B</td>
<td>85</td>
<td>9:30am - 11:45am</td>
</tr>
<tr>
<td>Shafer, Anna</td>
<td>Reduced mismatch negativity is associated with decreased Heschl's gyrus volume in first episode schizophrenia</td>
<td>Ballroom B</td>
<td>86</td>
<td>8:30am - 9:30am</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>10:30am - 11:45am</td>
</tr>
<tr>
<td>Silverstein, R. Gina</td>
<td>Postpartum psychological distress associated with systematized emergency team response during labor and delivery</td>
<td>Ballroom B</td>
<td>87</td>
<td>9:30am - 11:45am</td>
</tr>
<tr>
<td>Sun, Xiaolin</td>
<td>Pseudophosphorylation of MAP2c increases MAP2 protein accumulation</td>
<td>Ballroom B</td>
<td>88</td>
<td>8:30am - 9:30am</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>10:30am - 11:45am</td>
</tr>
<tr>
<td>Szücs, Anna, MD</td>
<td>Personality and vulnerability to suicide in the elderly</td>
<td>Ballroom B</td>
<td>89</td>
<td>9:30am - 11:45am</td>
</tr>
<tr>
<td>Tarcjona, Goda</td>
<td>Gamma oscillations in auditory steady-state stimulation among adolescents with psychosis</td>
<td>Ballroom B</td>
<td>90</td>
<td>8:30am - 9:30am</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>10:30am - 11:45am</td>
</tr>
<tr>
<td>Name</td>
<td>Poster Title</td>
<td>Poster Location</td>
<td>ID #</td>
<td>Poster Session Time</td>
</tr>
<tr>
<td>-----------------------------</td>
<td>------------------------------------------------------------------------------</td>
<td>-----------------</td>
<td>------</td>
<td>--------------------------------------</td>
</tr>
<tr>
<td>Tervo-Clemmens, Brenden, MS</td>
<td>Early cannabis use and neurocognitive risk: A prospective cohort fMRI study</td>
<td>Ballroom B</td>
<td>91</td>
<td>9:30am - 11:45am</td>
</tr>
<tr>
<td>Tiani, Alaina, BS</td>
<td>Health behaviors by adolescents with ADHD: Associations with ADHD symptoms and symptom subtype</td>
<td>Ballroom B</td>
<td>92</td>
<td>8:30am - 9:30am 10:30am - 11:45am</td>
</tr>
<tr>
<td>Transue, Emilie</td>
<td>Clustering emotion dysregulation in autism spectrum disorders</td>
<td>Ballroom B</td>
<td>93</td>
<td>9:30am - 11:45am</td>
</tr>
<tr>
<td>Vadnie, Chelsea, PhD</td>
<td>Using optogenetics to determine the role of the suprachiasmatic nucleus in mood-like behaviors</td>
<td>Ballroom B</td>
<td>94</td>
<td>8:30am - 9:30am 10:30am - 11:45am</td>
</tr>
<tr>
<td>Versace, Amelia, MD</td>
<td>Global probabilistic tractography and symptom dimensions in a prospectively characterized sample of adults with a childhood diagnosis of ADHD</td>
<td>Ballroom B</td>
<td>95</td>
<td>9:30am - 11:45am</td>
</tr>
<tr>
<td>Vezzoli, Jessica, BS</td>
<td>Paternal age at birth of child with ASD and its association with symptom severity</td>
<td>Ballroom B</td>
<td>96</td>
<td>8:30am - 9:30am 10:30am - 11:45am</td>
</tr>
<tr>
<td>Victor, Sarah, MA</td>
<td>Predicting self-injurious thoughts and behaviors over time: The roles of self-conscious emotions and interpersonal stress</td>
<td>Ballroom B</td>
<td>97</td>
<td>9:30am - 11:45am</td>
</tr>
<tr>
<td>Walker Payne, Monica, MA</td>
<td>Evaluating youth peer support within high fidelity wraparound: Defining roles, tracking progress, and exploring preliminary outcomes</td>
<td>Ballroom B</td>
<td>98</td>
<td>8:30am - 9:30am 10:30am - 11:45am</td>
</tr>
<tr>
<td>Wang, Frances, MA</td>
<td>Role of genetically-influenced 5-HT functioning in a bifactor model of psychopathology</td>
<td>Ballroom B</td>
<td>99</td>
<td>9:30am - 11:45am</td>
</tr>
<tr>
<td>Wang, Yiming</td>
<td>Transcallosal auditory connectivity in first episode schizophrenia</td>
<td>Ballroom B</td>
<td>100</td>
<td>8:30am - 9:30am 10:30am - 11:45am</td>
</tr>
<tr>
<td>Wei, Wenjing</td>
<td>Increased cerebral blood flow in middle and posterior cingulate is associated with improvement in depression severity in a longitudinal treatment trial of late-life depression</td>
<td>Ballroom B</td>
<td>101</td>
<td>9:30am - 11:45am</td>
</tr>
<tr>
<td>Wesesky, Maribeth, BPS</td>
<td>Combined young and older adult mirtazapine pilot trials in AUD/MDD</td>
<td>Ballroom B</td>
<td>102</td>
<td>8:30am - 9:30am 10:30am - 11:45am</td>
</tr>
<tr>
<td>Westbrook, Kevin</td>
<td>Rostral-caudal effects of kalirin reduction on dendritic spines in APPSWE/PSEN1dE9 transgenic mice</td>
<td>Ballroom B</td>
<td>103</td>
<td>9:30am - 11:45am</td>
</tr>
<tr>
<td>Wilson, Jonathan, BS</td>
<td>Contributions of distinct ventral prefrontal subregions to value-based decision-making</td>
<td>Ballroom B</td>
<td>104</td>
<td>8:30am - 9:30am 10:30am - 11:45am</td>
</tr>
<tr>
<td>Wood, Jesse, PhD</td>
<td>Stimulation of medial orbitofrontal cortex terminals in ventromedial striatum causes neuroplastic changes in cortical networks</td>
<td>Ballroom B</td>
<td>105</td>
<td>9:30am - 11:45am</td>
</tr>
<tr>
<td>Woody, Mary, MS</td>
<td>Competition effects in visual cortex between emotional distractors and a primary task in remitted depression</td>
<td>Ballroom B</td>
<td>106</td>
<td>8:30am - 9:30am 10:30am - 11:45am</td>
</tr>
<tr>
<td>Zimmerman, Eric, BS</td>
<td>The nucleus reuniens of the midline thalamus gates prefrontal-hippocampal modulation of ventral tegmental area dopamine neuron activity</td>
<td>Ballroom B</td>
<td>107</td>
<td>9:30am - 11:45am</td>
</tr>
</tbody>
</table>
Research Day
Abstracts
**Presenter:** Heather E. Acuff  
**Education:** University of Pittsburgh  
**Current Position:** MD/PhD Student  
**Principal Area of Research Interest:** Pediatric Mood Disorders  
**Current Research Support:** NIMH R01 MH060952-16 (mPI: Mary Phillips, MD, MD (Cantab), PI: Boris Birmaher, MD), NIH/NCATS 1TL1 TR001858-01 (PI: Wishwa Kapoor, MD)  
**Mentor(s):** Mary L. Phillips, MD, MD (CANTAB)

**Determining relationships between white matter structure and function in offspring at risk for bipolar disorder: The bipolar offspring study**

**Author(s):** Acuff AE¹, Versace A², Bertocci MA², Hanford LC², and Phillips ML²  
**Affiliation(s):** ¹Medical Scientist Training Program, University of Pittsburgh School of Medicine and ²Department of Psychiatry, University of Pittsburgh School of Medicine

**Study:** Recent studies have identified abnormalities in white matter structure and functional activity for emotion processing in youth at risk for bipolar disorder (BD). However, the specificity of these relationships to BD has yet to be elucidated. Our objective was to study these structural-functional relationships in youth at risk for BD.

**Methods:** Offspring (aged 8-17) of parents with BD (OBP, n=33), a non-BD psychiatric diagnosis (OCP, n=37), and no diagnosis (OHP, n=25) underwent a structural scan using diffusion tensor imaging and a functional magnetic resonance imaging scan while performing a dynamic faces task. We used elastic net regression and correlation analyses to determine group differences in these structural-functional relationships.

**Results:** 27 variables explained 42.24% of the variance in activity in the amygdala and prefrontal cortical regions in response to negative emotions (lambda=0.549). Group interactions were found between OBP and OCP in the left uncinate fasciculus, inferior longitudinal fasciculus (ILF), and superior longitudinal fasciculus volume which accounted for 11.08% of this variance. Correlation analyses revealed significant differences in relationships between left ILF volume and left amygdala activity between OBP (positive correlations) and OCP (negative correlations) (p=0.012). These differences remained significant only in subjects without a psychiatric diagnosis (p=0.048).

**Conclusion:** These findings suggest that the relationship between left ILF volume and left amygdala activity significantly distinguishes youth at risk for BD from youth at risk for similar conditions. This relationship may reflect a vulnerability mechanism predisposing to the development of BD in the future.

**Significance:** These relationships between white matter volume and functional activity may contribute to improved diagnostic accuracy in individuals developing BD.

**Funding Source(s):** NIMH R01 MH060952-16 (mPI: Mary Phillips, MD, MD (Cantab), PI: Boris Birmaher, MD); NIH/NCATS 1TL1 TR001858-01 (PI: Wishwa Kapoor, MD)
Adolescents’ gender and depressive symptoms are associated with amygdala functional connectivity during social reward

Author(s): Alarcón G¹, Eckstrand K², Mohanty A¹, and Forbes EE¹
Affiliation(s): ¹Department of Psychiatry, University of Pittsburgh School of Medicine and ²Western Psychiatric Institute and Clinic of UPMC

Study: Amygdala resting state functional connectivity (FC) has been implicated in major depression; however, few studies have examined amygdala task-related FC in relation to depressive symptoms during adolescence. Social reward is one such relevant context given the amygdala’s role in emotion processing, social reward processing alterations in depression and adolescents’ heightened sensitivity to reward and social information. Here, we measured FC during social reward and explored moderating effects of gender and substance use exposure (SUE), due to their associations with depressive symptoms.

Methods: Forty-six healthy adolescents completed questionnaires assessing substance use (Youth Risk Behavior Survey) and depressive symptoms (Center for Epidemiologic Studies Depression Scale), and a social reward task during functional magnetic resonance imaging. Depressive symptoms were regressed against whole-brain FC of bilateral amygdalae using the CONN toolbox (voxel and cluster p<0.0001, FDR). Post-hoc multivariate ANOVAs assessed the effects of gender and SUE, controlling for age, on FC.

Results: Depressive symptoms were positively associated with FC within amygdalae and between amygdala and subgenual cingulate cortex (SCC). A significant interaction between gender and SUE was observed for amygdala-SCC FC, such that boys with no SUE had the strongest FC.

Conclusion: Top-down modulation of the amygdala by SCC ordinarily functions to regulate emotional experiences; however, in social reward contexts, this function may be weakened in youth with SUE and in girls, manifesting in fewer depressive symptoms.

Significance: These findings highlight the importance social context when determining the utility of amygdala FC as a predictor of depressive symptoms.

Funding Source(s): R21 DA033612 (PI: Erika Forbes, PhD)
Obesity & executive function in older adults: The moderating role of physical activity

Author(s): Alessi M\(^1\), Gujral S\(^2\), and Erickson K\(^3\)
Affiliation(s): \(^1\)Western Psychiatric Institute and Clinic of UPMC; \(^2\)Department of Psychology University of Pittsburgh; and \(^3\)Center for Neural Basis of Cognition, Carnegie Mellon University and University of Pittsburgh

Study: Obesity is associated with impaired executive function and this association may vary with age. Physical activity is one lifestyle factor that has been shown to improve executive functioning. Higher levels of physical activity may mitigate obesity’s negative association with executive function.

Methods: This study examined the extent to which physical activity moderates the association between obesity and executive function in a sample of older adults (n = 110, ages 55-90). Ordinary Least Squares Regression Models were used to test the independent association between BMI and cognitive performance and whether accelerometer-based measures of physical activity moderate the association between BMI and cognitive performance. In order to investigate these relationships at both general levels of physical activity and specific bouts of exercise, two-way ANOVAs assessed the association between BMI and a categorical bout measure on cognitive performance.

Results: Specifically, high BMI predicted poorer accuracy on the Flanker task ($\beta = -.312, p = .009$), while high PA predicted greater accuracy on the Stroop task ($\beta = .289, p = .003$). On the Task Switch paradigm, physical activity moderated the association between BMI and reaction time switch cost, such that at high body mass, greater amounts of physical activity were associated with better task performance ($\beta = -.957, p = .006$). Two-way ANOVAs revealed a significant interaction between BMI and exercise, such that obesity predicted poor accuracy on Flanker ($F(1) = 9.00, p = .0004$) and Stroop ($F(1) = 4.28, p = .041$) at zero levels of exercise, while both obese and non-obese adults who exercised performed comparably on either task.

Conclusion: BMI and physical activity independently and differentially predicted executive function in our sample of older adults. These findings support the beneficial effect of physical activity on executive function, particularly in more obese older adults, and suggest that the effect of BMI on cognition may vary as a function of physical activity.

Significance: This study utilized objective armband data to measure physical activity and exercise levels in a sample of older adults, and examined the interaction between obesity and physical activity on cognitive function.

Funding Source(s): NIH R01 DK095172
**Toward a mechanistic biomarker of prodromal psychosis? The relationship between pre-attentive information processing and stress**

*Author(s):* Bachman P\(^1\), Mathalon DH\(^2\), Walker EF\(^3\), Malin BE\(^1\), and the North American Prodrome Longitudinal Study Investigators

*Affiliation(s):* \(^1\)Pittsburgh Department of Psychiatry, University of Pittsburgh School of Medicine; \(^2\)Department of Psychiatry, University of California, San Francisco; and \(^3\)Department of Psychology, Emory University

**Study:** Growing focus on secondary prevention of schizophrenia has fostered study of people judged to be at clinical high risk (CHR) for psychosis due to presence of subclinical signs and symptoms. Identification of physiological indices (or relationships among indices) that prove predictive of psychosis is the first step in the search for biomarkers of psychosis pathogenesis.

**Methods:** Using EEG data collected as part of the North America Prodrome Longitudinal Study (“NAPLS”), we tested associations between amplitude of the Mismatch Negativity (MMN) event-related potential (ERP) and cortisol concentration in saliva collected at rest – both collected at baseline. Groups included: CHR youth who transitioned to psychosis during follow-up, CHR youth whose symptoms remitted, CHR youth who remained symptomatic–but not psychotic–at the conclusion of follow-up, and typically developing controls.

**Results:** CHR youth who later transitioned to full psychosis showed a significant association between baseline MMN amplitude and baseline cortisol level ($r=0.348$, $p<0.01$). CHR youth whose symptoms remitted, like the controls, showed no such association (remitters: $r=0.043$, $p=0.67$; controls: $r=-0.015$, $p=0.84$). CHR youth who remained symptomatic, but not psychotic, through follow up showed an intermediate level of association ($r=0.194$, $p=0.12$).

**Conclusion:** Here we show evidence of a relationship between resting cortisol level and MMN, present selectively in CHR participants who later transitioned to psychosis. This association implicates both indices in the same (or closely related) pathogenic pathway to full psychosis.

**Significance:** In addition to suggesting that resting cortisol level may is functionally related to a cortically-mediated, pre-attentive process, during emerging psychosis, the relationship between the two measures adds a multi-variate candidate to the field’s set of potential physiological predictors of later illness.

**Funding Source(s):** NIMH K23, Department of Psychiatry, University of Pittsburgh School of Medicine
Drinking motives predict severity of binge drinking in underage drinkers

Author(s): Bachrach RL¹, Creswell KG², Skrzynski CJ², and Chung T¹
Affiliation(s): ¹Department of Psychiatry, University of Pittsburgh Medical Center and ²Department of Psychology, Carnegie Mellon University

Study: Many college students and young adults drink at levels far beyond the “standard” binge thresholds of 5+ (male) or 4+ (female) drinks per occasion, often consuming twice or even three times these amounts in a single sitting (i.e., 10/8+ and 15/12+ drinks). The consumption of such large quantities of alcohol can cause severe acute and long-term problems. As such, work that uncovers what motivates young people to drink at “high” or “extreme” levels is necessary for preventing high-intensity binge behavior. This study aimed to understand whether specific drinking motives predict severity of binge in a sample of underage drinkers (ages 18-20).

Methods: Underage current drinkers were recruited via a TurkPrime panel to participate in a study on health behaviors. Participants (N = 677, M_age = 19.25, 87.8% female) completed a web survey on drinking motives (i.e., coping, enhancement, social, and conformity reasons for drinking; Drinking Motives Questionnaire-Revised; Cooper, 1994) and frequency of binge drinking in the past year, defined as: “standard” (5/4+ drinks), “high” (10/8+ drinks), and “extreme” (15/12+ drinks). Ordinal logistic regression was conducted to predict level of binge drinking from the four drinking motive scales, controlling for sex, age, education, and ethnicity. Binge drinking severity, in the past year, was coded as an ordered categorical variable (0=non-bingers, 1=“standard” binge ≥1 time, 2= “high” binge ≥1 time, 3= “extreme” binge ≥1 time).

Results: Approximately one-third of the sample (33.8%) endorsed binging at the most extreme levels (15/12+) at least once in the past year. In addition, 17.1% binged at high levels (10/8+), 25.2% binged at standard levels (5/4+), and 17.1% denied ever binging in the past year. Logistic regression indicated that coping, enhancement, and conformity motives, but not social motives, significantly predicted the log odds of moving up one level in binge severity (as did being male). Thus, for every 1-unit increase in coping, enhancement, and conformity motives, individuals were 1.34, 1.44, and 1.47 (respectively) times more likely to binge at higher levels (ps<.01).

Conclusion: The prevalence of extreme binge drinking is high among underage drinkers and the link between coping, enhancement, and conformity drinking motives and severity of binge is significant. Social motives did not predict binge severity, suggesting that interventions to reduce binge drinking could specifically target coping, enhancement, and conformity drinking motives.

Significance: Interventions that focus on skills to cope with negative mood, engage in healthy activities to enhance positive mood, and resist peer influence, may help reduce binge drinking.

Funding Source(s): NIAAA training grant T32AA007453 (PI: Marie Cornelius, PhD)
Relationships among pre-pregnancy weight and gestational weight gain early in pregnancy

Author(s): Benno MT, Kolko RP, and Levine MD

Affiliation(s): 1Western Psychiatric Institute and Clinic of UPMC and 2Department of Psychiatry, University of Pittsburgh School of Medicine

Study: Research shows that excessive weight gain during pregnancy is associated with postpartum weight retention and adverse pregnancy outcomes. Women with higher weight prior to pregnancy are at increased risk for excessive gestational weight gain (GWG). Thus, we aimed to examine pre-pregnancy weight status in relation to other pregnancy specific variables and early GWG in a sample of pregnant women with overweight and obesity.

Methods: Participants included pregnant women (N = 200) with a body mass index (BMI) ≥25.0 kg/m², and gestational age < 20 weeks. Women self-reported their weight and height, which were used to determine their pre-pregnancy weight status (overweight or obese). At study enrollment, weight was measured and early GWG was calculated as the difference between current weight and self-reported pre-pregnancy weight. Women reported demographic and pregnancy-related information, and completed a semi-structured psychiatric interview. We used t-tests to evaluate women’s pre-pregnancy weight status in relation to their early GWG, pregnancy specific variables, and total number of lifetime psychiatric disorders.

Results: Across all women, the average GWG in early pregnancy was $M = 8.22$ lbs. ± $13.02$. Women with pre-pregnancy obesity gained more weight ($M = 9.70 ± 15.12$) early in pregnancy than women with pre-pregnancy overweight ($M = 6.34 ± 9.46$, $t(189.23) = -1.92$, $p = .056$, $d = .26$). Women in the obese group reported having a higher number of pregnancies ($M = 3.18 ± 2.73$, $t(185.99) = -1.96$, $p = .051$) and children ($M = 1.34 ± 1.55$, $t(195.84) = -1.93$, $p = .055$) than women in the overweight group ($M = 2.57 ± 1.63$; $M = 0.98 ± 1.09$, respectively). The two weight groups showed no significant differences in other characteristics such as age, gestational age, and total number of lifetime psychiatric disorders ($ps > .076$).

Conclusion: Women with obesity prior to pregnancy gain more weight early in pregnancy and have a higher number of pregnancies and children compared to women with overweight prior to pregnancy.

Significance: Women at high risk for excessive GWG gain a large amount of their total gestational weight in the first half of pregnancy. Moreover, women with obesity, for whom the total recommended GWG is smaller than other women, gain more than their peers with overweight, suggesting the need for further studies throughout the duration of pregnancy.

Funding Source(s): NICHD R01 HD068802 (PI: Michele Levine, PhD)
Ketamine reduces yohimbine+cue-induced reinstatement of ethanol seeking and depressive-like behavior in female rats

Author(s): Bertholomey ML¹, McElroy BD², and Torregrossa MM²
Affiliation(s): ¹Department of Psychiatry, University of Pittsburgh School of Medicine and ²Department of Neuroscience, University of Pittsburgh

Study: Alcohol use and major depressive disorder are frequently comorbid. Poor treatment responses evident in both disorders are further complicated when they co-occur, underscoring the need for better therapies. One promising candidate is ketamine, which has been shown to have rapid and long-lasting effects in individuals with treatment-resistant depression and in rodent stress models. However, though women are more likely to have this comorbidity, few studies have examined sex-specific effects of ketamine on depressive symptoms, and none have done so for alcohol drinking or seeking. Therefore, the goal of the present experiment was to determine both acute and long-term effects of ketamine on both alcohol-motivated and depressive-like behaviors in female rats.

Methods: Rats were injected with an antidepressant (low) dose of ketamine (10mg/kg), an anesthetic (high) dose of ketamine (90mg/kg), or saline at postnatal day p27. Rats were then trained to self-administer a 10% ethanol+0.1% saccharin solution beginning around p70. Following 21 days of self-administration, ethanol drinking was extinguished, and rats were tested for the effects of low-dose ketamine on the reinstatement of ethanol seeking following exposure to ethanol-related cues and the pharmacological stressor, yohimbine. Reinstatement tests were repeated at weekly intervals for 4 weeks. Finally, rats were tested for the effects of low-dose ketamine on depressive-like behavior in the forced swim test (FST).

Results: Though adolescent pretreatment with ketamine did not alter ethanol self-administration, acute low-dose ketamine treatment robustly reduced cue+yohimbine-induced reinstatement of ethanol seeking, which tended to last up to 3 weeks post-treatment in subsequent reinstatement tests in rats that had received low dose ketamine prepubertally. Ketamine also produced significant decreases in immobility in the FST, suggesting an antidepressant effect.

Conclusion: Acute low-dose ketamine treatment reduces both alcohol-motivated and depressive-like behavior under stressful conditions in female rats.

Significance: These data confirm the antidepressant effects of ketamine in female rats that have been previously shown in males, but also demonstrates that ketamine may be an effective treatment for stress-induced alcohol seeking.

Funding Source(s): K01DA071345, R01DA042029, R21AA025547, Pennsylvania Department of Health (PI: Mary Torregrossa, PhD), and the DSF Charitable Foundation 132RA03
How brains are built: Community neuroscience education to improve child outcomes


Affiliation(s): Departments of Neuroscience, Natural Science, Health Sciences, Epidemiology, Behavioral and Community Health Science, and Psychiatry, University of Pittsburgh

Study: Children who have faced significant early life stresses are at a much higher risk of not reaching their maximal potential in terms of education, physical health, mental health, and economic success in the workplace. Increasing the availability of supportive and enriching experiences can improve children’s outcomes, but in stressed communities there is often little knowledge of how to help children strengthen brain pathways they need for life skills.

Methods: The Working for Kids: Building Skills™ (WFK) educational platform was designed based on principles of developmental neuroscience to educate the general public about how to strengthen brain pathways needed to succeed with life skills. The educational tools are fun, easy to use, and designed to be useful for those with a variety of backgrounds. Topics covered explain how experiences shape brain development, the importance of supportive environments, and the value of community supports in counteracting the effects of early life stresses. 132 professionals (social workers, home visitors, public health professionals) and 74 pre-professional students were trained and survey data to assess how well they learned the principles of brain development was collected. 400 additional professionals played the Brain Architecture Game.

Results: Overall, people taking the entire WFK training program correctly answered 89.5±2.89% of the questions on developmental neuroscience correctly. The greatest number of people have received training using the Brain Architecture Game, which teaches how life experiences and community supports act together to shape brain development. For this, professionals answered 89.31±1.31% of questions correctly, while pre-professional students answered significantly more questions correctly (94.86±1.13%, p=0.004). 44% were particularly interested in how life experiences shape brain development, 34.6% rated the Brain Architecture Game most interesting, while 10.5% were intrigued by the posters and visual materials.

Conclusion: WFK training effectively teaches how to strengthen children’s brain development.

Significance: WFK training has the potential of breaking the transgenerational pipeline whereby children growing up in stressed environments are doomed to become adults with low skill levels.

Funding Source(s): Pittsburgh Innovator’s Challenge Award (NIH UL1 RR024153), NSF Grant 1644507, NSF I-Corps Site Grant at the Univ. Pittsburgh (1st Gear Program), Bales Family Foundation
**Presenter:** Miranda Bridgwater, BS  
**Education:** University of Pittsburgh  
**Current Position:** Student Research Assistant  
**Principal Area of Research Interest:** Social cognition in the offspring of individuals with schizophrenia  
**Current Research Support:** Not applicable  
**Mentor(s):** Gretchen L. Haas, PhD and Leslie E. Horton, PhD

**The relationship between premorbid adjustment and emotional intelligence in first-episode schizophrenia**

**Author(s):** Bridgwater MAS¹, Horton LE¹, and Haas G¹, ²  
**Affiliation(s):** ¹Department of Psychiatry, University of Pittsburgh School of Medicine and ²VA Pittsburgh Healthcare System

**Study:** Research shows that individuals with schizophrenia exhibit deficits in emotional intelligence that may impair social functioning. This study addresses the question of whether indicators of social maladjustment during childhood and early adolescence might be associated with later deficits in emotional intelligence observed in the early phase of schizophrenia.

**Methods:** This study included 119 participants in the NIMH Conte Center studies of first-episode schizophrenia (ages 14-40): those who met DSM-IV criteria for a first episode of schizophrenia (n = 40) or another psychotic disorder (n =22) and age- and sex-matched healthy control participants (n =57). In addition to a baseline diagnostic and symptom assessment interview, trained clinical interviewers administered the Cannon-Spoor Premorbid Adjustment Scale (PAS) and asked participants to complete the Managing Emotions Scale of the Mayer-Salovey-Caruso Emotional Intelligence Test (MSCEIT), an index of emotional intelligence.

**Results:** Across the three groups, individuals with schizophrenia (SZ) had the lowest emotional intelligence scores on the MSCEIT, scoring lower (p<.05) than the HC participants. Those with other psychoses (OP) scored at a level mid-way between the SZ and HC groups, although not significantly different from the other groups. PAS scores reflecting maladjustment (deviation from normal adjustment) during childhood and early adolescent premorbid development were negatively associated with MSCEIT Managing Emotion scores for all subjects (p<.001) and at a trend level (p<.10) for the SZ and HC groups, but not for the OP.

**Conclusion:** In this study, individuals experiencing a first episode of schizophrenia scored more poorly than mentally healthy individuals on a standardized measure of emotional intelligence. Poor performance on the Managing Emotions subscale was associated with poor childhood and early adolescent adjustment for all subjects and at a trend level for the SZ and HC groups alone.

**Significance:** To our knowledge, no previously published studies have examined the relationship between premorbid adjustment and emotional intelligence in first episode schizophrenia and other psychoses. Findings from this study suggest that social maladjustment may predate deficits in social intelligence in the early (first episode) phase of schizophrenia.

**Funding Source(s):** MH045156 and MH084053 (PI: David Lewis, MD), UL1 RR024153 (PI: Steven E. Reis, MD), and NIH/NCRR/ GGRC M01 RR00056 (PI: Arthur Levine, MD)
A greater decline in physical activity appears to underlie the gain in body weight associated with mild hyperandrogenemia and consumption of a Western-Style Diet (WSD) in adolescent female monkeys

Study: Polycystic ovary syndrome (PCOS), a form of infertility that affects 4-8% of reproductive aged women, is characterized by mild hyperandrogenemia, cystic ovaries and an increased prevalence of obesity. Pilot studies from our lab, using peripubertal nonhuman primates, suggested that hyperandrogenemia and high fat diet, together, can lead to both the ovarian and metabolic symptoms associated with PCOS. The current study was designed to examine the chronic effects of elevated testosterone (T), western-style diet (WSD), and a combination of T+WSD on metabolic and reproductive function in more detail in adolescent female primates.

Methods: Forty female rhesus macaques, at the time of menarche (2.5 years of age), were assigned to one of four treatment groups (n=10/group) receiving: (1) cholesterol implants and a regular monkey chow diet with 14% of the calories coming from fat (C); (2) low dose T implants (serum range 1-1.4 ng/mL) and a chow diet (T); (3) cholesterol implants and a WSD with 36% of the calories coming from fat (WSD); or (4) T implants and a WSD (T+WSD). Through the course of the study, all monkeys had glucose tolerance tests (GTT), bone density scans (DEXA), and ovarian ultrasounds every six months and wore a collar mounted accelerometer.

Results: T+WSD animals had increased weight gain over the three-year treatment period compared to C animals (193% vs 113% p = 0.004), and the development of insulin resistance and cystic ovaries. However, there was no significant differences in weight or fat gain in the T- or WSD- treated groups compared to the C group. Neither food intake nor metabolic rate differed significantly between treatment groups. In all monkeys, daily physical activity levels declined as monkeys matured from 2.5 to 5.5 years of age (p <0.001). A random effects linear regression showed that both T and WSD were significantly associated with a greater decline in activity (p<0.05), although there was no interaction between the two (p = 0.70).

Conclusion: We conclude that a greater decrease in adolescent activity likely plays a substantial role in the development of the metabolic changes in PCOS in response to T and WSD.

Significance: This finding suggests that larger decreases in adolescent physical activity triggered by hyperandrogenemia and WSD play a significant role in the development PCOS.

Funding Source(s): NICHD NCTRI program U54 HD071836 and P51 OD011092
Psychophysiological assessment of emotional reactivity during parent-child conflict as a predictor of reactive aggression in daily life

Author(s): Byrd AL\textsuperscript{1}, Verabes T\textsuperscript{1}, Jennings JR\textsuperscript{1}, and Stepp SD\textsuperscript{1}

Affiliation(s): \textsuperscript{1}Department of Psychiatry, University of Pittsburgh School of Medicine

Study: Reactive aggression (RA) has been defined as an extreme, maladaptive response to stress and it represents a transdiagnostic indicator that permeates nearly all psychological disorders in youth. Individual variability in emotional reactivity (ER) is believed to underlie increased risk for engaging in RA. However, prior research shows conflicting results regarding the directionality of this association that likely reflects a failure to comprehensively assess ER. Despite research suggesting that ER is comprised of multiple components, previous studies have utilized psychophysiological assessments that measure ER as a unidimensional construct, conflating sympathetic and parasympathetic function or assessing either sympathetic or parasympathetic function in isolation. Recent theory emphasizes the importance of the independent assessment and integration of autonomic systems via the examination of cardiac autonomic balance (CAB), or the ratio of parasympathetic to sympathetic activation. CAB is thought to represent an index of autonomic flexibility in response to stress and abnormalities in this index are thought to be indicative of biological vulnerability of psychopathology.

Methods: The current study examined parasympathetic and sympathetic function in response to stress to comprehensively assess ER as a biological vulnerability for RA. Participants were adolescents (n=54; ages 11-13) in psychiatric treatment for any mood or behavior problem. Parasympathetic (respiratory sinus arrhythmia; RSA) and sympathetic (pre-ejection period; PEP) function were assessed during 1) resting baseline and 2) conflict discussion task. Additionally, adolescents completed a 4-day Ecological Momentary Assessment (EMA) protocol that assessed RA in daily life using 10 time-based prompts over the course of a long weekend.

Results: Preliminary analyses suggested that CAB was negatively associated with reports of RA in daily life. Specifically, decreases in CAB during conflict predicted engagement in RA in daily life. Prospective associations between CAB and RA at 9-months will also be examined.

Conclusion: Results will be discussed within the context of the broader literature and focus on elucidating dysregulated autonomic function as a risk factor to highlight areas for targeted intervention among at-risk youth.

Significance: Findings highlight the importance of examining patterns of reciprocal activation across both branches of the ANS to better characterize ER as a biological vulnerability for RA.

Funding Source(s): NIMH F32 NRSA Postdoctoral Fellowship (MH110077; PI: Amy Byrd, PhD) using infrastructure from Dr. Stephanie Stepp’s R01 (MH101088)
Examining a rule-based avoidance paradigm in individuals with Obsessive-Compulsive Disorder

Author(s): Chase HW¹, Greenberg T¹, Versace A¹, Graur S¹, Bonar L¹, Haber S², and Phillips ML¹
Affiliation(s): ¹Department of Psychiatry, University of Pittsburgh School of Medicine and ²Department of Pharmacology and Physiology, University of Rochester

Study: Gillan and colleagues (Am J Psych 2015) showed that overtraining of an avoidance paradigm leads to decreased activation in the medial prefrontal cortex (mPFC) in individuals with obsessive compulsive disorder (OCD) compared to controls. We sought to extend these findings using a rule-based avoidance paradigm which included a rule shift (devaluation).

Methods: The participant cohort included 11 healthy (HC) and 9 OCD individuals. Participants performed an avoidance task which was overtrained before entering the scanner. The paradigm required pressing one of two buttons in order to prevent a negative outcome from occurring following two stimuli (A/B). A third (control) stimulus (C) did not require active avoidance. The paradigm also included a rule change where avoidance responses were no longer required (devaluation). A simultaneous multislice (SMS) sequence was employed to acquire functional MRI data (TR/TE=1500/31ms; 4xSMS acceleration; 2mm slice thickness).

Results: Healthy controls showed greater activity in the mPFC during active avoidance (A/B > C) than OCD (peak voxel: x=-6, y=38, z=-12; t=5.06, p<0.001 uncorrected). 30% of all participants did not modulate their behavior following a rule change, but this was not more common in the OCD group (HC=5; OCD=1).

Conclusion: Consistent with previous findings, individuals with OCD show reduced activation during active avoidance in the mPFC following overtraining than HC. However, the majority of OCD patients were able to alter their response pattern following a rule change. Together, these findings provide preliminary evidence to suggest that a rule-based system may be relatively intact in OCD, despite the abnormalities in mPFC activity during avoidance.

Significance: The findings provide support for models of OCD which emphasize dysfunction of the medial prefrontal cortex. However, they modify conclusions of previous studies regarding avoidance habits, suggesting that avoidance behavior in OCD can be flexible under certain circumstance.

Funding Source(s): 1 P50 MH106435-01A1 to Haber (Overall PI), Phillips (Project 2 PI)
**Symptoms of depression increase girls’ trajectories of sexual risk behavior from ages 14 to 18**

**Author(s):** Choukas-Bradley S, Hipwell AE, and Stepp S

**Affiliation(s):** 1Department of Psychiatry, University of Pittsburgh School of Medicine

**Study:** Adolescence is a developmental period during which girls are at heightened risk for increases in both depressive symptoms and sexual risk behavior (SRB). However, little is known about whether depressive symptoms increase girls’ engagement in SRB over time, or whether these associations are unique or better explained by cross-diagnostic mechanisms (e.g., emotion regulation, as seen in prior work related to borderline personality disorder, BPD). Given the significant health risks associated with adolescents’ SRB, particularly among girls, research is needed that examines longitudinal associations between girls’ depressive symptoms and SRB.

**Methods:** Data from the Pittsburgh Girls Study (PGS), an urban community sample, were used. The full sample includes girls who were ages 5-8 in 2000, identified via city enumeration and interviewed annually for 16 years. Participants for the current study included 1,619 girls ages 14-18 from 3 original cohorts; the youngest cohort could not be included due to changes in the SRB assessment. Adolescents self-reported age 14 depressive symptoms and past-year SRB annually from ages 14-18 (number of partners, inconsistent birth control, STI diagnosis, sexual behavior under the influence of substances). Two count variables were created to reflect each participant’s number of SRBs and depressive symptoms. Several covariates were assessed: minority race, household receipt of public assistance, sexual orientation, and pubertal development.

**Results:** Latent growth curve models were estimated in Mplus 7.4 using a maximum likelihood estimator. Associations were examined between age 14 depressive symptoms and the intercept and slope of SRB, controlling for the effects of covariates on the intercept. Model fit statistics indicated a good fit to the data. Results revealed that, after controlling for within-construct stability, age 14 depressive symptoms were associated with higher age 14 SRB ($\beta=.055$, $p=.001$), as well as with stronger increases in SRB from ages 14 to 18 ($\beta=.062$, $p=.002$). Additional analyses will examine the unique effects of depression, controlling for symptoms of BPD; reciprocal influences of SRB and depression; and specific mechanisms that may underlie the observed associations (e.g., emotion regulation, characteristics of dating relationships).

**Conclusion:** Adolescent girls’ symptoms of depression at age 14 are associated with increased risk for the longitudinal development of SRB.

**Significance:** The findings highlight the need for future work to identify points of intervention for depressed adolescent girls at risk for SRB.

**Funding Source(s):** R01 MH056630 (PI: Rolf Loeber), NIJ JF-FX-0058 (PIs: Alison Hipwell/Stephanie Stepp), R01 DA012237 (PI: Tammy Chung), and the FISA Foundation, Falk Fund
Transdiagnostic comparison of dysregulated erbB4 splicing and parvalbumin expression across multiple psychiatric disorders

Author(s): Chung DW1, Chung Y1, Bazmi HH1, and Lewis DA1
Affiliation(s): 1Department of Psychiatry, University of Pittsburgh School of Medicine

Study: In schizophrenia, higher minor-to-major ErbB4 splice variant ratios are thought to contribute to lower parvalbumin interneuron activity and activity-dependent downregulations of parvalbumin expression. In this study, we explored whether this relationship is observed in 1) schizophrenia subjects when compared to two different sets of comparison subjects and 2) other psychiatric disorders associated with parvalbumin dysfunction.

Methods: Quantitative PCR was performed to assess mRNA levels of ErbB4 major (JM-b) and minor (JM-a) splicing variants and parvalbumin in DLPFC of 23 triads of schizophrenia and two independently matched unaffected comparison subjects (n=69 subjects). Levels of these transcripts were also assessed in 40 matched tetrads of schizophrenia, bipolar disorder, major depressive disorder and unaffected comparison subjects (n=160 subjects). Transcript levels across subject groups were analyzed using ANCOVA.

Results: In the 23 triads, higher JM-a and lower JM-b levels were observed in schizophrenia relative to both comparison groups. In the 40 tetrads, the reciprocal changes in JM-a and JM-b levels were replicated in schizophrenia, but were not present in bipolar or major depressive disorder. Moreover, a significantly greater deficit in parvalbumin levels was observed in schizophrenia relative to bipolar disorder or major depressive disorder. In both studies, the JM-a:JM-b ratio was negatively correlated with parvalbumin levels in all diagnostic groups.

Conclusion: Abnormal ErbB4 splicing at the JM locus 1) is evident in schizophrenia subjects regardless of the comparison group and 2) might contribute to the mechanisms driving lower parvalbumin expression in schizophrenia but not in bipolar or major depressive disorder.

Significance: Since the activity of cortical parvalbumin interneurons is required to generate the DLPFC activity subserving certain complex cognitive processes, our study suggests that dysregulated ErbB4 splicing is a critical molecular determinant of the severity of DLPFC dysfunction and cognitive impairment across multiple psychiatric disorders.

Funding Source(s): MH043784 (PI: David Lewis, MD) and MH103204 (PI: David Lewis, MD)
Care transitions in the psychiatric hospital: Are older adults at greater risk?

Author(s): Conlon M\textsuperscript{1}, Tew J\textsuperscript{1}, Gopalan P\textsuperscript{1}, Azzam P\textsuperscript{1}, Solai L\textsuperscript{1}, and Karp J\textsuperscript{1}

Affiliation(s): \textsuperscript{1}Department of Psychiatry, University of Pittsburgh School of Medicine

Study: A care transition is the transfer of a patient from one care setting to another. Patients undergoing a care transition are vulnerable to duplication of services, conflicting care recommendations, and errors in medication reconciliation. In addition, care transitions are a source of patient and family distress. Limited research has been done comparing the frequency of care transitions in geriatric and non-geriatric adults in the inpatient psychiatric setting to see whether psychiatically hospitalized older adults are more vulnerable to care transitions.

Methods: We conducted a retrospective chart review of patients ($N = 100$) admitted to Western Psychiatric Institute and Clinic between November 2016 and January 2017. Two cohorts were collected: one of geriatric adults (age $\geq 60; n = 50$) and one of non-geriatric adults (age 18-59; $n = 50$). Patients were accrued using a prospective opportunity sampling approach. Only hospitalizations at least 72 hours in length were included. For each case, we tallied the number of care transitions and recorded the length of stay in emergency settings (i.e., psychiatric and medical emergency departments). A care transition was defined as the transfer from the psychiatric setting (either the psychiatric emergency department or psychiatric hospital) to the medical setting (either the medical emergency department or medical hospital) and then back again to the psychiatric setting. We also collected clinical and demographic information for all patients. We used a two-sided $t$-test to examine the difference in length of stay in emergency settings for the two cohorts. We used a Chi-square test to examine the difference in the frequency of care transitions between these two cohorts.

Results: The rate of care transitions in the geriatric cohort was 14% ($n = 7$). None of the cases in the adult non-geriatric cohort experienced a care transition. The geriatric cohort was significantly more likely to experience a care transfer ($\chi^2(1) = 7.53$, $p = .012$) than the non-geriatric cohort. The number of minutes spent in emergency settings was longer for geriatric adults ($M = 387.66 \pm 163.39$) than non-geriatric adults ($M = 332.52 \pm 176.16$; $t(98) = -1.62$, $p = .108$; $d = .32$), however this difference was not statistically significant.

Conclusion: This study demonstrates that inpatient psychiatric care transitions are more common in the geriatric population than in the non-geriatric adult population.

Significance: This work supports the need to target quality improvement interventions that improve the care transition process to the geriatric population as these individuals are more vulnerable to experiencing a care transition during a psychiatric hospitalization.

Funding Source(s): None
Dysregulation of cortical input to central striatum in the Sapap3-KO OCD mouse model

**Author(s):** Corbit V\(^1,2,4\), Gittis A\(^1,3,4\), and Ahmari S\(^1,2,4\)

**Affiliation(s):** \(^1\)Center for Neuroscience, \(^2\)Translational Neuroscience Program, University of Pittsburgh; \(^3\)Biological Sciences Department, Carnegie Mellon University; and \(^4\)Center for the Neural Basis of Cognition

**Study:** Obsessive-Compulsive Disorder (OCD) is defined by the inability to suppress compulsive behaviors, and hyperactivity in corticostriatal circuits is observed in OCD patients. Lateral orbitofrontal cortex (IOFC) and supplementary motor areas are hyperactive in OCD patients, and a recent meta-analysis has identified them as the best targets for repetitive transcranial magnetic stimulation (rTMS) treatment for OCD. In mouse, these cortical regions (IOFC and M2) project to central striatum (CS), and this circuitry is dysregulated in an OCD-relevant mouse model, the Sapap3-KO mouse. Additionally, fast-spiking interneurons (FSIs) are thought to play a role in behavioral suppression through their influence on striatal output neurons (MSNs). Thus, investigating how IOFC and M2 influence CS is essential to understanding how corticostriatal microcircuits affect compulsive behaviors.

**Methods:** Channelrhodopsin2 was injected into each cortical region of Sapap3-KO and WT mice to record light-evoked excitatory post-synaptic currents (EPSCs) using acute slice physiology.

**Results:** LOFC-evoked EPSCs onto MSNs were weaker in KO mice relative to WTs, while IOFC inputs to FSIs were unchanged. The ratio of EPSC amplitudes confirmed that IOFC input to FSIs is increased relative to nearby MSNs, suggesting IOFC evoked feedforward inhibition is stronger in Sapap3-KOs. In contrast, M2-evoked EPSCs were increased onto both MSNs and FSIs in the CS of Sapap3-KOs, indicating a general increase in CS drive from M2. These data from IOFC and M2 predict an increase in excitatory drive to FSIs, but not MSNs. Electrical stimulation confirmed that FSIs exhibit greater excitatory drive in KOs, while MSNs do not.

**Conclusion:** These data suggest that primary cortical control of CS may shift from IOFC to M2, potentially causing the repetitive grooming behavior seen in the Sapap3-KO mice.

**Significance:** These results bring new focus to the role of supplementary motor cortical regions in OCD and contribute insight about stimulation-based treatments. Moreover, greater influence of CS FSIs suggests that interneuron dysfunction may play a role in OCD. Taken together, these results reveal corticostriatal abnormalities that may cause compulsive behaviors in OCD.

**Funding Source(s):** BRAINS R01MH104255 (PI: Susanne Ahmari), Burroughs Wellcome Career Award for Medical Scientists (PI: Susanne Ahmari, MD, PhD), NIH R00 NS076524-03 (PI: Aryn Gittis, PhD)
Sleep disturbance and emotion regulation dysfunction in depression: Self-report and neural evidence

Author(s): Cummings L₁, Graur S₁, and Fournier J₁
Affiliation(s): ¹University of Pittsburgh School of Medicine, Department of Psychiatry

Study: When presented with negative stimuli, individuals with depression often struggle to engage in cognitive reappraisal (CR), an emotion regulation strategy whereby individuals reinterpret the meaning of an emotional stimulus in order to change their emotional response to it. Previous work has demonstrated that sleep disturbances (SD) are associated with poor CR ability. Thus, SD may contribute to CR deficits among depressed individuals. Limited research exists, however, regarding how SDs affect the functioning of brain regions necessary for CR among depressed adults. Thus, this study examined whether SDs were associated with the functioning of neural regions underlying CR ability in clinical depression.

Methods: A sample of 38 adults who met criteria for a major depressive episode (MDD) on the SCID IV and 24 psychiatrically healthy adults completed self-report measures of SD (PROMIS-SD) and a clinician-administered measure of depression (HAMD). fMRI data were collected during a CR task during which participants viewed negative interpersonal scenes and either attended to the scene or reappraised the content in order to alter their emotional reactions. Linear regressions were performed to test for effects of diagnostic status and SD on neural activation in an a priori ROI: the interior frontal junction (IFJ), a brain region which has been implicated in tasks that engage cognitive control during the presentation of emotional stimuli.

Results: Across all participants, SD (b = -0.641, p < .012) diagnostic group (b = -0.95, p < .02) predicted IFJ activation, while controlling for depression severity. The interaction between SD and diagnostic group was not significant. A secondary regression analysis confirmed SDs predicted IFJ activation within just the MDD group as well (b = -0.341, p < .037).

Conclusion: Both SD and diagnostic status independently affect levels of neural activation in brain regions associated with CR. Although our results did not show a significant interaction, future studies should examine whether reduced sleep quality has an additive effect with diagnostic status, which may further reduce CR ability in depression.

Significance: This study provides neural evidence of the relationship between sleep disturbances and cognitive reappraisal among a sample of clinically depressed adults. Interventions seeking to alter emotion dysregulation among depressed adults might benefit from adjunctive strategies that target sleep disturbances.

Funding Source(s): NIMH grant: 5K23MH097889
**Human three-dimensional neuronal platforms for drug screening**

**Author(s):** D’Aiuto L\(^1\), Naciri JN\(^1\), Demers M\(^1\), and Nimgaonkar V\(^1\)

**Affiliation(s):** \(^1\)Department of Psychiatry, University of Pittsburgh School of Medicine

**Study:** Conventional high throughput drug screens employ two-dimensional (2D) cell cultures. However, it is recognized that the inefficiency of drug development (approximately 85% drugs fail during early clinical trials), can be attributed partly to the inadequate representation of the human tissue environment in these cultures. Indeed, cellular responses in 2D monolayer cultures differ from their *in vivo* analogs for several reasons, such as: i) impaired cell-cell communication; ii) reduced intercellular contacts; and iii) lack of appropriate extracellular matrix-cell adhesion interactions. Hence, the need for the development of preclinical models that can more accurately predict clinical outcomes that will save both time and cost. The first step for the generation of physiologically relevant cellular models is the addition of the “third dimension” to the classic 2D cultures. This is a “*conditio sine qua non*” dictated by the evidence that physiological responses, cell-to-cell signaling, and gene expression profile of three-dimensional (3D) cultures more closely resemble *in vivo* conditions.

**Methods:** We employed an approach that we defined as ‘self-assembling’ to generate scaffold-free 3D neuronal cultures in optical active 96-well plates and 96-Transwell plates starting from neural progenitor cells (NPCs) derived from induced pluripotent stem cells (iPSC). To test their suitability for drug screening, 3D neuronal cultures were infected with the neurotropic virus HSV-1 along with increasing amounts of antiviral drug acyclovir. We used a genetically engineered HSV-1 KOS construct incorporating enhanced green fluorescent protein (EGFP) and red fluorescent protein (RFP) as reporter genes. The drug concentration that inhibit the viral infection by 50 % (IC50) was determined using both flow cytometry (FC) and the CX7 High Content Screening (HCS) platform (ThermoFisher, Inc).

**Results:** An elaborate three-dimensional organization of neurons and glial cells was revealed by high resolution confocal microscopy. FC analysis of both 3D neuronal culture system showed >80% cell viability and no significant well-to-well variation in both cell density and the ratios of Tuj1+ or MAP2+ cells /GFAP+ cells. The IC50 for acyclovir determined by both FC and HCS was comparable (3.144 \(\mu\)M and 3.121 \(\mu\)M, respectively).

**Conclusion:** Our 3D human neuronal cultures along with a novel confocal-based HCS platform (CX7) provide an unprecedented opportunity to screen drugs for CNS infections and psychiatric disorders.

**Significance:** Our study paves the way for a rapid and robust high throughput drug screening using human 3D neuronal culture platforms.

**Funding Source(s):** R21 NS096405-01A1 (PI: Leonardo D’Aiuto), R01 MH063480-11A1 (PI: Vishwajit Nimgaonkar); O7R-1712 Stanley Foundation (PI: Vishwajit Nimgaonkar)
NPAS2 knockout increases intravenous cocaine self-administration

Author(s): DePoy L\(^1\), Logan R\(^1\), and McClung C\(^1\)
Affiliation(s): \(^1\)Department of Psychiatry, University of Pittsburgh School of Medicine

Study: The development of substance dependence is associated with disruptions in circadian rhythms and circadian genes. A dominant negative mutation in circadian locomotor output kaput (CLOCK) increases both cocaine reward and self-administration. However, the role of its homologue, neuronal PAS domain protein 2 (NPAS2), in cocaine self-administration remains unclear, despite NPAS2 knockout contrastingly decreasing cocaine reward.

Methods: We performed intravenous cocaine self-administration using male and female mice with a mutation in NPAS2. Mice first acquired an operant response for food and then were implanted with an indwelling jugular catheter. After recovery, mice acquired cocaine self-administration and then dose-response testing was conducted, both at a fixed ratio and progressive ratio schedule.

Results: NPAS2 knockout did not impact acquisition of a food response, however, it did accelerate acquisition of a cocaine-reinforced response. In addition, NPAS2 knockout increased the total number of infusions earned, to a greater extent in males. Cocaine is also a more efficacious reinforcer in NPAS2 knockout mice as evidenced by an upward shift in dose-response curves. NPAS2 knockout also increases breakpoint ratio during a progressive ratio paradigm.

Conclusion: NPAS2 knockout increases cocaine intake, propensity to self-administer cocaine, as well as, the reinforcing and motivational properties of cocaine. This divergence from decreased cocaine reward seen in NPAS2 knockout mice is likely due to the volitional control over drug intake during self-administration compared to conditioned place preference. Further research is required to understand the differences between NPAS2 regulation of cocaine reward and drug consumption.

Significance: Understanding the role of NPAS2, compared to CLOCK, in addiction-related behaviors is critical. NPAS2 is more highly enriched in the forebrain, including the nucleus accumbens, which could indicate a greater role for NPAS2 in reward. Furthermore, these contradictory findings, with NPAS2 knockout decreasing cocaine reward while increasing cocaine self-administration, emphasizes the importance of studying drug self-administration, which is more appropriate model of drug use and might better measure vulnerability to addiction.

Funding Source(s): DA039865 (PI: Colleen McClung, PhD)
Presenter: Samuel J. Dienel  
Education: University of Pittsburgh  
Current Position: MD/PhD Candidate  
Principal Area of Research Interest: Schizophrenia  
Current Research Support: Medical Sciences Training Grant T32 GM08208  
Mentor(s): David A. Lewis, MD  

Development of transcripts regulating dendritic spines in layer 3 pyramidal cells of the monkey prefrontal cortex: Implications for the pathogenesis of schizophrenia  
Author(s): Dienel SJ\textsuperscript{1,2}, Bazmi HH\textsuperscript{2}, and Lewis DA\textsuperscript{2,3}  
Affiliation(s): \textsuperscript{1}Medical Scientist Training Program, University of Pittsburgh; \textsuperscript{2}Translational Neuroscience Program, Department of Psychiatry, School of Medicine, University of Pittsburgh; \textsuperscript{3}Department of Neuroscience, Dietrich School of Arts and Sciences, University of Pittsburgh  

Study: Certain cognitive deficits in schizophrenia appear to emerge from altered postnatal development of the dorsolateral prefrontal cortex (DLPFC). Dendritic spines on DLPFC layer 3 pyramidal cells are essential for certain cognitive functions, change in density over development, and are reduced in number in schizophrenia. Altered expression of molecular regulators of actin filament assembly and stability, which are essential for spine formation and maintenance, are thought to contribute to the pathogenesis of spine deficits in the disease. However, the normal developmental expression patterns of these molecular regulators of dendritic spines, which might provide insight into the timing of spine deficits in schizophrenia, are unknown.  

Methods: We quantified the expression from birth to adulthood of key transcripts regulating dendritic spine density in monkey DLPFC. Layer 3 pyramidal cells, and tissue samples containing layers 3 or 6, were captured by laser microdissection and selected transcripts were quantified using PCR.  

Results: In layer 3 pyramidal cells, the expression levels of most of the transcripts studied changed early, and not late, in postnatal development. These developmental shifts in expression were generally not detected in tissue homogenates of layers 3 or 6, suggesting that the changes may be enriched in layer 3 pyramidal cells.  

Conclusion: The timing of these shifts in expression suggests that early, rather than later, postnatal development may be a vulnerable period for layer 3 pyramidal neurons. Disruption of the normal developmental trajectories of these transcripts may contribute to layer 3 pyramidal neuron spine deficits in individuals who are later diagnosed with schizophrenia.  

Significance: The finding that these expression changes are most common in early postnatal development suggests that the schizophrenia-associated changes in these transcripts might occur during that same developmental period. Thus, the spine deficits on DLPFC layer 3 pyramidal cells in the disease may arise due a disturbance in spinogenesis. An early loss in dendritic spines may mediate the pre-clinical symptoms of impaired cognitive function in individuals who go on to develop schizophrenia.  

Funding Source(s): NIH grant MH051234 (PI: David A. Lewis, MD)
Student pharmacists’ perceived competence and knowledge in conducting SBIRT

Author(s): Drab D¹, Goldschen L², Quintilliani J¹, Unger H¹, Reynolds M¹, and Douaihy A²
Affiliation(s): ¹School of Pharmacy, University of Pittsburgh and ²Department of Psychiatry, University of Pittsburgh School of Medicine

Study: Receiving training in substance use disorders is an essential component of education for pharmacy, medical, and other healthcare professional students. Screening, Brief Intervention, and Referral to Treatment (SBIRT) is an evidence-based public health approach used to identify, reduce, and prevent problematic alcohol and drug use. Training in SBIRT has been incorporated into the curriculum in the School of Pharmacy. This study examined the efficacy of the training to improve student knowledge of identification of problematic substance use, perceived competence in utilizing the SBIRT model, and its application in clinical settings.

Methods: Two classes of University of Pittsburgh pharmacy students completed SBIRT training via online modules and interactive skills building sessions. Students were asked to complete a survey before and after the training; 186 students completed the surveys. Survey responses relating to the knowledge of problematic substance use (8 items), perceived competence in addressing substance use with patients (13 items), and clinical application of SBIRT principles and methods (13 items) were examined. Application, knowledge, and competency scales were evaluated across the two time points utilizing paired samples t-test. This study was reviewed and approved by the University of Pittsburgh IRB, Protocol # 16080644.

Results: From pre- to post-training, the application mean score improved from 21.13 to 24.27, (t= -2.112, df =18, p=0.037). Knowledge scale improved from 3.67 to 5.80 (t= -13.377, df =175, p=0.000). Competence scale score improved from 25.73 to 35.57 (t= -11.763, df =163, p=0.000).

Conclusion: There was significant improvement in the students’ knowledge about problematic substance use, self-reported competency in discussing substance use with their patients, and increased application of the SBIRT model when interacting with their patients as a result of the SBIRT training.

Significance: SBIRT training provides a foundation and a higher level of comfort for trainees to facilitate discussions about substance use with their patients. The knowledge of SBIRT model will allow trainees to capitalize on the frequent encounters they have with patients to intervene early and refer to the appropriate level of treatment.

Funding Source(s): SAMHSA Grants #TI-026423-01 (PI: Maureen Reynolds, PhD) and TI-026446-01 (PI: Antoine Douaihy, MD)
Presenter: Kristen L. Eckstrand, MD, PhD
Education: Vanderbilt University Medical Center
Current Position: Resident Psychiatrist
Principal Area of Research Interest: Affective neuroscience, Childhood trauma and adversity, LGBT health, Development of risk-taking behavior
Current Research Support: Not applicable
Mentor(s): Mary L. Phillips, MD, MD (CANTAB) and Erika E. Forbes, PhD

Anterior cingulate connectivity during reward processing mediates the relationship between trauma exposure and depressive and anxiety states in young adults
Authors: Eckstrand KL¹, Hanford LC², Chase HW², Lockovich J¹, Stiffler R¹, Aslam HA¹, Bebko G², Forbes EE², and Phillips ML²
Affiliations: ¹Western Psychiatric Institute and Clinic of UPMC and ²Department of Psychiatry, University of Pittsburgh School of Medicine

Study: Exposure to trauma during childhood has been associated with the development of depression and anxiety. While prior research has focused on emotional distress following trauma and the relation to threat processing, little research has focused on its relation to reward capacity. In this study, we examined the impact of trauma exposure on neural activity during reward processing and emotional states in young adults.

Methods: 111 young adults [78F/33M, 21.7±1.9yrs] completed self-report measures of trauma and emotional states, and underwent functional magnetic resonance imaging during a standardized monetary reward task. Trauma-associated neural activation and psychophysiological interaction were analyzed during reward prediction error (RPE) using linear regression models in SPM12 with a cluster extent threshold of $p_{corr}<0.05$. Neurally mediated associations between trauma and emotional states were also examined. Age, sex, race, IQ, and pre-existing psychological distress were included as covariates.

Results: Trauma exposure was associated with greater anterior cingulate cortex (ACC; xyz=-4,30,-6) activation during RPE, and decreased ACC connectivity with the right insula [xyz=46,2,12], middle frontal [xyz=36,44,38], inferior parietal [xyz=40,-40,50], middle temporal [xyz=64,-38,4], and supramarginal [xyz=60,-16,26] regions. ACC connectivity mediated the relationship between greater trauma exposure and worsening depressive and anxiety states ($p_{corr}<0.05$).

Conclusion: The combined pattern of greater ACC activation and reduced ACC connectivity following trauma exposure may reflect a pattern of aberrant regulatory mechanisms in the context of unexpected reward, where greater trauma results in abnormal recruitment of a prefrontal cortical region implicated in suppressive-style emotion regulation (ACC), together with a disconnection with other PFC regions implicated in self- and higher-order appraisal processes.

Significance: This current results highlight the importance of studying reward processing in understanding the development of affective symptoms among trauma-exposed individuals.

Funding Source(s): NIMH, R01MH100041 (PI: Mary Phillips, MD, MD (CANTAB))
Predicting quality of life in distressed young adults: Cortico-thalamic BOLD signal and reward processing

Author(s): E. Kale Edmiston\(^1\), Henry Chase\(^1\), Richelle Stiffler\(^1\), Jeanette Lockovich\(^1\), Haris Aslam\(^1\), Simona Graur\(^1\), Genna Bebko\(^1\), and Mary L. Phillips\(^1\)

Affiliation(s): \(^1\)Department of Psychiatry, University of Pittsburgh School of Medicine

Study: Identification of neurobiological factors that predict quality of life (QoL) in mood and anxiety disorders could help identify young adults requiring more targeted treatment. Alterations in reward processing are a core component of mood and anxiety disorders. Functional MRI research indicates associations between BOLD during reward processing and mood and anxiety symptoms. However, it is unclear how such alterations might predict later QoL.

Methods: In this fMRI study, twenty-eight young adults (ages 18-25) experiencing psychological distress completed an uncertain reward task in scanner. Participants then returned for a six-month follow-up and completed the Quality of Life Enjoyment and Satisfaction Questionnaire (QLESQ). Correlation between BOLD signal during reward expectancy or BOLD signal during prediction error and QoL, as assessed by the change in QLESQ Total Scores at time one and six-month follow-up, was modeled.

Results: There were significant positive correlations between change in QoL at follow-up and BOLD signal during reward expectancy in the dorsomedial thalamus, cuneus, and left primary visual cortex, such that increased BOLD was associated with improved QoL (p<0.001, uncorrected). There was also a significant positive correlation between QoL at follow-up and BOLD in the left premotor cortex during the prediction error portion of the task.

Conclusion: Our findings indicate that enhanced activity of cortico-thalamic regions during reward processing is predictive of later QoL in a distressed sample of young adults.

Significance: These findings may help to identify neurobiological features associated with improved outcomes in mood and anxiety disorders, potentially leading towards targeted therapeutic interventions.

Funding Source(s): NIMH 2R01 MH73953
The relationship between impulsivity and body mass index depends on how impulsivity is measured:

**Findings from a comprehensive meta-analysis**

**Author(s):** Emery RL¹ and Levine, MD²

**Affiliation(s):** ¹Department of Psychology, University of Pittsburgh and ²Department of Psychiatry, University of Pittsburgh School of Medicine

**Study:** Although impulsivity has been implicated in the development and maintenance of obesity, evidence linking impulsivity to obesity has been mixed. These mixed findings may be related to differences in the type of impulsivity measures used and the varied domains of impulsivity assessed by each measure. Accordingly, the present meta-analysis aimed to examine the impact of measurement selection on the relationship between impulsivity and body mass index (BMI).

**Methods:** A total of 142 articles met inclusion criteria and were comprised of 315,818 participants. Effect sizes consisted of Fisher’s z-transformed correlation coefficients, which were weighted by the inverse variance to establish the grand mean estimate of the relationship between impulsivity and BMI. Overall weighted mean effect sizes also were computed for each type and domain of impulsivity measure. Moderator analyses were conducted using a mixed-effects approach to determine if the relationship between impulsivity and BMI varied between the types of impulsivity measures used.

**Results:** On average, participants were 32.25 (SD=12.41) years of age, with a BMI of 26.63 (SD = 5.73) kg/m². The overall relationship between impulsivity and BMI was small but significant \( r = 0.07 \). Behavioral task measures of impulsivity produced significantly larger effect sizes \( r = 0.10 \) than did questionnaire measures of impulsivity \( r = 0.05 \). Domains of impulsivity that assessed disinhibited behaviors \( r = 0.10 \), attentional deficits \( r = 0.11 \), impulsive decision-making \( r = 0.10 \) and cognitive inflexibility \( r = 0.17 \) produced significant effect sizes.

**Conclusion:** These findings demonstrate that impulsivity is positively associated with BMI and further document that this association varies by the type of impulsivity measure used and the domain of impulsivity assessed.

**Significance:** The present meta-analysis is the most comprehensive effort designed to understand how questionnaire and behavioral task measures of impulsivity differentially relate to BMI. Findings from this study ultimately help to clarify who is at risk for overweight and obesity and further provide a preliminary model for how those individuals may be at risk.

**Funding Source(s):** Not applicable
Right posterior superior temporal sulcus and temporoparietal junction response to social reward moderates the relation between naturalistic emotional closeness and positive affect among adolescents

**Author(s):** Flores L, Eckstrand K, Silk J, Ambrosia M, Allen N, and Forbes E

**Affiliation(s):** 1VISN 4 Mental Illness Research, Education and Clinical Center (MIRECC), VA Pittsburgh Healthcare System; 2Department of Psychiatry, University of Pittsburgh School of Medicine; 3Department of Psychology, University of Pittsburgh; 4Department of Psychology, University of Oregon

**Study:** Experiencing emotional closeness can be rewarding and is related to lower anhedonic depressive symptoms. Function in brain regions implicated in social processing—such as right posterior superior temporal sulcus and temporoparietal junction (pSTS/TPJ)—may alter the positive association between naturalistic emotional closeness and positive affect.

**Methods:** Participants consisted of 34 typically developing adolescents. As part of a two-week ecological momentary assessment, participants received multiple phone calls per day and responded whether they were with someone and how close they felt to them. They also rated their current positive affect and their peak level of happiness over the past hour. In addition, participants completed a social reward fMRI task in which they received social feedback from peers represented by standardized faces.

**Results:** Multilevel modeling was used to examine right pSTS/TPJ as a moderator in associations between emotional closeness and positive affect. Surprisingly, adolescents with greater right pSTS/TPJ social reward response exhibited a weaker positive association between emotional closeness and concurrent positive affect than adolescents with lower right pSTS/TPJ response, $t(185)=-2.52$, $p=.013$. However, adolescents with greater right pSTS/TPJ response demonstrated a positive association between emotional closeness and peak happiness a few hours later, whereas adolescents with lower right pSTS/TPJ response did not, $t(158)=2.46$, $p=.015$.

**Conclusion:** Overall, the findings suggest that although neural response to social reward in key social processing regions may buffer the short-term mood effects of emotional closeness, it helps sustain affective benefits from emotional closeness.

**Significance:** Future research may demonstrate that the ability to sustain affective benefits from emotional closeness may serve as a protective factor against depression.

**Funding Source(s):** NIDA grant DA033612 (PI: Erika E. Forbes, PhD)
An analysis of eating disorders and reward processing in a high-risk female sample

Author(s): Flynn E¹, Guyer A², Keenan K³, Hipwell A¹, and Forbes E¹
Affiliation(s): ¹Western Psychiatric Institute and Clinic of UPMC; ²Department of Psychiatry, University of Pittsburgh; ³University of Chicago; and ⁴University of California at Davis

Study: Eating disorders (ED) are more prevalent in women, emerge in adolescence, and are postulated to involve disrupted reward processing. Previous studies of neural reward circuitry in ED reported altered reward function in clinical binging purging subtype samples in response to food cues, which preclude interpretation of reward function generally; thus highlighting the need to understand underlying neurocognitive differences and predispositions for reward processing across the continuum of ED symptoms in the general population. This study aims to understand the neural correlates of reward in ED by focusing on an aspect of ED that varies in the larger population of young women. We hypothesized participants with dieting behaviors would have altered functioning in reward regions.

Methods: 116 girls from the Pittsburgh Girls Emotions Study (PGS-E) were included in this sample. At age 16 participants completed the Eating Attitudes Test (EAT), a self-report measure used to capture cognitions and behaviors associated with ED that contains a dieting subscale. Participants completed a monetary reward fMRI task in a 3T Siemens TIM Trip scanner at age 16. Data preprocessing and analysis were preformed using SPM8.

Results: A regression analysis indicated higher levels of dieting were associated with greater BOLD response in the dorsolateral prefrontal cortex (130 voxels, t=4.82, 58 28 6) and the thalamus (66 voxels, t=4.83, 14 -22 2).

Conclusion: In high-risk adolescent girls, dieting is associated with altered response to reward in regions implicated in self-regulation (DLPFC) and reward processing (thalamus). This could reflect the experience of dieting, and its behavioral features of restricting caloric intake and its affective features of overriding reward signals by regulating hunger.

Significance: Dieting could involve the reward of attempting to control one’s own behavior and motivation but could also involve denying basic reward motivation. Thus, it could alter neural circuitry relevant to motivation, affect, and self-control through repeated experience of concerns about food reward and behavioral efforts to avoid such reward. Clinically, altered reward circuitry could serve as a mechanism for disrupted eating behavior in its extreme forms of binging (i.e., undercontrolled intake) or excessive caloric restriction (i.e., overcontrolled intake).

Funding Source(s): R01MH104418 and R01MH056630
The postpartum stress scale and smoking relapse

**Author(s):** Freyberg R\(^1\) and Levine M\(^1\)

**Affiliation(s):** \(^1\)Department of Psychiatry, University of Pittsburgh, School of Medicine

**Study:** The Postpartum Stressors Scale (PPSS) was recently developed as a brief measure of postpartum stress that could easily be incorporated clinical and research contexts. However, the scale was originally validated using a largely upper-middle class, white, educated population. Thus, the aims of the current study were to examine the factor structure of this scale among a more diverse population of women who quit smoking during pregnancy, and to explore the relationship between stress and smoking status across the first 6 months postpartum.

**Methods:** 300 postpartum women (\(M_{age} = 25.06, SD = 5.66\)) who had quit smoking completed the PPSS along with additional assessments at 12 and 24 weeks of age. The majority of our participants identified as African-American (54%), nearly 46% of our participants had a high school degree or less, and the majority of our participants were currently in a relationship.

**Results:** A principle Components Analysis (PCA) with varimax rotation was initially performed using the nine item scale incorporated in the previous validation study. To explore the concordance between this PCA and the initial validation sample, we removed items from the initial scale based on low endorsement and performed an additional PCA with varimax rotation using these new items. New factors encompassing practical, interpersonal, and maternal concerns emerged revealing different sources of stress for our participant population. Participants who had relapsed to smoking at 12 weeks postpartum reported significantly more stress on scales that assessed practical and interpersonal stress (both \(p < .05\)). At 24 weeks, women who relapsed had significantly higher maternal stress scores at 24 weeks (\(p = .006\)).

**Conclusion:** These results provide information on the conceptualization and experience of stress among a diverse sample of postpartum women and its impact on relapse rates. We demonstrated that the factor structure that emerged for the PPSS was different than what was previously documented, and propose that demographic differences between the two samples and differences in the administration of the scale may have led to differences in how the questionnaire was completed. Importantly, postpartum women who endorsed greater levels of postpartum-specific stress were more likely to return to smoking postpartum.

**Significance:** The current study emphasizes the need for further research exploring the role of ethnic, social, and socioeconomic factors in the postpartum period and how stress during the postpartum period affects smoking relapse.

**Funding Source(s):** RO1 DA 021608 (PI: Michele D. Levine, PhD)
**Presenter:** Sarah N. Fribance  
**Education:** University of Pittsburgh  
**Current Position:** Undergraduate Student  
**Principal Area of Research Interest:** First episode schizophrenia  
**Current Research Support:** Center for Translational Mental Health Research Undergraduate Fellowship, NARSAD, NIH R01 MH108568  
**Mentor(s):** Dean Salisbury, PhD

### Deficits in attentional modulation of auditory stimuli in first episode schizophrenia

**Author(s):** Fribance S\(^1\), Coffman B\(^1\), Murphy T\(^1\), Haigh S\(^1\), Leiter J\(^1\) and Salisbury D\(^1\)  
**Affiliation(s):** \(^1\)Department of Psychiatry, University of Pittsburgh School of Medicine

**Study:** The N1 auditory evoked potential (AEP) is reduced in long-term schizophrenia (Sz) and in the first episode schizophrenia spectrum (FE). N1 is increased by attention to tones, and this modulation is impaired in Sz. It is not known whether FE can modulate N1 sensory signals by attention. This study examined N1 in attend and ignore tasks to access N1 modulation by attention (Nd) in FE early in disease course.

**Methods:** Thirteen FE and 11 matched healthy control (HC) participants heard sounds while watching a silent video. Participants heard repetitious tones in a typical AEP task (1k Hz, 50 ms duration, 5 ms rise/fall, 80 dB), spaced 1050 ms to 1550 ms apart. In one condition, participants were told to ignore tones, while in the other condition participants pressed a button to every 7\(^{th}\) tone. EEG data was recorded and filtered between 0.5 Hz and 20 Hz. N1 amplitude was calculated as average voltage between 100 ms and 110 ms at Cz.

**Results:** Overall, there was no significant difference in N1 between groups (p =0.27). Attention increased N1 (p =0.03). Of primary importance, N1 amplitude was differentially affected by attention between groups (p =0.002). Analyses revealed that HC showed larger N1 with attention (p =0.01), but FE did not show the same Nd effect (p =0.27).

**Conclusion:** FE did not appear to enhance the auditory N1 with attention. This may reflect a long-range functional disconnection between cognitive control cortical areas in the frontal lobes and auditory sensory cortex in the temporal lobes early in disease course. The lack of significant differences between groups in the Ignore condition suggests the N1 deficit observed here, and previously reported for oddball tasks in FE, may be more an attention effect than a sensory deficit.

**Significance:** Further examination of the underlying pathophysiology and structural pathology may lead to a better understanding of the processes giving rise to schizophrenia. Clinically, the lack of attention-related Nd in FE suggests it may serve as a sensitive biomarker for the detection of the schizophrenia prodrome among clinical high-risk individuals.

**Funding Source(s):** NARSAD and NIH R01 MH108568 (PI: Dean Salisbury, PhD)
Dysregulated phosphoproteome expression in the auditory cortex in schizophrenia

Author(s): Garver M\textsuperscript{1}, Newman J\textsuperscript{1}, Sweet R\textsuperscript{1}, Yates N\textsuperscript{2}, and MacDonald ML\textsuperscript{1}
Affiliation(s): \textsuperscript{1}Department of Psychiatry, University of Pittsburgh School of Medicine and \textsuperscript{2}Biomedical Mass Spectrometry Core, University of Pittsburgh

Study: Pathologic alterations to synaptic protein networks are believed to underlie synapse loss and disease symptoms in schizophrenia. Phosphorylation plays an important role in synaptic protein trafficking and activity. Here, for the first time, we utilize phosphoproteomic mass spectrometry to analyze human postmortem brain tissue from schizophrenia and matched control subjects, identifying synaptic phosphoprotein and phosphoprotein network alterations linked to spine loss in schizophrenia.

Methods: Grey matter homogenates were prepared from right hemisphere auditory cortex grey matter of 16 schizophrenia and matched control subjects. Samples were digested with trypsin, subject to phosphopeptide enrichment by TiO\textsubscript{2}, and analyzed by DDA (top 4) LC-MS/MS on an LTQ Orbitrap XL. Spine density measurements were determined in the right hemisphere of the same subjects by quantitative fluorescence confocal microscopy. Term enrichment was conducted in DAVID. Co-phosphorylation networks will be constructed for the schizophrenia and control groups separately by WGCNA and compared.

Results: We observed 883 unique phosphorylation sites from 479 protein groups. Of these phosphorylation sites, 106 were significantly dysregulated in schizophrenia (q < 0.05) accounting for multiple hypothesis testing. Proteins with dysregulated phosphosites were significantly enriched for terms relating to postsynaptic density function and the cytoskeleton. Over 20 of these sites are significantly correlated with spine density, suggesting a link to, if not a role in, spine loss in schizophrenia. Co-expression network analyses, utilizing weighted gene co-expression network analysis (WGCNA) type approaches, are currently underway to map and compare phosphoprotein networks in schizophrenia tissue.

Conclusion: Schizophrenia individuals exhibit altered phosphoproteome expression, with 20 dysregulated phosphopeptides correlated to spine density.

Significance: This study employs phosphoproteomic mass spectrometry to investigate the dynamic post translational modification, phosphorylation, and its role in the synaptic alternations observed in Schizophrenia.

Funding Source(s): MH 071533, K01 MH 107756
Approaches to recruitment in a pediatric community sample

Author(s): George-Milford B¹, Brent D¹, Biernesser C¹, and Moore T¹
Affiliation(s): ¹Department of Psychiatry, University of Pittsburgh School of Medicine

Study: Employing recruitment techniques within the Youth Computerized Adaptive test (YCAT) study maximized enrollment of 1400 youth ages 7-17, who were in mental health treatment and controls. Promotion of sharing participants across a research institution/university with multiple, unique research studies aids in overall health of many research grants.

Methods: A multi-step approach to recruitment was used within a community sample. Steps included: 1) planning recruitment strategies with a detailed timeline of recruitment activities throughout the grant; 2) snowball sampling of referral sources that directed study staff to numerous other referral sources who interact with the study target population; 3) implementation of recruitment strategies via immersion of study staff in the target population with the goal of developing close relationships and then educating those referral sources to send participants to the study and executing strategies “campaign style” (i.e. continuously educating all referral sources in tandem with traditional forms of recruitment); and 4) tracking recruitment strategies which impacted screening, consenting processes, and follow up with research participants.

Results: Community outreach and education of referral sources (both inside and outside of University of Pittsburgh/UPMC) were the most effective strategies from which referrals were made to the study, garnering 1622 referrals. Traditional forms of advertising such as flyers and online/print ads garnered 495 referrals and “word of mouth” garnered 134 referrals. Very limited direct recruiting of individuals took place by the research staff, thereby allowing study staff to focus on screening and enrollment, while maximizing the number of referrals received. During lower enrollment periods on the grant, using campaign style recruiting techniques allowed some referral sources to swell while others waned. Through this plan, the grant met all recruitment milestones set by NIMH standards.

Conclusion: There are several recommendations born out of this process. 1) Educating referral sources and immersion in target recruitment population maximizes referrals while allowing study staff to focus on other important grant tasks; 2) Campaign style recruiting implemented by a team is essential; 3) Appropriate tracking and ongoing analysis of recruitment strategies, monitored daily is necessary; 4) A recruitment line item in grant budget is critical; 5) It helps to develop a means to share and keep referrals.

Significance: The development of a successful recruitment plan to recruit a broad, pediatric population can be generalizable to multiple studies.

Funding Source(s): NIMH grant MH100155 (PI: Robert Gibbons, PhD)
Self-efficacy in smoking restraint, but not motivation, predicts postpartum smoking resumption among women

Author(s): Germeroth LJ\textsuperscript{1}, Emery RL\textsuperscript{1}, Kolko RP\textsuperscript{1}, Salk RH\textsuperscript{1}, Cheng Y\textsuperscript{2}, and Levine MD\textsuperscript{1}

Affiliation(s): \textsuperscript{1}Department of Psychiatry, University of Pittsburgh School of Medicine and \textsuperscript{2}Department of Statistics, University of Pittsburgh

Study: Women commonly quit smoking during pregnancy, but most resume smoking within the first year postpartum. Low motivation to remain quit from smoking and low self-efficacy in maintaining abstinence are two factors that may contribute to resumption of smoking behavior postpartum. The present study assessed motivation and self-efficacy to stay quit as predictors of initial smoking lapse and full-blown relapse through 1 year postpartum.

Methods: Three hundred pregnant, recently quit smokers ($M$ age = 24.99, $SD$ = 5.64 years) participating in one of two postpartum relapse prevention interventions completed a prenatal baseline session and follow-up sessions 12, 24, and 52 weeks postpartum. Participants completed measures of motivation to remain quit (Reasons for Quitting Questionnaire), self-efficacy in refraining from smoking (Self-Efficacy Questionnaire), and a Timeline Follow-Back interview of any smoking since delivery. The primary outcomes, time to lapse and time to relapse, were determined by counting the number of days between delivery and (a) the first day at least 1 cigarette was smoked (lapse) and (b) the first day of 7 consecutive days of smoking (relapse).

Results: Cox regression analyses, adjusted for treatment group, number of weeks quit at baseline, age, race, and education, indicated that women with higher self-efficacy in refraining from smoking were less likely to lapse than women with lower self-efficacy at each postpartum follow-up (e.g., Week 52: HR = 0.99, 95% CI = 0.97-1.00, $p$ = .01). Self-efficacy, however, did not predict relapse, and motivation was not predictive of time to lapse or relapse at any point through 52 weeks postpartum (all $p$s between .23 and .98).

Conclusion: Self-efficacy in refraining from smoking consistently predicted smoking lapse through 1 year postpartum. Motivation, however, did not provide unique predictive value. Further work is needed to understand how prenatal self-efficacy and motivation may interact to influence postpartum smoking behavior.

Significance: The present findings underscore the importance of assessing and increasing prenatal self-efficacy to remain quit in smoking cessation interventions.

Funding Source(s): NIDA grant R01DA021608 (PI: Michele Levine, PhD)
Coping with eating disorders on a college campus: A qualitative study

Author(s): Goldschen L\textsuperscript{1}, Lundblad W\textsuperscript{2}, Fertig AM\textsuperscript{2}, and Chang JC\textsuperscript{3}

Affiliation(s): \textsuperscript{1}University of Pittsburgh School of Medicine; \textsuperscript{2}Department of Psychiatry, University of Pittsburgh School of Medicine; and \textsuperscript{3}Department of Obstetrics, Gynecology & Reproductive Sciences, University of Pittsburgh School of Medicine

Study: Anorexia Nervosa and Bulimia Nervosa are eating disorders that are more prevalent on college campuses than in the general population. While college counseling centers report record-high numbers for students seeking mental health services (including eating disorders), it is unknown how students with eating disorders use and perceive these resources. Our study’s objective is to understand the experiences of undergraduate students with eating disorders regarding managing their disorder during college, preferences for treatment, and their challenges when seeking care.

Methods: Undergraduate students who self-identify having an eating disorder were recruited through fliers and Project Heal, the undergraduate eating disorder advocacy organization. We conducted semi-structured individual interviews and two investigators separately coded verbatim transcripts.

Results: Fifteen undergraduate students participated in the interviews. Participants included freshmen and recent alumni. Participants reported a combination of restricting, binging, purging, and self-harm behaviors. Preliminary analysis of the transcripts has noted the following themes: 1) participants attributed a negative influence on their eating disorder recovery to the unhealthy diet culture on college campuses; 2) participants described mental illness stigma on college campuses as a barrier to access treatment for their eating disorders; 3) participants emphasized a need and desire for peer support for students with eating disorders on University of Pittsburgh’s campus.

Conclusion: Our preliminary findings suggest a need to provide additional campus support and resources to students with eating disorders as well as to pursue efforts to change the college eating environment and reduce stigma regarding mental illness.

Significance: This study will provide students with eating disorders a voice to express their experience, a forum to share their needs, and an opportunity to share preferred treatment options. This insight will be invaluable to both the undergraduate counseling center and the UPMC Center for Eating Disorders so they can tailor their programs to the needs of these students.

Funding Source(s): T32 MH018951 (PI: David Brent, MD)
Emotion dysregulation in youth with autism, but not autism symptom severity, is associated with greater use of intensive care services

Author(s): Golt J\(^1\) and Mazefsky C\(^1,2\)
Affiliation(s): \(^1\)Western Psychiatric Institute and Clinic of UPMC and \(^2\)Department of Psychiatry, University of Pittsburgh School of Medicine

Study: Although there is increasing evidence that individuals with autism spectrum disorder (ASD) have impaired emotion regulation, the effect of emotion dysregulation in this population has not been well studied. This study investigated how severity of emotion dysregulation in youth with ASD impacts the amount and types of services utilized.

Methods: Parents of 1,228 6-17 year old youth with ASD completed a battery of questionnaires online. The Emotion Dysregulation Inventory (EDI), a new measure developed using PROMIS principles, was utilized to measure emotional reactivity and dysphoria over the past 7 days. Parents also completed a treatment history form that captured current medications and treatments, recent crisis interventions, and other gold standard assessments of behavior and ASD symptoms. Logistic regression to predict services and other outcomes from EDI scores were conducted, controlling for age and autism symptom severity.

Results: Higher levels of emotion dysregulation using the EDI Reactivity factor significantly predicted a greater likelihood of emergency attention or crisis care among youth with ASD, including in home crisis evaluation, police contact, or psychiatric hospitalizations \((p<0.001)\). Those with higher EDI scores also were significantly more likely to use antipsychotics, psychostimulants, and antidepressants \((p<0.001)\), as well as mood stabilizers \((p<0.03)\). Higher EDI Reactivity scores also significantly predicted the likelihood of school suspensions or school contact due to a behavior issue \((p<0.001)\). Finally, higher EDI scores significantly associated with a greater likelihood of individual or in-home therapies \((p<0.001)\). Interestingly, ASD symptom severity was not significantly associated with increased risk in any of these models, with the exception of individual and in-home services.

Conclusion: Greater emotion dysregulation is associated with an increased use of services and medications, more instances of crisis interventions for behavior at home and school, and police contact among youth with ASD, whereas ASD symptom severity was unrelated to the likelihood of these services and interventions when emotion dysregulation was taken into account.

Significance: Although early intervention for ASD typically emphasizes the social and communication aspects of the disorder, these findings highlight the importance of early identification and treatment of emotion dysregulation in children with ASD.

Funding Source(s): NIH R01HD079512 (PI: Carla Mazefsky, PhD)
Impulsive sensation seeking de-couples the putamen from the posterior cingulate cortex

Author(s): Graur S\textsuperscript{1}, Chase HW\textsuperscript{1}, Greenberg T\textsuperscript{1}, Stiffler R\textsuperscript{1}, Aslam H\textsuperscript{1}, Lockovich JC\textsuperscript{1}, Bebko G\textsuperscript{1}, and Phillips ML\textsuperscript{1}

Affiliation(s): \textsuperscript{1}Department of Psychiatry, University of Pittsburgh School of Medicine

Study: Impulsivity and sensation seeking (ISS) constitute a cluster of traits predicting maladaptive decision making and risky behaviors. Previously, we associated a subset of self-report scales (BIS-11 Motor/Attention; UPPS-P Positive/negative urgency; BAS fun seeking) with enhanced reward anticipation-related activity in the ventral striatum. Presently, we seek to identify whether individual differences in ISS is associated with altered resting functional connectivity using striatum subregions (bilateral putamen, caudate head, and nucleus accumbens). This would provide evidence of an ISS-related alteration in the functional properties of the region that might extend beyond reward-related stimuli.

Methods: Resting state functional MR images were obtained in cohorts of 68 healthy controls and 55 distressed individuals. A composite score of ISS was derived from the questionnaires described above. A multiband (MB) sequence was employed to acquire functional MRI data (TR/TE=1500/30ms; 3xMB acceleration; 2.3mm slice thickness). Standard seed-based resting state preprocessing methodology was applied.

Results: Increasing ISS decoupled the relationship between the left putamen and the posterior cingulate cortex/precuneus (MNI coordinates: x=6, y=-58, z=32; k=314, t=4.36, cluster corrected p\textsubscript{FWE}=0.001, with cluster forming p<0.001). No other findings reached significance after correcting for 6 seeds (p\textsubscript{FWE}<0.008).

Conclusion: Decoupling of the precuneus from the striatum could reflect an alteration in regulation of regions supporting motivation, decision-making and executive/cognitive processing from those subserving self-awareness and reflection, and drive impulsive behavior. The association with left putamen, as opposed to other striatal regions, suggests that abnormal resting connectivity and reward expectancy-related activation associated with ISS may be neuroanatomically distinct.

Significance: Current data suggests that impulse related symptoms in mood disorders and neural substrates could help inform new treatment strategies.

Funding Source(s): NIMH MH100041 “Reward, pathophysiologic dimensions and psychological distress in young adults” (PI: Mary Phillips, MD)
Sensitivity to the disinhibiting effects of alcohol for adults with and without a history of ADHD

**Author(s):** Green CD, White SJ, Molina BSG and Pedersen SL

**Affiliation(s):** 1Department of Psychiatry, University of Pittsburgh School of Medicine

**Study:** Childhood ADHD predicts increased alcohol problems in adulthood (Pedersen et al., 2016). Sensitivity to the disinhibiting effects of alcohol can contribute to alcohol problems (Marczinski, Combs, & Fillmore, 2007) and prior research with small samples (n = 20) has demonstrated that adults with ADHD may be more sensitive to these effects (Weafer, Fillmore, & Millich, 2009). The current study extends this research to adults with a history of childhood ADHD that vary in their current symptomatology and explores racial differences. Additionally, we examined the association between sensitivity to the disinhibiting effects and alcohol use and alcohol problems.

**Methods:** Adult drinkers (N = 221; 51.6% ADHD; 48.4% nonADHD; 74.2% male; 64.7% White; M age = 27.97) completed a within-subjects counterbalanced alcohol administration study (alcohol and non-alcohol sessions). During the alcohol session, participants consumed a moderate dose of alcohol (~.08%) over a 30-minute period. The Cued Go/No-Go task, an index of behavioral disinhibition, was completed on the ascending (35 mins post-alcohol consumption, MBrAC = .069) and descending limbs of the BrAC curve (80 mins post-alcohol consumption, MBrAC = .067), as well as in the non-alcohol session. Additionally, participants completed self-reported measures of quantity and frequency of alcohol use and alcohol problems.

**Results:** Regression analysis with sex, age, race, session order, and BrAC as covariates indicated that participants with ADHD had increased behavioral disinhibition than those without ADHD on the ascending (M_{BrAC} = .069, β = -.138, p<.05) and descending limb (M_{BrAC} = .067, β = -.202, p<.05). Black drinkers experienced a sharper increase in behavioral disinhibition on the ascending limb than White drinkers (β = .151, p<.05). Heightened behavioral disinhibition on the descending limb was related to more past 12 month alcohol problems (β = -.224, p<.05).

**Conclusion:** Adults with a history of ADHD experienced sharper increases in behavioral disinhibition following alcohol consumption compared to those without ADHD. Additionally, Black drinkers may be more sensitive to these effects compared to White drinkers.

**Significance:** These findings highlight the possibility that one reason why childhood ADHD relates to alcohol problems in adulthood is sensitivity to the disinhibiting effects of alcohol and may identify a proximal point of intervention in this at risk population. Similarly, Black drinkers experience more alcohol problems at comparable levels of drinking compared to White drinkers and acute alcohol response may partially explain these health disparities.

**Funding Source(s):** K01 AA021135 (PI: Sarah Pedersen, PhD), ABMRF (PI: Sarah Pedersen, PhD)
Presenter: Tsafrir Greenberg, PhD
Education: Stony Brook University
Current Position: Research Instructor in Psychiatry
Principal Area of Research Interest: Neuroimaging of affective processes associated with mood and anxiety symptoms
Mentor: Mary L. Phillips, MD, MD (CANTAB)

Anxiety mediates the relationship between amygdala activity during emotion processing and poor quality of life in young adults
Authors: Greenberg T1*, Bertocci MA1*, Chase HW1, Stiffler R1, Aslam HA1, Graur S1, Bebko G1, Lockovich JC1, and Phillip ML1 (* These authors contributed equally to this work.)
Affiliation: 1Department of Psychiatry, University of Pittsburgh School of Medicine

Study: Young adults often experience psychological distress. Yet, there are no objective neural markers to accurately identify individuals who will develop future psychopathology, and to guide interventions. We aimed to identify directional relationships between fronto-amygdala emotional regulation circuitry activity, personality traits, and symptoms associated with psychological distress, and quality of life (QoL).

Methods: A hundred and twenty 18-25 year-olds, n=51 psychologically distressed and n=69 healthy individuals, completed a face emotion processing task during functional magnetic resonance imaging, clinical and behavioral measures, and QoL assessment.

Results: Penalized regression, accounting for large numbers of independent variables, showed that increased state and trait anxiety, cohort, and measures of general and anhedonic depression severity predicted poorer QoL (all exponents>0.87). Only state and trait anxiety predicted emotion processing-related fronto-amygdala activity (all exponents=1.00). State and trait anxiety fully mediated the relationship between amygdala activity and QoL (p-value increased from .001 to .29: left amygdala, and from .003 to .94: right amygdala). State anxiety fully mediated the relationship between left ventrolateral prefrontal cortical (vlPFC) activity and QoL (p-value increased from .01 to .18). The relationship between state and trait anxiety and QoL was not mediated by amygdala or left vlPFC activity.

Conclusion: We identify specific, directional relationships linking amygdala and left vlPFC activity, state and trait anxiety, and poor QoL across different diagnoses.

Significance: Our findings highlight roles of amygdala and left vlPFC activity as neural predictors of anxiety and poor QoL, and as potentially important targets for novel interventions to reduce anxiety and, in turn, improve QoL in young adults.

Funding Source(s): NIMH R01MH100041 (PI: Mary L. Phillips, MD, MD (CANTAB))
A schizophrenia-associated missense mutation in kalirin converges on multiple rhoA-dependent pathways involved in cytoskeletal morphology

Author(s): Grubisha MJ, Russell T, Ferguson C, Wills ZP, Fish KN, Homanics GE, Penzes P and Sweet RA

Affiliation(s): 1Department of Psychiatry, University of Pittsburgh Medical School; 2Department of Anesthesiology, University of Pittsburgh School of Medicine; 3Departments of Physiology and Psychiatry and Behavioral Sciences, Northwestern University Feinberg School of Medicine; and 4Mental Illness Research, Education, and Clinical Center, VA Pittsburgh Healthcare System

Study: Kalirin (KAL) is a Rho GEF that is highly involved in regulation of cytoskeletal morphology within dendrites. There are several isoforms of the protein that arise from differential splicing. A missense mutation (P2255T, PTKAL9) in the KAL9 isoform has been associated with schizophrenia. We hypothesized that the PT mutation alters KAL9’s Rho GEF activity, an effect which contributes to morphological alterations in pyramidal cells associated with schizophrenia.

Methods: Rho activation assays were performed in an in vitro culture system. Dendritic complexity was analyzed via Sholl analysis on KAL9 transfected rat E17 primary cortical cultures. A humanized mouse model of the PTKAL9 mutation was created using CRISPR/Cas9 genome editing. Frontal pole homogenate was collected and RNAseq was performed. Differential gene expression was calculated and pathway analysis was performed.

Results: In mature cortical neurons in vitro, overexpression of PTKAL9 confers increased RhoA activation and decreased dendritic complexity. Frontal pole cortex from PTKAL9 mice shows differential expression of multiple genes which are enriched in neuron development pathways using gene ontology classifications. Of these differentially regulated genes, multiple RhoA-dependent signaling pathways which are involved in cytoskeleton dynamics were identified.

Conclusion: PTKAL9 appears to have increased RhoA activity compared to WT, resulting in perturbation of multiple convergent pathways involved in signaling to the cytoskeleton in a RhoA-dependent manner. These signaling pathway perturbations may underlie some of the observed functional impairments seen in pyramidal cells in schizophrenia.

Significance: Using a disease-associated mutation to model convergent pathway perturbations involved in cytoskeleton remodeling may aid the development of novel pharmacotherapeutics for schizophrenia.

Funding Source(s): MH071533, AG027224, and VAPHS grant BX000542 (PI: Robert Sweet, MD)
Deficits in complex MMN to group size deviance in first-episode schizophrenia-spectrum psychosis

Author(s): Haigh SM1, Coffman BA1, Murphy TK1, Ward KL1, and Salisbury DF1
Affiliation(s): 1Clinical Neurophysiology Research Laboratory (CNRL), Department of Psychiatry, University of Pittsburgh School of Medicine

Study: Individuals with long-term schizophrenia (SZ) show reductions in simple mismatch negativity (MMN) to infrequent stimulus parameter deviance, and in complex MMN to infrequent pattern deviance. First episode schizophrenia-spectrum individuals (FE) show less reduction of simple MMN. Complex pattern deviance may be more suitable for elucidating subtle deficits in auditory perception at first-episode, and may be a useful biomarker for the presence of schizophrenia.

Methods: We measured simple MMN to pitch and duration deviants, and complex MMN to an extra fourth tone amongst standard groups of three tones (1 kHz, 50 ms duration, 5 ms rise/fall, 80 dB, 330 ms SOA, 800 ms ITI) in 24 SZ, and 23 matched healthy controls (HCSZ), and in 24 FE (within 6 months of first-episode), and 23 matched healthy controls (HCFE).

Results: For simple MMN, SZ showed reductions in pitch (p < .001) and duration (p < .008), and for complex MMN (p = .043). Simple MMN was not significantly reduced in FE (pitch p = .215, duration (p = .705), but complex MMN was (p = .003).

Conclusion: Both simple MMN and complex MMN are impaired in long-term schizophrenia, whilst only complex MMN was impaired in FE; simple MMN was not impaired at first break. The late MMN must be associated with deficits in pure novelty detection, as there was no stimulus-specific information that indicated a deviant tone. Therefore, both individuals with both long-term and first-episode schizophrenia show specific deficits in pure novelty detection.

Significance: Complex MMN may be a more sensitive biomarker of the presence of schizophrenia early in disease course. To assess whether complex MMN has greater sensitivity to detect incipient psychosis, both simple MMN and complex MMN will be measured in prodromal individuals.

Funding Source(s): NIH R01 MH094328 (PI: Dean F Salisbury, PhD)
Heart rate variability and depressive symptoms among high-risk late adolescents: The role of sleep

Author(s): Hamilton JL\textsuperscript{1,2} and Alloy LB\textsuperscript{1}
Affiliation(s): \textsuperscript{1}Department of Psychology, Temple University and \textsuperscript{2}Department of Psychiatry, University of Pittsburgh School of Medicine

Study: Heart rate variability (HRV) is considered to be a physiological marker of self-regulation, with considerable research documenting that lower resting HRV is associated with poorer emotion regulation, executive functioning, and current and past depression. However, individual differences of HRV levels among those with a depression history remain unclear, particularly related to their prospective risk for depression recurrence. Furthermore, sleep deprivation and insomnia severely impact self-regulation abilities, even among health individuals. Therefore, we evaluated whether insomnia symptoms exacerbated the effects of lower resting HRV on depressive symptoms among late adolescents with a depression history.

Methods: Participants included late adolescents and emerging adults (N= 105; 73% female; 71% Caucasian; 80% heterosexual) who met criteria for a history of major or subthreshold depression based on a diagnostic interview (SADS-L). Participants completed a baseline assessment, which included measures of depressive symptoms and a socio-evaluative stressor task (TSST) while being hooked up to electrocardiogram (ECG) to assess heart rate variability (HRV). For two weeks, participants completed a daily diary of depressive (PROMIS-SF) and insomnia symptoms (ISI).

Results: Multilevel modeling in Mplus indicated that lower resting HRV prospectively predicted higher depressive symptoms over the next two weeks. Further, we found a significant interaction between sleep and resting HRV predicting prospective depressive symptoms. This interaction was such that lower resting HRV predicted depressive symptoms, but only among those with more symptoms of insomnia (difficulty falling and staying asleep).

Conclusion: Among individuals a history of depression, those with more self-regulation difficulty (as indexed by the physiological marker of HRV) are at greater risk for prospective depressive symptoms. Further, sleep exacerbates the effects of self-regulation on depressive symptoms.

Significance: The present findings highlight the importance of considering intragroup differences of HRV and sleep on depression risk, particularly among individuals at heightened risk for depression recurrence.

Funding Source(s): F31MH106184-01
Maternal caregiving moderates the association between emotionality and network topology in infants

Author(s): Hanford L\textsuperscript{1}, Schmithorst V\textsuperscript{2}, Lee V\textsuperscript{2}, Panigrahy A\textsuperscript{2}, Ridley J\textsuperscript{1}, Versace A\textsuperscript{1}, Hipwell A\textsuperscript{1}, and Phillips M\textsuperscript{1}

Affiliation(s): \textsuperscript{1}Department of Psychiatry, University of Pittsburgh and \textsuperscript{2}Children's Hospital of Pittsburgh of UPMC

Study: Infancy is a period of expansive brain growth and development. It is also a time of heightened sensitivity to external influences, some of which have long-lasting implications on neuronal structure and function. One such influence can be the quality of maternal caregiving received. The current study investigates: (1) the relationship between infant emotionality and resting state connectivity network measures; and (2) the potential moderating effects of maternal caregiving on this relationship.

Methods: At approximately 3 months (n=23, average age = 3.5 months, 11 female), infants underwent resting state functional magnetic resonance imaging and were filmed in face-to-face interaction with the mother. Behavioral indices of positive (PE) and negative (NE) emotionality and maternal mental state talk (MST) were coded by independent observers. Network measures were calculated through graph theory techniques. Mixed-effect general linear models were developed to examine the relationship between infant emotionality and nodal measures, including clustering coefficient (CC), eigenvector centrality (EC), nodal efficiency (NE) and participation (P). Next, the moderating effects of maternal MST were tested.

Results: Several significant associations of PE and NE-PE ratio with nodal metrics were seen. Of note, PE showed positive associations within bilateral caudate (EC, NE, P), middle orbital frontal and left middle frontal regions (CC), as well as negative associations within the left thalamus (NE, P) and inferior frontal gyrus (EC, NE). Finally, we observed moderation effects of maternal MST on the relationship between PE and nodal metrics within the bilateral orbitofrontal (EC, CC, NE), left middle frontal (NE), and bilateral inferior temporal regions (EC, NE, P).

Conclusion: Taken together, our results suggest increasing nodal importance of frontal and caudal structures with greater positive emotionality in 3-month-old infants. Later in life, this frontal activation may be indicative of greater top-down emotional regulatory network control.

Significance: Our preliminary results show the establishment of important brain-behaviour relationships; between resting state network topology and infant emotionality, and that this relationship can be altered by the strength of maternal attribution in infants as young as 3 months. Finding biological correlates of temperament during infancy would better our understanding of brain-behaviour relationships, but may also be helpful in predicting future psychological outcomes.

Funding Source(s): NICHD 106570 (PIs: Phillips/Hipwell)
**Presenter:** Connor Haszto  
**Education:** University of Pittsburgh  
**Current Position:** Undergraduate Student  
**Principal Area of Research Interest:** Schizophrenia  
**Current Research Support:** MH101566  
**Mentor(s):** Konasale Prasad, MD

### Meta-analysis of membrane phospholipid metabolites in schizophrenia

**Author(s):** Haszto C, Stanley J, and Prasad K  
**Affiliation(s):** 1University of Pittsburgh Deitrich School of Arts and Sciences; 2Wayne State University School of Medicine; and 3University of Pittsburgh School of Medicine

**Study:** Synaptic pathology is proposed to underlie schizophrenia (SZ). Synapses are primarily located in the neuropil that consists of synaptically dense region of dendrites, unmyelinated axons and glial filaments with relatively few cell bodies. Phosphorus magnetic resonance spectroscopy ($^{31}$P MRS) is a non-invasive method to specifically and reliably quantify changes in synaptic density by measuring membrane phospholipid (MPL) metabolites. MPL precursors, phosphocholine (PC) and phosphoethanolamine (PE) are elevated at the time and site of synaptic formation. Likewise, MPL catabolites, glycerophosphocholine (GPC) and glycerophospho-ethanolamine (GPE) are elevated at the time and site of synaptic pruning.

**Methods:** We extensively searched the bibliographic databases for peer-reviewed publications, namely PubMed, PsychInfo, Web of Sciences and others. We selected 42 published studies that reported $^{31}$P MRS data in SZ with adequate description of MRS methods. We analyzed the data on the frontal and temporal lobes using the MAVIS on R 3.2.1. Random effects models were built for PC+PE and GPC+GPE data from these regions.

**Results:** Sample size varied for each region and diagnostic group (SZ, Frontal PC+PE: 408; Temporal PC+PE: 95; Frontal GPC+GPE: 376; Temporal GPC+GPE: 107) (Controls, Frontal PC+PE: 341; Temporal PC+PE: 89; Frontal GPC+GPE: 316; Temporal GPC+GPE: 125). PC+PE was significantly decreased in the frontal (b=-0.90 (-1.57, -0.23), p=0.008) and the temporal (b=-0.22 (-0.43, 0.01), p=0.045) regions. Test of heterogeneity for the frontal PC+PE measurements suggested that the findings were not homogeneous (Q(df=20)=178.42, p<0.001). However, the temporal PC+PE was more homogeneously decreased (Q(df=11)=13.37, p=0.27). GPC+GPE showed nominal elevation in the frontal (b=0.35 (-0.03, 0.73), p=0.06) but significant elevation in the temporal (b=0.74 (0.45, 1.02), p<0.001) regions but showed significant heterogeneity in measurements across the studies.

**Conclusion:** Despite methodological differences, this meta-analysis shows decreased PC+PE in both frontal and temporal regions among SZ patients suggesting decreased neuropil formation. Increased GPC+GPE in both these regions in SZ compared to controls suggests increased synaptic pruning. Taken together, these findings suggest a decreased neuropil density, possibly contributed by a dual hit of decreased synapse formation with an increased synaptic pruning.

**Significance:** Significant changes in both synapse formation and pruning suggests that the pathophysiological pathways that contribute to both these processes together are likely to be more effective targets for novel drug discovery than either of them separately.

**Funding Source(s):** MH101566
Effects of nicotine versus placebo e-cigarette use on symptom relief during tobacco abstinence

Author(s): Herb TH¹, Karelitz JL², and Perkins KA³
Affiliation(s): ¹Western Psychiatric Institute and Clinic of UPMC; ²Department of Psychology, University of Pittsburgh; and ³Department of Psychiatry, University of Pittsburgh School of Medicine

Study: Because electronic cigarettes (e-cigs) containing nicotine may relieve smoking abstinence symptoms similar to NRT medication, we used within-subjects designs to test these effects in non-quitting and quitting smokers across two studies.

Methods: In Study 1, 28 non-quitting smokers abstained overnight prior to each of 3 sessions, varying by within-subjects e-cig condition. Counterbalanced sessions involved either no e-cig or 4 exposures (each 10 puffs) over 2 hours to e-cigs that either did (36 mg/ml) or did not (0 mg/ml) contain nicotine. MNWS withdrawal and single “craving” item were assessed for these sessions. Study 2 was a cross-over design involving 10 smokers preparing to quit soon. Participants engaged in two 4-day “practice” quit periods on separate weeks. All received either a nicotine or placebo e-cig on Monday to use ad lib while trying to stop smoking on Tuesday-Friday. One week of smoking resumption separated the two e-cig weeks. MNWS and QSU craving were assessed daily during both e-cig weeks.

Results: Study 1 results show that withdrawal symptom relief was greater after nicotine vs. placebo e-cig (p<.05), but not after placebo vs. no e-cig. This suggests that relief was due to nicotine alone and not simple e-cig use behavior. Study 2 results show QSU craving, especially Factor 1 (“Nothing would be better than smoking a cigarette right now”) was generally relieved by ad lib use of the nicotine vs. placebo e-cig. However, there was no significant relief shown for MNWS withdrawal.

Conclusion: Our studies show some relief due to nicotine e-cig use, both during temporary abstinence in non-quitting smokers (Study 1) as well as during >24 hour abstinence in smokers planning to quit permanently (Study 2).

Significance: Present findings are consistent with the notion that e-cigs could potentially be used as an effective cigarette smoking cessation tool due to their ability to decrease cigarette withdrawal symptoms. More controlled research is needed on the effects of nicotine from e-cig use in relieving abstinence-related symptoms, with larger and diverse study samples assessed over longer durations of tobacco cessation.

Funding Source(s): NIH Grants DA035774 (PI: Kenneth Perkins, PhD) and T32HL7560 (PI: Joshua Karelitz, PhD)
**Blinding of psychotherapy and pharmacology in clinical trials**

**Authors:** Herbstsomer RA\(^1\), Swartz HA\(^1\), and Wallace M\(^3\)

**Affiliation:** \(^1\)Department of Psychiatry, University of Pittsburgh School of Medicine

**Study:** The gold standard in clinical research is the randomized, double-blinded, placebo-controlled trial. Blinding conceals the identity of the intervention from investigators, assessors, and participants, thus reducing expectancy bias, which is necessary for a scientifically rigorous trial. Many assume that blinding is more effective in the context of pharmacology trials than psychotherapy studies, but this has never been formally tested. This study compares the effectiveness of blinding in one trial comparing pharmacotherapies and one comparing psychotherapies.

**Methods:** Study 1 subjects included 65 male and female adults with bipolar II disorder, currently depressed, treated with Interpersonal and Social Rhythm Therapy and randomized to either quetiapine (n=36) or placebo (n=29). Study 2 subjects included 35 adult females with major depressive disorder randomized to receive either Brief Supportive Psychotherapy (BSP; n=16) or Interpersonal Psychotherapy for Mothers (IPT-MOMS; n=19). Participants were provided either a list of side effects of quetiapine or a short conceptual description of the two psychotherapies, depending on the trial, prior to randomization, and then asked to guess which treatment they had received after completion. In the pharmacotherapy trial, treatment was provided in a double blind fashion. In the psychotherapy trial, treatment was single blind (therapists were aware of the therapy provided but participants were not).

**Results:** Participants in the pharmacology trial were able to identify their treatment assignment more frequently than chance predicts (n=46, 82%, p<.001). Those assigned to quetiapine were not more likely to identify their assignment than those assigned to placebo. In the psychotherapy trial, 69% (n=24, p=.02) of participants were able to identify their assignment correctly. A significantly larger (p=0.01) percentage of participants correctly identified their assignment to BSP (n=14, 88%) than those assigned to IPT-MOMs (n=9; 48% correct).

**Conclusion:** Although blinding procedures were applied in both trials, over 60% of participants in both the pharmacology and psychotherapy trials were able to identify treatment assignments. High rates of blinding failure may jeopardize the rigor of the studies and appears to be relevant to both psychotherapy and pharmacology interventions. In addition, BSP, which is commonly used as a “control” in psychotherapy clinical trials, was readily identified by participants.

**Significance:** These findings suggest that it may be necessary to re-evaluate practices used to blind pharmacotherapy and psychotherapy trials to reduce bias in clinical trials.

**Funding Source(s):** NIMH grants MH084831 and MH083647 (PI: Holly Swartz, MD)
Circadian perturbation reveals susceptibility and resilience to reward-related behavior in adolescence

Authors: Hildebrand MH¹, Vadnie CA¹, Bertholomey M¹, McElroy B¹, Logan RW³, Torregrossa M¹, McClung CA¹

Affiliations: ¹Department of Psychiatry, University of Pittsburgh School of Medicine

Study: Adolescence is a vulnerable time for perturbations in sleep patterns and circadian rhythms. Adolescents prefer later sleep and wake times, which has been attributed to a biologically driven delay in circadian rhythms. Since school start times are early in the morning, many adolescents may experience chronic circadian misalignment and sleep deprivation. Numerous studies support that sleep and circadian rhythm disruptions are risk factors for increased reward seeking behavior, suggesting that adolescents with poor sleep quality and misaligned rhythms may be more susceptible to uncontrolled reward seeking. Thus, we sought to determine the effects of circadian disruption on reward-related behavior in adolescent rats.

Methods: The circadian rhythms and sleep patterns of adolescent male Wistar rats were monitored in non-invasive Piezo Sleep boxes (Signal Solutions LLC) from age P25-P35 in constant dark to determine their sleep/circadian phenotype. Rats were subsequently tested for operant self-administration of sucrose pellets during their active phase from age P39-P56 to determine if their motivation for reward was associated with their sleep/circadian phenotype. On the final two days, rats responded on a random ratio (RR3) schedule during their inactive phase to determine if there were associations between reward-related behavior and sleep/circadian phenotype during an acute disruption of sleep and circadian rhythms.

Results: The change in performing operant sucrose self-administration during their active phase relative to their inactive phase produced two distinct phenotypes. Resilient rats (n=4) decreased ~20% in their performance, whereas susceptible rats (n=4) had less than a 10% decrease in performance during the inactive phase. These two groups differed in their responding for sucrose reward (p = 0.037). The susceptible group had more fragmented sleep than the resilient group (p = 0.021) and showed a trend for having a shorter circadian activity period (p = 0.058).

Conclusion: Adolescent rats that had more fragmented sleep showed increased reward-related behavior during their inactive phase. This suggests that poor sleep quality might increase reward-seeking behavior.

Significance: Developing a model system to understand the mechanisms underlying the associations between sleep and circadian phenotypes and reward-related behavior could allow us to develop novel treatments to reduce substance use disorders in adolescents.

Funding Source: Hillman Foundation seed grant from UPBI (PIs: Colleen McClung, PhD; Mary Torregrossa, PhD; Ryan Logan, PhD)
Exploring reward system responsivity in the nucleus accumbens across chronicity of binge eating in female rats

Author(s): Hildebrandt BA\textsuperscript{1,2}, Sinclair, EB\textsuperscript{1}, Sisk CL\textsuperscript{3}, and Klump KL\textsuperscript{1}
Affiliation(s): \textsuperscript{1}Department of Psychiatry, University of Pittsburgh School of Medicine; \textsuperscript{2}Department of Psychology, Michigan State University; and \textsuperscript{3}Department of Neuroscience, Michigan State University

Study: Binge eating (BE) is characterized by an overconsumption of palatable food, a natural reinforcer, pointing to an increased interest in the role of reward-based processes in BE. To date, results have been mixed across studies examining reward system responsivity and BE, showing both increased and decreased activation in the nucleus accumbens and other brain structures within reward pathways. One contributing factor to differences in results might be chronicity of BE (i.e., early vs. chronic), where the reward system is initially hyper-responsive to BE, but over time, the system becomes hypo-responsive to BE. Despite chronicity of illness being a plausible mechanism to explain differences in reward-related responsivity, no studies have examined duration of BE as a potential factor contributing to differences in responsivity over time.

Methods: 120 Sprague-Dawley female rats were exposed to intermittent, palatable food feeding tests. Binge eating prone (BEP) and binge eating resistant (BER) rats were identified using well-established methods, and randomly assigned to the early stage (i.e., six feeding tests) or chronic stage (i.e., 24 feeding tests) group. Fos expression, a measure of neural activation, was quantified in the nucleus accumbens and compared across the BER and BEP groups.

Results: BEP rats had higher levels of c-Fos expression in the nucleus accumbens core and shell at the early stage of BE compared to BER rats, suggesting an initial hyper-responsivity to palatable food in BEP rats. At the chronic stage, BEP rats showed lower levels of c-Fos in the nucleus accumbens core and shell, suggesting a pattern of downregulation in responsivity to palatable food over time.

Conclusion: Duration of BE leads to differences in neural function of the reward system. This change was specific to BEP rats, suggesting that the downregulation is in response to long-term, consistent, high-levels of palatable food intake.

Significance: Results from the current study suggest a need to control of stage of BE in future studies by including duration of illness as a covariate or examining different stages of BE as independent groups.

Funding Source(s): Foundation Funding: Global Foundation for Eating Disorders (PIs: Britny Hildebrandt, MA; Kelly Klump, PhD; Cheryl Sisk, PhD)
Presenter: Gil Hoftman, MD, PhD  
Education: University of Pittsburgh Medical Center, WPIC  
Current Position: Resident  
Principal Area of Research Interest: Schizophrenia, Cognition, Neurodevelopment  
Current Research Support: Department of Psychiatry  
Mentor(s): David Lewis, MD

Altered gradients of glutamate and GABA transcripts in the cortical visuospatial working memory network in schizophrenia

Author(s): Hoftman GD\textsuperscript{1}, Dienel SJ\textsuperscript{1}, Bazmi HH\textsuperscript{1}, Zhang Y\textsuperscript{2}, Chen K\textsuperscript{2}, and Lewis DA\textsuperscript{1}  
Affiliation(s): \textsuperscript{1}Department of Psychiatry, University of Pittsburgh School of Medicine and \textsuperscript{2}Department of Statistics, University of Pittsburgh

Study: Visuospatial working memory (vsWM), which is impaired in schizophrenia, requires information transfer across multiple nodes in the cerebral cortex, including visual, posterior parietal, and dorsolateral prefrontal regions. Information is conveyed across these regions via the excitatory projections of glutamatergic pyramidal neurons located in layer 3, whose activity is modulated by local inhibitory GABAergic neurons. Key properties of these neurons differ across these cortical regions. Consequently, in schizophrenia, alterations in the expression of gene products regulating these properties could disrupt vsWM function in different ways, depending upon the region(s) affected.

Methods: Here, we quantified the expression of markers of glutamate and GABA neurotransmission selectively in layer 3 of four cortical regions in the vsWM network from 20 matched pairs of schizophrenia and unaffected comparison subjects. Laser microdissection was used to dissect layer 3 from V1, V2, PPC, and PFC from 20 matched pairs of schizophrenia and control subjects.

Results: In comparison subjects, levels of glutamate transcripts tended to increase, whereas GABA transcript levels tended to decrease, from caudal-to-rostral across cortical regions of the vsWM network. Composite measures across all transcripts revealed a significant effect of region, with the glutamate measure lowest in primary visual cortex (V1) and highest in the dorsolateral prefrontal cortex (DLPFC), whereas the GABA measure showed the opposite pattern. In schizophrenia subjects, the expression levels of many of these transcripts were altered. However, this disease effect differed across regions such that the caudal-to-rostral increase in the glutamate measure was blunted and the caudal-to-rostral decline in the GABA measure was enhanced in the illness.

Conclusions: Differential alterations in layer 3 glutamate and GABA neurotransmission across cortical regions may contribute to vsWM deficits in schizophrenia.

Significance: Studying a distributed cortical circuit thought to underlie cognitive dysfunction in schizophrenia is critical for dissecting disease pathology with greater precision. In this study, we have uncovered previously unknown relationships in transcript gradients that require further study into their potential functional impact on cognitive impairments in schizophrenia.

Funding Source(s): Department of Psychiatry, University of Pittsburgh School of Medicine and the Conte Center for Translational Mental Health Research 1P50MH103204 (PI: David Lewis, MD)
Congruent parental report of child symptom severity: A study of fathers with a history of childhood ADHD and their preschool aged children

Author(s): Hunter D, Joseph H, Pedersen S, Perlman S, Pelham W, and Molina BSG

Affiliation(s): 1 Department of Psychiatry, University of Pittsburgh School of Medicine and 2 Department of Psychology, Florida International University

Study: Research on children with ADHD has primarily utilized maternal report of the child’s behavior. Given higher rates of ADHD in males, fathers are more likely than mothers to have a diagnosis of ADHD. Paternal history of ADHD could influence reporting of child behavior. The current study examined differences in mother and father report of child behaviors as a function of paternal ADHD status. We hypothesized that differences in parent report of child symptom severity would be more frequent for internalizing than externalizing behaviors. Paternal ADHD would be associated with greater disagreement in the maternal and paternal reported symptoms.

Methods: Male participants (N=21, ADHD=13, No ADHD=8) from the Pittsburgh ADHD Longitudinal Study (PALS) with children between the ages of 3-7 (M=5, SD=0.83) along with the child’s biological mother completed the Child Behavior Checklist (CBCL).

Results: Mean differences in parent reported symptoms were significant for internalizing problems (M_mother=44.00, SD=9.97; M_father=49.19, SD=9.52; t = 2.258; p = 0.035) but not externalizing problems (M_mother=46.48, SD=13.75; M_father=51.24, SD=9.76; t = 1.957; p = 0.064). There was greater than one standard deviation difference in mother and father reported symptoms 33% of the time for internalizing and 38% of the time for externalizing problems. The percent incongruently reported symptoms were greater for mother-father pairs when the father had ADHD. The differences between mother and father report, based on paternal ADHD status, were more pronounced for child internalizing problems (46% ADHD and 14% no ADHD) than externalizing problems (46% ADHD and 33% no ADHD).

Conclusion: Even in a small pilot study, significant differences were found between maternal and paternal report of child symptom severity for internalizing problems and a trend towards significance for externalizing problems. Paternal ADHD may contribute to an increased report of symptom severity for internalizing problems.

Significance: For clinical and research purposes additional work with observational data and third informant (e.g. teacher) is needed to clarify these differences between maternal and paternal report. How paternal history of ADHD may impact reporting of child behaviors is unknown, the increased differences in reporting could influence treatment outcomes.

Funding Source(s): AACAP Pilot Award for Attention Disorders (PI: Heather Joseph, DO) and AA011873 (PI: Brooke Molina, PhD)
Simultaneous in vivo calcium imaging and cortico-striatal hyperstimulation generated perseverative grooming in awake behaving mice

Author(s): Hyde J1, LaPalombara Z2, and Ahmari S1

Affiliation(s): 1Department of Psychiatry, University of Pittsburgh School of Medicine

Study: Obsessive compulsive disorder (OCD) is characterized by intrusive obsessive thoughts and abnormal repetitive behaviors. This is accompanied by abnormalities in corticostriatal structure and function, as demonstrated in human imaging studies. In mice, work from our lab has shown that hyperstimulation of orbitofrontal cortex (OFC) projections to the ventromedial striatum (VMS) generates perseverative grooming behavior. Building on these results and the recent development of miniaturized, head-mounted microscopes capable of simultaneous optogenetic stimulation and calcium imaging, we can now directly visualize VMS activity during OFC-VMS hyperstimulation in our mouse model. With this advanced dual optogenetic stimulation and calcium imaging technology, we hypothesized that OFC-VMS hyperstimulation would produce elevated VMS firing rates as measured by in vivo calcium imaging.

Methods: 10 male EMX-cre mice were used in this study (CB57BL/6J background). Mice were injected with AAV8.DiO.csCrimson or AAV5.DiO.mCherry in the OFC and the genetically encoded calcium indicator AAV9.syn.GCaMP6M in the VMS, and implanted with a microendoscope (6.1mm x 0.5mm GRIN lens) in VMS. 4 weeks after virus injections the mice were fitted with microscope baseplates. Mice were habituated to experimental conditions for 7 days. An Inscopix nVoke microscope was used to simultaneously stimulate OFC-VMS projections and record calcium activity in striatal medium spiny neurons for 5 days. Calcium transient data was extracted from processed calcium videos to analyze event frequency and time-locked activity. ANOVA testing was used to compare groups.

Results: Optogenetic stimulation increased perseverative grooming over the 5-day stimulation period. Calcium imaging results show the average calcium events per minute is statistically unaffected by stimulation prior to, during, or after stimulation. However, the data suggest a trend towards increased calcium event rates with each day of stimulation.

Conclusion: We demonstrated that simultaneous optogenetic stimulation and calcium imaging is capable of generating perseverative grooming behavior in mice. While stimulation did not directly change the population firing rates, a better-powered experiment may show that event rates increase with stimulation.

Significance: This project demonstrates the feasibility of using in vivo calcium imaging to simultaneously visualize neural activity and optogenetically induce perseverative grooming.

Funding Source(s): MQ Fellows, NIMH R01MH104255, NIMH 5F32MH108226-02
Presenter: Karen P. Jakubowski, MS
Education: University of Pittsburgh
Current Position: Doctoral student in Clinical and Biological-Health Psychology
Principal Area of Research Interest: Early life adversity, sleep, and cardiovascular disease
Current Research Support: Not applicable
Mentor(s): Karen A. Matthews, PhD

Associations between cumulative adverse childhood experiences and cardiometabolic disease and mortality: A systematic review and meta-analysis
Author(s): Jakubowski KP\textsuperscript{1}, Cundiff JM\textsuperscript{2}, and Matthews KA\textsuperscript{1,3}
Affiliation(s): \textsuperscript{1}Department of Psychology, University of Pittsburgh; \textsuperscript{2}Department of Psychological Sciences, Texas Tech University; \textsuperscript{3}Department of Psychiatry, University of Pittsburgh School of Medicine

Study: Evidence suggests that adverse childhood experiences may negatively influence cardiovascular (CV)-related disease and mortality. Because many studies are post-hoc analyses of large data sets, there is notable heterogeneity in terms of the type of items in cumulative adversity indices, sample sizes and demographics, and covariates. The present review used quantitative meta-analysis to examine the association and potential moderators.

Methods: The search returned 2,342 articles. Included studies had a measure of cumulative adversity (an index that included at least 2 adverse childhood experiences from age 0 to 18) and at least one CV-related outcome (CV clinical events: hypertension, stroke, coronary heart disease; CV clinical risk scores: Framingham risk; and metabolic outcomes: diabetes, metabolic syndrome), or mortality measured at age 19 or older in a non-psychiatric population. Effect sizes were reported as regression weights, odds ratios (OR), or hazard ratios (HR), and were drawn from fully adjusted models. Given differences in the interpretation of OR versus HR, effects were pooled separately. Overall, 11 HR studies (19 effects) based on 212,246 participants and 23 OR studies (45 effects) based on 160,650 participants were included.

Results: Cumulative adversity was associated with risk for CV-related outcomes (OR [95%CI]=1.30 [1.22-1.38]) and time to event for CV-related outcomes and mortality (HR=1.39 [1.21-1.60]). Combined risk for CV clinical events, CV risk scores, and mortality was elevated relative to metabolic outcomes (OR=1.43 [1.31-1.56] vs. OR=1.18 [1.08-1.29]); this pattern was not seen in HR studies. Results varied somewhat by analytic strategy, number of covariates, and whether childhood SES was included in the cumulative adversity index.

Conclusion: There is a small but significant estimated effect of cumulative childhood adversity on adult cardiometabolic disease and mortality. The overall effect is similar to the effect of other psychosocial risk factors on cardiometabolic outcomes and death (e.g., hostility, social isolation).

Significance: The present findings highlight that the extant literature lacks a consistent operational and conceptual definition of adversity, particularly with regard to whether or how to include childhood SES. Thus, it is time for a conceptual perspective on the types and timing of events that have maximal impact on adult cardiometabolic disease and mortality.

Funding Source(s): HL07560 (PI: Karen Matthews, PhD)
Presenter: Gabrielle N. Kaplan, BS
Education: North Carolina State University
Current Position: CNUP Graduate Student
Principal Area of Research Interest: Bipolar disorder, circadian rhythms
Current Research Support: Not applicable
Mentor(s): Colleen McClung, PhD and Ryan Logan, PhD

Mitochondrial complex I alterations in a mouse model of bipolar mania
Author(s): Kaplan GN1, Khattar NK2, Kretz ES2, Friedlander RM2, Logan RW1, and McClung CA1
Affiliation(s): 1Department of Psychiatry, University of Pittsburgh School of Medicine and 2Department of Neurological Surgery, University of Pittsburgh School of Medicine

Study: A confluence of evidence points towards an underlying dysfunction of mitochondrial complex I in bipolar disorder (BD) which may lead to an increase in oxidative stress and inflammation. The Clock mutant mice (ClockΔ19), which has been shown to display a behavioral repertoire similar to bipolar mania, serves as a model in which we can investigate both the circadian control of complex I and potential neuronal mitochondrial dysfunction in the prefrontal cortex, a critical structure known to regulate mood and decision making in the brain.

Methods: Live mitochondria from WT and ClockΔ19 mouse PFC brain tissue were isolated using a Percoll gradient to obtain non-synaptosomal and synaptosomal fractions. Mitochondria then underwent high-resolution respirometry measures to obtain rate of oxygen consumption. RCR (respiratory control rate) was calculated by dividing State 3 (ADP-stimulated) and State 2 (substrate-stimulated) oxygen consumption rates. Frontal cortex mitochondria from WT and ClockΔ19 mice were also used for protein assays to compare mitochondrial subunit expression across oxidative phosphorylation (OXPHOS) complexes. Mitochondrial protein lysates were run on a Western blot and blotted using an antibody cocktail of against critical subunits of each of the 5 OXPHOS complexes (Abcam ab110413).

Results: Human postmortem studies conducted in the PFC of patients with BD have shown a decrease in mitochondrial complex I function and expression. Our data shows a similar decrease in complex I-driven respiratory rate as determined by the addition of glutamate-malate and ADP to synaptosomal mitochondria from the PFC of ClockΔ19 mice. Additionally, we demonstrate alterations to protein levels specific to complex I and its downstream targets.

Conclusion: These results show a decrease in mitochondrial expression and respiratory function that can be attributed to alterations in complex I in the presence of a dominant negative CLOCK protein. As the “entry enzyme” of cellular respiration, complex I integrity has significant implications for ATP production, management of reactive oxygen species (ROS) levels, and maintenance of the NAD-NADH ratio.

Significance: Through these preliminary studies, we demonstrate that the ClockΔ19 mouse, as a model for bipolar mania, recapitulates the mitochondrial alterations found in human postmortem tissue and will serve as a model for future studies investigating the direct links between circadian clock machinery, cellular metabolism, and mitochondrial respiration.

Funding Source(s): NIH R21 DA041872 and NIH R01 MH106460
**Functional activation during emotion processing in late-life depression: Early markers of treatment response**

_Author(s):_ Karim HT¹, Andreescu C², Karp J², Reynolds C III², and Aizenstein HJ¹, ²

_Affiliation(s):_ ¹Departments of Bioengineering and ²Psychiatry, University of Pittsburgh

**Study:** Treatment of major depression (MDD) often requires multiple trials of medications before an effective therapy can be identified, this poses a serious issue as it is associated with an increased risk of suicide and can contribute to worsening co-morbidities. In late-life depression (LLD), as the time required to respond to a single medication is on average longer (6 weeks compared to 4) – these risks may be worsened. Several studies have shown changes in functional activation/connectivity following acute doses as measured by functional magnetic resonance imaging (fMRI). In this study, we aimed to investigate early changes in functional brain activation (during emotion reactivity) that occur during a treatment trial.

_Methods:_ LLD patients (N=33, 23 F, greater than 60 years old) were enrolled into a 12-week Venlafaxine treatment trial where an fMRI scan was collected at baseline, 12 hours following a placebo, 12 hours following their first dose, a week after beginning treatment, and at the end of the trial. Participants performed an emotion reactivity task (faces/shapes) and matched two faces to a cue (either angry/fearful) and a control (matching shapes). Montgomery-Asberg Depression Rating Scale (MADRS) measured depression severity, and remitters had a score less than 10 for at least two weeks. After spatial preprocessing and modeling of activation – we investigated whether there were significant group by time effects. Multiple comparisons correction was conducted using statistical non-parametric mapping (cluster forming threshold of 0.001), which controlled for the family-wise error (p<0.05).

**Results:** We found a significant group by time interaction in the left insula, superior temporal gyrus, thalamus, supramarginal gyrus, inferior parietal gyrus, and the right insula that did not occur following placebo. Remitters had relatively lower activation that increased following treatment (reversed in non-remitters). We found that the initial dose (placebo vs. acute period) showed a significant interaction in the left parahippocampus. Similarly, remitters showed a significant increase in activation while non-remitters showed a significant decrease.

**Conclusion:** The changes identified across the 12-week treatment interval may reflect the gradual increased activity in implicit emotion regulation in the remitters and continued and progressive disruption in the non-remitters.

**Significance:** This study provides insight into early treatment markers in LLD.

_Funding Source(s):_ NIMH R01 MH076079, 5R01 AG033575, MH 086686, P30 MH90333, 5R01, MH083660, and Charles F. Reynolds III and Ellen Gay Detlefsen Chair in Geriatric Psychiatry
Peer influences on alcohol use among young adults with ADHD histories

Author(s): Kennedy TM¹, Walther CAP², Pedersen SL¹, Mckone KMP¹, Gnagy EM³, Pelham WE³, and Molina BSG¹,⁴

Affiliation(s): ¹Department of Psychiatry, University of Pittsburgh School of Medicine; ²Department of Psychology, University of Houston-Clear Lake; ³Department of Psychology, Florida International University; and ⁴Department of Psychology, University of Pittsburgh

Study: Perceived peer substance use strongly predicts adolescents’ alcohol use – especially among adolescents with a history of ADHD (Marshal et al., 2003; Belendiuk et al., 2016). However, the extent to which these associations continue into adulthood among individuals with childhood ADHD is unknown. The present study examined the relation between peer substance use and adults’ own alcohol use longitudinally across a broad age range (early adulthood to age 29) and compared these associations for those with versus without ADHD histories. We hypothesized stronger relations for adults with ADHD histories.

Methods: As part of the Pittsburgh ADHD Longitudinal Study, 443 individuals (248 ADHD, 195 nonADHD; 88.9% male; 81.9% White) completed measures of perceived substance use by their friends (i.e., alcohol, marijuana, and other drugs), their own alcohol use (past 12-month frequencies of drinking alcohol, binge drinking, and drunkenness), and demographic information (e.g., gender, SES, marital status, college enrollment) approximately biannually at ages 18-29.

Results: Controlling for baseline demographics and age 21 alcohol use, hierarchical OLS regressions revealed that peer substance use at age 21 was related to past-year frequency of drinking alcohol ($β = .16, p < .01$), binge drinking ($β = .30, p < .001$), and drunkenness ($β = .34, p < .001$) at age 22. Moreover, peer use at age 21 continued to relate positively to frequency of binge drinking ($β = .20, p < .01$) and drunkenness ($β = .29, p < .001$) at age 29. There were no significant moderating effects of ADHD history at either age. A latent growth curve model of peer substance use from age 18-29 suggested a piecewise linear pattern for both ADHD and nonADHD groups, increasing to age 21 then remaining stable to age 29 ($SBχ^2 = 108.75, p = .002; CFI = .946; RMSEA = .031; SRMR = .097$).

Conclusion: Peer substance use is a long-lasting factor in young adults’ alcohol use, both for those with and without ADHD. Correlated growth between perceived peer use and one’s own alcohol use as a function of ADHD history will also be examined; declines in peer drinking after age 21 may differentially relate to alcohol use by older individuals with versus without ADHD.

Significance: Peer contexts remain influential in alcohol use through young adulthood. Interventions to reduce high-risk drinking should target interactions with substance-using peers.

Funding Source(s): NIAAA grant R37 AA011873 (PI: Brooke S. G. Molina, PhD)
OPTIMUM: Optimizing outcomes of treatment-resistant depression in older adults

Author(s): Kincman JM, Stack J, Chickering S; Emanuel J, Anderson A, Ingram J, Gaston Thiry L, Weber E, Whyte EM, Lenze EJ; Gebara MA, Reynolds III CF, Rollman BL, and Karp JF

Affiliation(s): 1Western Psychiatric Institute and Clinic of UPMC; Departments of 2General Internal Medicine and 3Psychiatry, University of Pittsburgh School of Medicine; and 4Department of Psychiatry, Washington University School of Medicine

Study: Treatment-resistant depression (TRD) is a major health problem for the growing population of older adults. We are launching a patient-centered, multi-site, pragmatic trial to compare the risks and benefits of antidepressant treatment options in older adults with TRD. Stakeholder input will help guide all aspects of the project from design to dissemination, with qualitative interviews giving added voice to patient and clinician viewpoints.

Methods: Acute treatment will follow a step-wise study design conducted in clinical settings. Participants will either switch to a new drug or add a drug to their existing antidepressant medications in Step 1 and Step 2 for up to 10 weeks each as clinically indicated. Participants will be followed by phone to assess symptoms, side effects, and provide medication adherence measurement and counseling. Primary care and mental health clinical partners will administer treatments with decision support from the study team. Participants will be followed for 12 months after acute treatment to monitor long-term safety and effectiveness. We will conduct semi-structured (qualitative) telephone interviews of patients and of clinicians to maintain a focus on lived experience of depression and antidepressant treatment.

Results: Input from focus groups and surveys with older adult patients and treatment providers helped shape our study design. Specifically, well-being and long-term symptom remission are the outcomes that matter to patients. Additional evidence on long-term treatment safety in older adults was important to both patients and providers. Patients prefer to receive treatment from their own care providers, with support and guidance from the researchers, preferably by phone.

Conclusion: These findings shaped our study design, particularly the use of decision support as a co-intervention, akin to collaborative care. The goal of this decision support is safe and effective use of the antidepressants in this elderly population.

Significance: This study, when completed, will be the largest and most definitive study to date of TRD in older adults. We are actively seeking input and involvement from community primary care providers and patients or caregivers affected by TRD.

Funding Source(s): PCORI Award (TRD-1511-33321)
Mothers' loss of control over eating during pregnancy in relation to their infants' appetitive traits

Author(s): Kolko RP¹, Salk RH¹, Sweeny GM², Marcus MD¹, and Levine MD¹

Affiliation(s): ¹Department of Psychiatry, University of Pittsburgh School of Medicine and ²Western Psychiatric Institute and Clinic of UPMC

Study: Infant appetitive traits confer risk for childhood obesity, although little is known about early precursors of these traits. Mothers’ eating behavior during pregnancy may predict their infants’ appetitive traits. Thus, we characterized mothers’ loss of control eating (LOC; a behavioral phenotype associated with obesity) during early pregnancy, and their infants’ appetitive traits at 6 months.

Methods: Women with overweight/obesity (N = 86; pre-pregnancy BMI≥25, 12-20 weeks gestation) completed interviews to assess LOC in early pregnancy. Women subsequently reported on their infants’ appetitive traits before solid food introduction using the Baby Eating Behaviour Questionnaire (food responsiveness, enjoyment of food, satiety responsiveness, slowness in eating, and general appetite). We examined associations between maternal LOC during pregnancy and infant appetitive traits in bivariate analyses as well as regression models that accounted for relevant covariates, including maternal and infant demographic factors.

Results: Maternal LOC was associated with higher infant food responsiveness (t(84) = -2.36, p = .021, d = .58), even after adjusting for covariates (β = .25, p = .039). The other BEBQ subscales were not related to LOC (p < .130).

Conclusion: Mothers’ LOC in early pregnancy was associated with an obesity-related appetitive trait in their infants. These findings indicate a prospective link between maternal eating behavior during pregnancy and infant eating.

Significance: This is the first study to examine early precursors of infant appetitive traits and demonstrate that mothers’ eating behavior during pregnancy predicts their infants’ appetitive behavior. Although additional studies using direct observations of infant behavior are needed, LOC in pregnancy may be a marker for obesity risk and obesity-related appetite patterns in infants.

Funding Source(s): NICHD R01 HD068802 (PI: Michele Levine, PhD) and NIMH T32 MH018269 (PI: Tina Goldstein, PhD)
Fingolimod treatment alters phospho-peptides with roles in dendritic morphology

Author(s): Krivinko JM\textsuperscript{1}, Erickson SL\textsuperscript{1}, MacDonald ML\textsuperscript{1}, Garver ME\textsuperscript{1}, and Sweet RA\textsuperscript{1,2,3}

Affiliation(s): Departments of \textsuperscript{1}Psychiatry and \textsuperscript{2}Neurology, University of Pittsburgh School of Medicine; and \textsuperscript{3}Mental Illness Research, Education, and Clinical Center, VA Pittsburgh Healthcare System

Study: Alzheimer Disease (AD) is characterized by cognitive deterioration, but the presence of additional neuropsychiatric disturbances such as psychosis in AD (AD+P) denotes a more severe AD phenotype with greater functional impairment and more rapid cognitive decline compared to when psychosis is absent (AD-P). Despite this observation, there are currently no licensed pharmacotherapies which target the underlying neurobiology of AD+P. Our lab has demonstrated that AD+P and a related mouse model are characterized by global deficits in synaptic protein levels compared to AD-P, with more specific deficits in postsynaptic density-enriched proteins (Krivinko et al, in preparation). In vitro work from our lab and others' has shown that fingolimod, an FDA-approved Multiple Sclerosis treatment, alters phosphorylation of several dendritic spine modifiers, including p21-activated kinases (PAKs). However, it is currently unknown whether fingolimod-induced alterations in the phospho-proteome correlate with aberrant behaviors in a murine model of amyloid-beta overexpression.

Methods: Fingolimod (5mg/kg, i.p.) or normal saline was administered to 3-month old C57Bl/6J mice (n=12) for 7 days after which mice were sacrificed, and cerebral cortex extracted for liquid chromatography/quantitative mass spectrometry (MS) with titanium dioxide phospho-enrichment. This drug treatment regimen was also administered to APP\textsubscript{SWE}/PSEN1dE9 (n=20) and WT (n=20) mice, during which performance in an open field and habituation/prepulse inhibition of the acoustic startle response was tested.

Results: 640 phospho-peptides were detected by MS. The top 10% most altered proteins by fingolimod treatment was significantly enriched for the gene ontology term “microtubule cytoskeletal organization” relative to a background of 360 unique proteins identified (p=.02). PAK3 was among the top 10 proteins altered by fingolimod treatment. Fingolimod’s effects on aberrant behaviors in APP\textsubscript{SWE}/PSEN1dE9 mice will be presented.

Conclusion: Fingolimod appears to alter levels of phospho-proteins related to dendritic spine morphology in cortical homogenates from WT mice.

Significance: Fingolimod’s ability to alter proteins involved in synaptic morphology in WT mice highlights the need to investigate such an effect in APP\textsubscript{SWE}/PSEN1dE9 mice, as these results may aid to inform the development of novel pharmacotherapies for AD+P.

Funding Source(s): Veterans Health Administration, BX000452
Measuring expression of candidate genes for Mediating reduced dendritic spine density in schizophrenia

Author(s): Kuflewski J\textsuperscript{1,2}, Sweet RA\textsuperscript{2}, and McKinney BC\textsuperscript{2}

Affiliation(s): \textsuperscript{1}Carnegie Mellon University and \textsuperscript{2}Department of Psychiatry, University of Pittsburgh School of Medicine

Study: Reduced dendritic spine density (DSD) is consistently observed in the superior temporal gyrus (STG) of subjects with schizophrenia (SZ), but the molecular mechanisms that give rise to reduced DSD are poorly understood. DNA methylation (DNAm), the addition of a methyl group to a cytosine nucleotide, is a regulator of gene expression and alterations in DNAm are hypothesized to contribute to reduced DSD in SZ by altering expression of a subset of genes. Recently, we identified 2 candidate genes for mediating reduced DSD in SZ through a DNAm-dependent expression change: brain-specific angiogenesis inhibitor 1-associated protein 2 (BAIAP2) and discs large, drosophila, homolog of, 1 (DLG1). Here, we validate a quantitative polymerase chain reaction (qPCR) approach that will be used to measure BAIAP2 and DLG1 gene expression in the STG of SZ and control subjects.

Methods: Total RNA was (1) isolated from STG gray matter of 22 SZ subjects and 22 control subjects, (2) assigned an integrity number (a measure of quality) using ribosomal ratios, and (3) reverse-transcribed into copy DNA (cDNA). qPCR primers for measuring BAIAP2 and DLG1 expression were designed, and their specificity and efficiency were assessed using melting curve analysis and standard curves, respectively.

Results: Isolated total RNA was of high quality and successfully reverse-transcribed. qPCR primers designed were specific and efficient for amplifying the targeted cDNA regions.

Conclusion: The qPCR primers are of sufficient specificity and efficiency to be used with high-quality cDNA generated from the SZ and control samples to test the hypothesis that BAIAP2 and DLG1 are expressed at different levels in SZ subjects compared to control subjects.

Significance: A better understanding of the molecular mechanisms that contribute to reduced DSD in SZ will provide insight into SZ neurobiology. The experiments described here are important early steps for measuring gene expression in postmortem brain by qPCR and testing hypotheses about the molecular mechanisms of reduced DSD in SZ.

Funding Source(s): CMU Summer Undergraduate Research Fellowship, NIH Grants KL2 TR001856 (BCM), K23 MH112798 (BCM), RO1 MH071533 (RAS)
Patterns of sensory rating due to the interaction of menthol status and nicotine content

**Author(s):** Kukich MJ, Karelitz JL, Kunkle N, and Perkins KA

**Affiliation(s):** 1Department of Psychiatry, University of Pittsburgh School of Medicine

**Study:** Determining if the amount of nicotine in a cigarette in conjunction with menthol preference collectively or independently affects participants’ subjective responses on a sensory questionnaire. It is predicted that when a cigarette contains a low amount of nicotine, there will be a decline in subjective ratings of sensory items. In addition, participants who smoke menthol cigarettes, versus non-menthol, will rate sensory items higher. Finally, smoking cigarettes with a higher nicotine content will affect participants’ subjective ratings of favorable items, such as “liking” and “satisfying” in the presence of menthol flavoring.

**Methods:** Dependent smokers completing discrimination training trials (4 puffs each), preferring menthol (n=42) or non-menthol (n=29) flavoring, were included. Participants included both males and females (m=30, f=41) ranging in age from 18-65 (n=71). Nicotine content (16 mg, “high” vs. 0.4 mg, “ultra low”) was manipulated within-subjects and menthol status (menthol vs. non-menthol) was compared between-subjects to measure subjective ratings (0-100 visual analog scale) on sensory items for “likeability”, “satisfaction”, “amount of nicotine”, “strength”, “harshness”, “flavor”, “smoothness”, and “similarity to own cigarette brand”.

**Results:** Results suggested that there was a significant interaction between nicotine content and menthol preference for participant ratings of “harshness” of the cigarette. Secondarily, there was a main effect of nicotine content for all subjective measures, excluding “smoothness”.

**Conclusion:** Nicotine content (high vs. ultra low) significantly affected participants’ ratings on subjective measures, excluding “smoothness”. When participants smoked a cigarette with a high amount of nicotine, sensory items were rated higher. In comparison, when a low nicotine cigarette was smoked, there was a decline in sensory ratings. With the exception of “harshness”, the presence of menthol did not have an effect on subjective ratings. Ultimately, the presence of menthol (a preference indicated by participants) had an effect on sensory ratings of “harshness” when participants were smoking a cigarette with an ultra-low nicotine content.

**Significance:** The analysis of physical subjective responses could be viewed in conjunction with sensory responses, further suggesting positive and negative effects of cigarettes, differing in flavor and nicotine content. Overall, the outcomes of the present study could contribute to the determination of the amount of nicotine content and flavoring needed to produce favorable effects in cigarettes.

**Funding Source(s):** NIH Grant DA035968 (PI: Kenneth Perkins, PhD)
Greater learning-dependent change in hippocampal circuitry relates to reward learning

Author(s): Larsen B\textsuperscript{1}, Calabro F\textsuperscript{2}, Murty V\textsuperscript{2}, Foran W\textsuperscript{2}, and Luna B\textsuperscript{2}

Affiliation(s): \textsuperscript{1}Department of Psychology, University of Pittsburgh and \textsuperscript{2}Department of Psychiatry, University of Pittsburgh School of Medicine

Study: The ability to encode and incorporate contextual information is enhanced during the adolescent period and is thought to be driven by the refinement of hippocampal systems. Building on initial diffusion weighted imaging studies that suggest changes in the white matter integrity of hippocampal systems after short-term training, we investigate white matter changes after a rewarded spatial learning task. We assess changes using Magnetization Transfer Imaging, which is sensitive to myelin content. Specifically, we investigate short-term learning dependent changes in the fornix, a white matter pathway involved in hippocampal-cortical spatial learning processes, in a developmental sample of young adults.

Methods: 81 adolescents and young adults aged 18-30y ($M = 23.4$, $SD = 3.6$) completed a rewarded spatial learning task in which they explored a 3x3 grid map and learned underlying reward probabilities. Before and after the spatial learning task we acquired magnetization transfer imaging data and derived the magnetization transfer ratio (MTR) as an indicator of myelin content. Difference between post-task and pre-task MTR in the fornix (identified using the JHU white matter atlas) was used as an indicator of task-induced plasticity. A total of 36 participants passed visual inspection for artifacts.

Results: We found that MTR in the fornix increased following the spatial learning task ($t = 6.33$, $p < .001$) and that the magnitude of this change changes with age following a quadratic function ($p = .005$), peaking prior to age 25. Further, the change in MTR in the fornix from pre-task to post-task was positively associated with the degree to which participants learned the relative spatial reward probabilities during the spatial learning task ($p = .004$).

Conclusion: This study demonstrates that MTR is sensitive to short-term task driven changes, potentially reflecting myelination. Specifically, we show that a rewarded spatial learning task induces measurable change in a white matter pathway that is central to spatial learning circuitry and that the degree of this change is associated with successful spatial learning. Further, we provide evidence for heightened plasticity during adolescence that decreases into adulthood.

Significance: Together, these findings provide compelling evidence for experience-dependent plasticity facilitating associative memory encoding that may underlie developmental improvements in spatial learning that persist until young adulthood.

Funding Source(s): NIMH grant MH067942 (PI: Beatriz Luna, PhD)
**Presenter:** Jessica C. Levenson, PhD  
**Education:** University of Pittsburgh  
**Current Position:** Research Instructor  
**Principal Area of Research Interest:** Development and treatment of interventions for sleep disturbance; sleep and psychopathology  
**Current Research Support:** American Sleep Medicine Foundation Focused Projects Award  
**Mentor(s):** Daniel Buysse, MD; Tina Goldstein, PhD; and Elizabeth Miller, MD, PhD

**Longitudinal sleep phenotypes among offspring of bipolar parents and community controls**

**Author(s):** Levenson JC\(^1\), Soehner A\(^1\), Rooks B\(^1\), Goldstein TR\(^1\), Diler R\(^1\), Merranko J\(^1\), Axelson D\(^2\), Goldstein BI\(^3\), Brent DA\(^1\), Hafeman D\(^1\), Hickey MB\(^1\), Monk K\(^1\), Sakolsky D\(^1\), Kupfer DJ\(^1\), and Birmaher B\(^1\)  
**Affiliation(s):**  
\(^1\)Department of Psychiatry, University of Pittsburgh School of Medicine;  
\(^2\)Nationwide Children’s Hospital Research Institute and The Ohio State University College of Medicine; and  
\(^3\)Department of Psychiatry, Sunnybrook Health Sciences Centre

**Study:** Sleep disturbances are a prominent feature of bipolar disorder (BP). However, it remains unclear how sleep phenotypes may evolve among at-risk youth, and their relevance to BP onset.

**Methods:** Pittsburgh Bipolar Offspring Study (BIOS) offspring (ages 10-18) and their parents completed assessments approximately every two years pertaining to current psychopathology and offspring sleep habits. A latent transition analysis (LTA) identified latent sleep groups within offspring based on their ratings of six sleep domains using the School Sleep Habits Survey. Demographic and clinical characteristics were compared between sleep groups. Logistic regression tested links between sleep group and BP onset at the subsequent assessment.

**Results:** The LTA model identified latent groups of good, poor, and variable sleepers. We observed an overall trend of good sleep becoming variable, and then poor, as youth age. Offspring in the poor sleep group were more likely to have psychopathology. Adjusting for age and depression, poor sleepers had nearly twice the odds of developing BP relative to good (OR=1.99, CI=0.45-8.91) or variable (OR=2.03, CI=0.72-5.72) sleepers. Limitations include the use of proximal sleep phenotypes to predict BP onset, and a self-report measure of sleep.

**Conclusions:** We found three non-overlapping sleep phenotype groups in a large sample of offspring of bipolar probands and offspring of demographically-matched community control parents. Clinicians should consider that youth will likely experience variable and/or poor sleep as they age, and that at-risk youth with poor sleep may be at increased risk of developing MDD and BP at their next assessment.

**Significance:** Sleep disturbances are a prominent and complex feature of BP, and this study begins to examine the longitudinal sleep phenotypes among youth at-risk for the disorder.

**Funding Source(s):** This study was supported by MH060952 (PI: Boris Birmaher, MD) and HL082610 (T32, PI: Daniel Buysse, MD).
Study: Functional imaging has strongly implicated cortico-striatal dysfunction in the pathophysiology of obsessive compulsive disorder (OCD). However, the mechanisms by which this dysfunction gives rise to OCD symptoms are unclear, with hyperactivity typically observed at baseline, and hypoactivity typically observed during cognitive testing. Studies in preclinical models provide a unique opportunity to investigate the precise mechanisms underlying these observations.

Methods: SAPAP3 knockout mice (KOs), a leading transgenic OCD model, were tested in an operant reversal learning paradigm to assess cognitive flexibility. Cortico-striatal activation during reversal learning was assessed via quantitative cFos expression, including cross-region analysis to infer network activity and comparison to reversal behavioral performance.

Results: SAPAP3-KOs were significantly impaired in reversal learning (p<0.001; n=22 controls, 29 KOs), including 40% failing to acquire a reversed contingency. Reversal learning-related cFos expression revealed correlations between the medial prefrontal cortex (mPFC) and the nucleus accumbens (NAc) exclusively in SAPAP3-KOs, suggesting hyperconnectivity in this circuit. This circuit also profoundly influenced reversal performance in SAPAP3 KOs; whereas increased cFos in mPFC/NAc was associated with more rapid reversal in control mice, higher cFos in these regions was associated with increased levels of perseverative cognition in KOs.

Conclusion: Our studies implicate aberrant neural activity in the mPFC-NAc circuit in disruption of cognitive flexibility in OCD. This circuit is critical in the regulation of reward- and affective-related behaviors, and future studies using in vivo calcium imaging in the SAPAP3 KOs will compare the role of this circuit in disruption of cognitive flexibility and other OCD-relevant behaviors.

Significance: Our results suggest that the use of OCD-relevant cognitive paradigms will be critical in future studies seeking to address cortico-striatal circuit dysfunction in OCD-relevant mouse models.

Funding Source(s): NIMH grant RO1 MH104255 (PI: Susanne Ahmari MD, PhD)
Anterior cingulate theta band oscillations support adolescent maturation of cognitive flexibility

Author(s): Marek S¹, Montez DF², Tervo-Clemmens B³, Foran W¹, Larsen B³, Calabro F²,⁴, and Luna B¹,²,³
Affiliation(s): ¹Center for Neuroscience, ²Department of Psychiatry, ³Department of Psychology, ⁴Department of Bioengineering, University of Pittsburgh

Study: Adolescence is a unique developmental period characterized by improvements in cognitive control abilities, including cognitive flexibility. Adult electrophysiological studies in both human and non-human primates have demonstrated increased theta band (4-8 Hz) activity within the anterior cingulate cortex (ACC) several hundred milliseconds after onset of a cue signaling the need to switch rule sets (i.e., cognitive flexibility). However, the developmental of ACC theta band oscillations and their contribution to the development of cognitive flexibility have not been examined.

Methods: Data were collected from 47 subjects aged 14-31 years. Subjects completed a modified version of the multi-source interference task in an MEG scanner in which subjects had to switch between two different trial types in pseudorandom fashion. After preprocessing and deconvolution of MEG data, we contrasted switch vs. repeat trials and projected these results into source space for each subject. We next executed a time/frequency decomposition and tested for age effects. Lastly, we related brain activity during task switching to behavioral performance, once again testing for developmental effects.

Results: Across all subjects, there was significantly greater activity in switch vs. repeat trials in the ACC within 200 ms of a cue signaling the need to switch tasks. Within the ACC, we observed a significant increase in theta band power when task switching, occurring shortly after switch trial onset. Theta band power during task switching decreased as a function of age. Across all subjects, increased theta band power was related to increased switch cost, on average. Additionally, increased theta band power resulted in a significantly greater switch cost for adolescents compared to adults.

Conclusion: ACC theta band power reflects an effort signal related to the instantiation of control during cognitive flexibility. Developmental decreases in theta band power during task switching suggests adolescents require greater neural recruitment in the ACC to instantiate control required to flexibly shift rule sets.

Significance: These findings present electrophysiological evidence that mechanisms supporting cognitive control instantiation are still immature during adolescence.

Funding Source(s): NIHM grant MH067942 (PI: Beatriz Luna, PhD)
Long-term, cognitive consequences of adolescent cannabinoid self-administration in female Sprague-Dawley rats

Author(s): McCalley DM, Kirschmann EK, and Torregrossa MM
Affiliation(s): 1Department of Neuroscience, University of Pittsburgh and 2Department of Psychiatry, University of Pittsburgh School of Medicine

Study: Given the prevalence of adolescent marijuana use, it is crucial to understand the long-term effects of cannabinoids on cognitive function. Some preclinical studies have found cognitive deficits after experimenter-administration of cannabinoids. However, little work has utilized a model of addiction, self-administration; and typically only males are studied. Here, we examined the effects of self- vs. experimenter-administration of the synthetic cannabinoid receptor agonist WIN55,212-2 (WIN) during adolescence on adult cognitive function in female rats.

Methods: Adolescent female Sprague-Dawley rats self-administered (SA) WIN or vehicle solution in daily 2-hr sessions from postnatal day (p)34-p57. Separate females received intraperitoneal (IP) injections of vehicle or WIN (0.2 mg/kg or 1.2 mg/kg) from p34-p53. In both SA and IP rats, short-term spatial memory (SM) was tested 24hr after last WIN exposure (p58/p54). Working memory (WM) was assessed under drug free conditions in adulthood.

Results: Adolescent females responding for infusions of WIN showed reliable discrimination for the active lever, whereas females responding for a vehicle solution did not. All rats displayed intact short-term SM 24hr after final WIN or vehicle exposure. All rats displayed equivalent WM performance in adulthood after a prolonged period of abstinence, regardless of adolescent history.

Conclusion: Adolescent female Sprague-Dawley rats will reliably self-administer WIN. Further, adolescent exposure to WIN via SA or IP injections did not yield any cognitive deficits in short-term SM or WM performance.

Significance: Legal policy regarding marijuana use has become increasingly relaxed, but the long-term consequences of cannabinoid use in adolescent females are not well-known. These results provide crucial information regarding long-term cognitive effects of adolescent cannabinoid use in females.

Funding Source(s): K01DA071345 and Pennsylvania Department of Health (PI: Mary Torregrossa, PhD)
Measuring the context of healing: Using PROMIS in chronic pain treatment

Author(s): McFarland C, Greco CM, Yu L, Dodds N, Johnston K, Lawrence S, Glick R, Morone N, Schneider M, Slutsky J, Pilkonis PA

Affiliation(s): 1Western Psychiatric Institute and Clinic of UPMC; 2University of Pittsburgh School of Medicine; 3University of Pittsburgh School of Health and Rehabilitation Sciences

Study: Nonspecific, contextual factors are seldom measured in research trials or clinics, yet they can influence outcomes. This project evaluated the Healing Encounters and Attitudes Lists (HEAL) and PROMIS measures during pain treatment. We hypothesized that HEAL scores would predict significant variance in outcome on measures such as global impression of improvement (CGI), PROMIS Pain Intensity, and PROMIS Pain Interference with life activities. We report here on predictive validity of the HEAL in persons initiating Complementary / Alternative (CAM) or Conventional Medicine treatment for chronic pain.

Methods: In this prospective observational study, persons with chronic pain starting a CAM (n=109) or conventional medicine treatment (n=100) during the previous month completed HEAL and PROMIS measures online at baseline and 2- and 4-months later. They rated clinical global improvement (CGI) at follow-ups.

Results: The average age of participants was 47.5 years (±15), 75% were female, 23% were non-white or multiracial, and 7% were of Hispanic ethnicity. Baseline HEAL Treatment Expectancy (TEX), Positive Outlook (POS) and Attitudes towards CAM were associated with follow-up PROMIS Pain Intensity. Baseline HEAL TEX, POS, CAM, and Spirituality (SPT) were associated with PROMIS Pain Interference. All baseline HEAL scores except Spirituality were associated with CGI at 2 and 4 months (Spearman rho, all p’s <0.05). In unadjusted regression models, baseline HEAL POS and SPT accounted for 17.7% of the variance in 2-month PROMIS Pain Interference, and HEAL Patient-Provider Connection (PPC) and CAM accounted for 9.4% of the variance in CGI at 2 months. In models adjusted for baseline pain, HEAL TEX contributed 2% to 4-month Pain Intensity.

Conclusion: Several HEAL measures were associated with PROMIS Pain treatment outcomes. The HEAL and other PROMIS health status instruments allow us to document patient-centered factors that may play a role in predicting outcomes of treatment for chronic pain.

Significance: Measuring nonspecific factors in treatment such as patients’ expectations and their views about the clinical setting may provide useful information for understanding ‘placebo’ effects. In addition, clinical settings may benefit by enhancing relevant contextual factors.

Funding Source(s): PCORI ME-1402-10114 (PI: Carol M. Greco, PhD)
**Presenter:** Ashlee Brooke McKeon, PhD, CRC  
**Education:** University of Pittsburgh  
**Current Position:** Postdoctoral Scholar  
**Principal Area of Research Interest:** Military samples with posttraumatic stress disorder  
**Current Research Support:** NHLBI 4T32HL082610-10 Buysse  
**Mentor(s):** Anne Germain, PhD

**Slow wave activity and sigma predict cognitive symptoms in combat-exposed military service members and veterans with posttraumatic stress disorder**  
**Author(s):** McKeon A\(^1\), Rode N\(^1\), Laxminarayan S\(^2\), Liu J\(^2\), Ramakrishnan S\(^2\), Reifman J\(^2\), and Germain A\(^1\)  
**Affiliation(s):** \(^1\)Department of Psychiatry, University of Pittsburgh and \(^2\)Department of Defense Biotechnology High Performance Computing Software Applications Institute, Telemedicine and Advanced Technology Research Center, US Army Medical Research and Materiel Command

**Study:** Slow wave activity (SWA) and sleep spindle activity have been linked to cognitive performance, but remain understudied in PTSD, and the contribution of traumatic brain injury (TBI) history to these relationships is unknown. This study examined SWA, sleep spindle activity, TBI history, and cognitive symptoms in military service members (SM) and veterans with and without PTSD.

**Methods:** 115 previously deployed military SM and veterans (76 male, 39 female) with (PTSD+; n=90) and without (PTSD-; n=25) PTSD, CAPS, followed by two consecutive sleep laboratory nights with full polysomnography, where relative delta (0.5-4Hz; a marker of SWA) and sigma power (12-16Hz) were extracted from C4 channel for whole, second night NREM sleep.

**Results:** The PTSD+ group demonstrated less SWA \(F_{1, 113} = 5.11, p = .03\) than the PTSD- group when controlling for sex and TBI history. The PTSD+ group had greater cognitive symptoms than the PTSD- group, which became increasingly robust when controlling for age, sex, and TBI history \(F_{1, 113} = 28.96, p < .001\). No group differences were observed with sigma. In the PTSD+ group, SWA significantly predicted cognitive symptoms when adjusting for TBI history, age, and sex \(F_{4,85} = 2.70, p = .036, R^2 = .336\), and age \((\beta = -.082, p = .05)\) and sex \((\beta = 2.33, p = .05)\) significantly contributed to model fit. Sigma significantly predicted cognitive symptoms when adjusting for TBI history, age, and sex \(F_{4,85} = 3.14, p = .02, R^2 = .359\), and both age \((\beta = -.089, p = .02)\) and sex \((\beta = 2.18, p = .06)\) significantly contributed to model fit.

**Conclusion:** PTSD is associated with less SWA and more cognitive symptoms when compared to trauma-exposed controls. SWA and sigma significantly predict cognitive symptoms, and age, sex, and TBI history may help to increase model fit.

**Significance:** The present findings highlight the importance of future research unpacking the effect of sleep features and personal factors on cognitive deficits in military samples with PTSD.

**Funding Source(s):** Department of Defense Congressionally Directed Medical Research Programs (PI: Anne Germain- W81XWH-06-1-0257, W81XWH-08-1-0637, W81XWH-12-2-0024; PI: Jaques Reifman- W81XWH-14-2-0145) and NIH (PI: Anne Germain- MH083035; PI: Daniel Buysse- 4T32HL082610-10)
Verbal episodic memory deficits in first-episode psychosis

Author(s): McKinney R\textsuperscript{1}, DuBrow S\textsuperscript{2}, Jalbrzikowski M\textsuperscript{2}, Haas G\textsuperscript{3}, Luna B\textsuperscript{3}, Vishnu P. Murty VP\textsuperscript{3}
Affiliation(s): \textsuperscript{1}Department of Psychology, Carnegie Mellon University; \textsuperscript{2}Department of Psychology, Princeton University, and; \textsuperscript{3}Department of Psychiatry, University of Pittsburgh School of Medicine

Study: Episodic memory deficits are among the most prominent cognitive impairments in psychosis, and are thought to relate to the core etiology of the disorder. Prior research has detailed these deficits in individuals with chronic psychosis as well as in those at high-risk for developing psychosis. However, research has yet to fully characterize differences in verbal episodic memory test between individuals with first-episode psychosis (FEP) and controls. We probed recall and memory intrusions (both semantically related and unrelated), and further the influence of antipsychotic medication and diagnosis on multiple measures of free recall.

Methods: Subjects included 115 patients with FEP (69 diagnosed with schizophrenia, 46 diagnosed with another psychotic disorder), and 60 controls. Verbal memory ability was measured using the Hopkins Verbal Learning Test – Revised (HVLT-R), in which participants are orally presented with a list of words from three semantic categories and asked to recall them over the course of three repeated exposures to the list of words.

Results: Patients showed impaired memory on first trial recall and overall recall as compared to controls (p<0.001). Separating by diagnosis, both schizophrenia and other psychotic disorder patients performed worse than controls (p<0.05), but there were no significant recall differences between the two groups. There were no differences reported between any of the groups in relation to semantic intrusions, but patients recalled more random intrusions than controls (p<0.05). Further, results remained significant when controlling for medication status, suggesting that our results were not due to anti-psychotic administration.

Conclusion: Verbal memory impairments are apparent during the first episode of psychosis, both in individuals with schizophrenia-related disorders and affective psychosis.

Significance: The present findings demonstrate a need to better understand the nature of episodic memory deficits in FEP, as this marks a critical transition from a prodromal state to clinical disorder. Future research will focus on more complex modeling of free recall data.

Funding Source(s): P50 MH103204 (PI: Beatriz Luna, PhD)
Social anxiety may not differentially explain ADHD-related early adult alcohol use

Author(s): McKone KMP\textsuperscript{1,4}, Kennedy TM\textsuperscript{1}, Walther CAP\textsuperscript{2}, Pedersen SL\textsuperscript{1}, Gnagy EM\textsuperscript{3}, Pelham WE\textsuperscript{3}, and Molina BSG\textsuperscript{1,4}

Affiliation(s): \textsuperscript{1}Department of Psychiatry, University of Pittsburgh School of Medicine; \textsuperscript{2}Department of Psychology, University of Houston-Clear Lake; \textsuperscript{3}Department of Psychology, Florida International University, and; \textsuperscript{4}Department of Psychology, University of Pittsburgh

Study: Adults with ADHD in childhood are at greater risk for heavy drinking and alcohol use disorder. Two factors often linked to these outcomes in normative samples are social anxiety and specific motives for drinking. However, the extent to which these factors confer additional risk to individuals with ADHD is unclear. In this study, we hypothesize that 1) adults with childhood ADHD will have higher levels of social anxiety; 2) social anxiety will positively predict social, coping, and conformity motives; and 3) drinking motives will positively predict alcohol outcomes.

Methods: Participants in the Pittsburgh ADHD Longitudinal Study (N = 537; 314 ADHD, 223 nonADHD; 89% male; 82% white) self-reported their current level of social anxiety (Fear of Negative Evaluation Scale), motives for drinking (social, coping, enhancement, conformity), and frequency of heavy drinking at age 21. AUD symptom score at age 21 was ascertained via structured clinical interview. Motives were only assessed for current drinkers (N = 352).

Results: ADHD was not associated with social anxiety, \( p = .97 \). Sequential OLS regression was used to examine all other hypotheses. High social anxiety predicted higher levels of all motives, all \( ps < .05 \). ADHD group predicted lower levels of social (\( \beta = -.22, p < .001 \)), enhancement (\( \beta = -.12, p < .05 \)), and, at low levels of social anxiety, conformity motives (\( \beta = -.145, p = .055 \)). All motives positively predicted AUD symptom score and heavy drinking, all \( ps < .01 \). Social anxiety negatively predicted heavy drinking (all \( ps < .05 \)), and, at high levels of social motives, positively predicted AUD score (\( \beta = .156, p < .01 \)).

Conclusion: Social anxiety and elevated drinking motives index key areas of risk for heavy drinking and AUD. Individuals with ADHD do not appear to be at differentially greater risk for alcohol use due to these factors. These findings counter the clinical wisdom that ADHD increases risk for alcohol use due to self-medication.

Significance: Social anxiety and elevated drinking motives are important risks for heavy drinking and AUD in young adulthood. Targeting these processes may aid in the prevention of alcohol binges and abuse. However, such interventions may not be as effective for those with ADHD.

Funding Source(s): AA011873 (PI: Brooke S.G. Molina, PhD)
Facilitating sturdy brain development in adolescents in the juvenile justice system

Author(s): Miragaia A¹, Kwon J², and Cameron JL³
Affiliation(s): Departments of ¹Epidemiology, ²Neuroscience, and ³Psychiatry, University of Pittsburgh

Study: Youth who have faced significant early life stresses and have not received interventions to help promote sturdy brain development are at a much higher risk of interfacing with the criminal justice system by the time they are adolescents. Working For Kids: Building Skills™ is an educational platform based on principles of developmental neuroscience designed to educate the general public about how to strengthen brain pathways needed to succeed with life skills. The educational tools are fun, easy to use, and designed to be useful for those with a variety of educational and cultural backgrounds. This study is designing and testing new educational tools to help adolescents build strong brain circuits for decision making, planning, complex reasoning, and behavior control.

Methods: High school teachers at Shuman Detention Center in Pittsburgh, PA received six sessions of Working For Kids: Building Skills™ training. Five teaching strategies were then developed for use with the regular subject matter taught in their existing high school classes. Strategies were designed to strengthen student’s decision making, complex reasoning, planning, problem solving, and conflict resolution skills. Teachers were asked to test out the strategies and provide survey data to allow evaluation of the strategies.

Results: In Strategy 1, students were asked to fill out a decision tree worksheet allowing them to identify decision points and consequences of each decision. In trials (n=9) of this strategy teachers have rated student’s attention at 6.8/10, and have indicated that they would be very likely to use the strategy again (8.8/10). Strategy 2 involving complex problem solving and Strategy 3 involving problem solving and conflict resolution, (n=6), teachers rated the effectiveness in teaching complex problem solving at 9/10, and indicated their intent to use the strategy again as a 10/10.

Conclusion: Teachers and students were receptive to using novel lesson strategies that strengthen brain circuits for decision making, planning, complex reasoning and behavior control. A clear strength of these strategies is that they involve active learning by the students.

Significance: Strengthening brain circuits for these skills may help adolescents break the cycle of recidivism.

Funding Source(s): Pittsburgh Innovator’s Challenge Award (NIH UL1 RR024153), NSF Grant 1644507, NSF I-Corps Site Grant at the University of Pittsburgh (1st Gear Program)
An investigation for neural basis of subjective cognitive decline

Author(s): Mizuno A¹, Karim HT², Rangarajan A², Klunk WE, Snitz BE¹, and Aizenstein HJ¹,²
Affiliation(s): ¹Department of Psychiatry, University of Pittsburgh School of Medicine and ²Department of Bioengineering, University of Pittsburgh School of Medicine

Study: Subjective Cognitive Decline (SCD) is a pre-clinical state that refers to individuals with high subjective concerns for cognitive decline (primarily in memory) without objective cognitive impairment. Research interest in SCD is emerging. SCD could represent the earliest stage of dementia; however, the course of progression and underlying neural basis is not understood. We compared brain activation during a memory-encoding task between healthy older individuals with no cognitive impairment and individuals with subjective concerns.

Methods: We recruited 44 of Normal Aging subjects and 16 self-refereed memory clinic subjects (mean age = 74.02, SD=7.04, range 61-93 years). All subjects were clinical unimpaired on neuropsychological assessment. We used the “face-name” memory encoding functional magnetic resonance imaging (fMRI) task. We built a general linear model for the dependence of voxel-wise activation on 1) a subjective concern score, 2) an objective memory score, and 3) their interaction. We used statistical non-parametric mapping to perform voxel-wise group level analyses and controlled the family wise error (FWE) rate at α<0.05. We also conducted one-way ANOVA to compare the mean activations among 4 groups: high-concern/high-memory-performance, high-concern/low-memory-performance, low-concern/high-memory-performance, and low-concern/low-memory-performance.

Results: We found that the bilateral thalamus and right anterior insula, which are parts of memory encoding system, showed significantly modulated activations depending on the level of subjective concerns and objective memory performance. Among individuals with high subjective concerns, reduced brain activation was associated with lower memory performance.

Conclusion: Although all participants were older individuals with unimpaired memory, we observed varied levels of recruitment of the memory encoding system depending on the level of subjective concerns and objective memory performance. The reduced activation among individuals who showed elevated concern with relatively lower memory performance may indicate unsuccessful recruitment of the memory encoding system, and this group may have the highest risk to develop dementia.

Significance: SCD could be a more heterogeneous clinical group than previous studies indicated.

Funding Source(s): T32 MH019986 (PIs: Charles F. Reynolds, III, MD and Howard Aizenstein, MD, PhD), P50 AG005133 (PI: Beth Snitz, PhD), P01 AG025204 (PI: William Klunk, MD, PhD), R37 AG025516 (PI: William Klunk, MD, PhD)
Developmental improvements in mean behavioral performance and behavioral variability are related to stabilizing gain signals

Author(s): Montez D\textsuperscript{1}, Calabro F\textsuperscript{1}, and Luna B\textsuperscript{1}
Affiliation(s): \textsuperscript{1}Department of Psychiatry, University of Pittsburgh School of Medicine

Study: During adolescent development, behavioral responses both improve on average as well as stabilize. Our previous work has found that excess behavioral variability in a memory-guided saccade (MGS) task during adolescence is associated with increased variability of whole-brain gain signals. Here, we develop a computational model of MGS task performance, which incorporates the effect of these whole-brain gain modulating signals, and demonstrate that their stabilization during adolescence is sufficient to account for the improvements in mean behavioral performance, behavioral variability, as well as the relationship between the speed and accuracy of behavioral responses.

Methods: We develop a computational model of MGS behavioral responses based on a high-dimensional drift-diffusion race model framework that incorporates variability in gain signals. The resulting model allows us to model reaction times as well as continuous metrics of response accuracy in the memory-guided saccade task.

Results: The relationship between the speed and accuracy of subjects’ responses is U-shaped and invariant across age. We find that by incorporating two balanced sources of independent variability affecting gain and response thresholds in a high-dimensional drift diffusion race model that we can account for this peculiar U-shaped relationship. In addition, the improvements in mean behavior and behavioral variability that are observed during adolescent development can be accounted for by a parallel reduction in the variability of both gain and response thresholds.

Conclusion: Computational modeling results indicate independent trial-to-trial variability in gain signals that affect working memory maintenance and response thresholds can account for the peculiar speed-accuracy relationships observed in our data. In addition to accounting for the stabilization of behavioral responses, e.g. reaction time variability and saccade precision, our computational model of memory-guided saccade performance can account for improvements in mean reaction time. Thus, it appears that many aspects of behavioral improvements observed during development may potentially be the results if the stabilization of widespread gain signals.

Significance: Computational modeling supports the hypothesis that improvements in mean behavioral performance as well as its stabilization during adolescent development is driven by a reduction in multiple sources of neural variability.

Funding Source(s): NIH grant MH067924 (PI: Luna, Beatriz. PhD)
Clinical presentation of inpatient youth with ASD and Comorbid Psychotic Spectrum Disorders

Study: Individuals with Autism Spectrum Disorder (ASD) are frequently comorbid with other psychiatric disorders. Particularly with regard to comorbid Schizophrenia Spectrum Disorder, the literature has focused on differential diagnosis. The clinical characteristics of this comorbid subgroup are largely unknown. We hypothesized that youth with ASD and a comorbid psychotic disorder would have more severe Schizophrenia-related symptoms and exhibit different manifestations of emotional and behavioral dysregulation compared to non-psychotic peers.

Methods: Participants were psychiatric inpatients with ASD from the six-site Autism Inpatient and Developmental Disorders Research Collaborative (ADDIRC). We compared a subgroup with psychotic or Schizophrenia-Spectrum discharge diagnoses (n = 19) to age-, gender-, and IQ-matched psychiatric inpatients with ASD without psychotic spectrum discharge diagnoses (n = 503) on clinical characteristics obtained by parent report and direct assessment.

Results: The groups did not significantly differ in emotion dysregulation in the domains of reactivity (p = .302) nor dysphoria (p = .301). Those in the Psychotic subgroup were reported to have more severe rates of auditory hallucinations (p = .000), strange ideas and beliefs (p = .000), and overall rates of interference in schoolwork and social interaction from these symptoms (p = .029). Additionally, these individuals more often had a family member with Schizophrenia (p = .022). Those in the Non-Psychotic group had more irritability (p = .039).

Conclusion: Inpatients with ASD with psychotic disorder diagnoses differed from non-psychotic inpatients with ASD in psychotic symptom severity, family history, and irritability. More research is needed to further characterize this unique subgroup of ASD subjects.

Significance: The results indicate that youth with ASD and psychotic symptoms present differently and highlight the need to better understand phenomenology. Development of subgroup profiles would create new avenues for future research.

Funding Source(s): Simons Foundation Autism Research Initiative and the Nancy Lurie Marks Family Foundation, (SFARI #296318 to M. Siegel.), NIH R01HD079512 (PI: Carla Mazefsky, PhD)
Context-dependent neurodevelopment of mesolimbic dopamine systems during adolescence

Author(s): Murty VP, Montez D, Foran W, Calabro F, and Luna B

Affiliation(s): 1Department of Psychiatry, University of Pittsburgh School of Medicine

Study: The mesolimbic dopamine system continues to mature throughout adolescence into early adulthood. Neuroimaging has characterized increases in ventral striatal activation across adolescence during reward-motivated behaviors; however, relatively less work has investigated interactions between the ventral tegmental area, the source of mesolimbic dopamine neurons, and its targets in the striatum. In the current study, we characterized this neural circuit in children, adolescents, and adults both during rewarding and neutral/resting-state contexts.

Methods: FMRI data was collected in 170 individuals ranging in age between 10-30 years old. Participants completed both a resting-state task (neutral context) and a reward-motivated anti-saccade task (rewarding context). To compare results across tasks, we characterized ‘background connectivity’ of the reward motivated anti-saccade task, which reflects intrinsic connectivity between regions after removing task-related activity.

Results: Results indicate a significant decrease in VTA-ventral striatal coupling in the rewarding context as individual’s approached adulthood (p < 0.001). Conversely, there were no differences in VTA-ventral striatal coupling as a function of age in the neutral context (i.e., resting state scan, p = 0.93).

Conclusion: These findings support a model by which connectivity of the VTA with its mesolimbic targets is relatively stable across adolescence, however, the ability to engage this circuit in motivational-relevant contexts continuous to mature into early adulthood.

Significance: These data not only characterize developmental trajectories of when and how the mesolimbic dopamine system is engaged throughout adolescence, but provide a normative template to test for psychopatholgy-related differences that emerge during adolescence.

Funding Source(s): NIMH R01 MH080243
Mural creation to develop aesthetic empathy

Author(s): Ohm D
Affiliation(s): 1Western Psychiatric Institute and Clinic of UPMC

Study: The study explored the impact of creating three hallway murals on perception and quality of care. After all, the first thing a patient views upon admission is the entrance hallway. This visual environment can be perceived as Scary, hopeful and anything in between. Study also includes measuring the extent that improving perception of care via enhanced visual environment impacts level of restraints and seclusions on the individual units. The study investigated the impact of long term mural creation to improve the psychiatric milieu. The purpose of this project is to explore these phenomena more closely and to develop effective ethical and aesthetic action to increase a sense of community and decrease marginalization of the psychiatric milieu. I intend to develop aesthetic empathy using a social service artist in residency framework while collaboratively creating murals. Essentially the goal is creating imagery with a caring impact on both staff and patients.

Methods: Reviewing quantitative seclusion and restraint numbers pre and post mural creation as well as acquiring brief qualitative surveys from patients involved in painting and developing murals themes. There is also response poetry from interns as well as interviews with Program Directors. This poetry is the run through an algorithm to identify themes and changes in perception.

Results: The data based on the survey results of client- artists, interviews with unit staff and art-based feedback indicates a transformative change in individuals’ perception of the milieu. The transformed perception is a more restorative recovery based environment where the client artists and unit staff were given a voice in the transformation. There seemed to be a significant correlation that the DARE project reduced seclusions and minimal measurable link to reducing restraints or unit violence.

Conclusion: The primary reason further study is needed is that, although mural creation seemed to improve perception of the milieu, there is the lack of significant data that by transforming perception you are reducing violence? There did seem to be a positive correlation between reducing seclusions and the developing aesthetically restorative environment- mural project.

Significance: The value of enhancing the aesthetic inpatient environment seemed to be threefold: 1) encouraging participation in mural creating provided the opportunity for patient and staff empowerment and investment in the milieu; 2) the impact of viewing the completed murals seemed to be restorative; and 3) the impact of the process of selecting imagery, developing the mural themes was consistent to a recovery-based treatment model.

Funding Source(s): None
Inflammation, striatal dopamine receptor binding and anhedonia in depression

**Author(s):** Pecina M, Burghardt P, Avery E, Hefferman J, Mickey B, and Zubieta J-K

**Affiliation(s):** 1Department of Psychiatry, University of Pittsburgh School of Medicine; 2College of Liberal Arts & Sciences, Wayne State University; 3Department of Psychiatry, University of Michigan; 4Department of Neurology, University of Wisconsin-Milwaukee; and 5Department of Psychiatry, University of Utah

**Study:** Growing evidence supports a potential relationship between inflammation and the dopamine (DA) system in Major Depressive Disorder (MDD). Still, a direct relationship between pro-inflammatory cytokines and striatal DA receptor measures in MDD has not yet been demonstrated. Based on pre-clinical data showing severe activation of astrocytes and microglia and pronounced inflammatory responses in DA D2 receptor-deficient mice, we hypothesized that in MDD patients, higher baseline levels of pro-inflammatory cytokines will be associated with: 1) reduced postsynaptic striatal DA D2 receptors and 2) higher anhedonia scores.

**Methods:** We measured striatal DA D2/3 receptor binding potential (BP) using positron emission tomography (PET) and the selective DA D2/3 receptor antagonist 11 C-raclopride in 20 non-smoking un-medicated subjects with MDD. Anhedonia scores were assessed using the Apathy Evaluation Scale (motivational anhedonia) and the Snaith-Hamilton Pleasure Scale (consummatory anhedonia). Blood samples were collected and analyzed according to standard procedures. Group analyses of PET were performed with mass univariate general linear models and parametric maps were extracted for quantification of regional changes in BPND, graphing and determination of correlations coefficients (p<0.001 uncorrected voxel-wise).

**Results:** Increased baseline pro-inflammatory plasma levels in patients with MDD were significantly correlated with higher apathy scores (INF-γ: r=0.5, p=0.038; TNF-α: r=0.5, p=0.048). No significant association was found between any of the pro-inflammatory cytokines and consummatory anhedonia scores (SHAPS) or overall depression severity scores (QIDS-16SR). Higher levels of INF-γ were significantly correlated with lower DA receptor BPND in the bilateral ventral striatum (VS) (left: -14, 4, -12; right: 18, 6, -12, K>5, p<0.001). Higher levels of IL-1α were also significantly correlated with lower DA receptor BPND in the bilateral ventral striatum (left: -16, 6, 6; right: 18, 4, -10, K>5, p<0.001). Apathy Evaluation Scale scores, but not SHAPS scores, were negatively correlated with measures of DA BPND in the left VS extracted from the analysis above (r=-0.4, p=0.046).

**Conclusion:** Our findings support the hypothesis that inter-individual variability in DA D2/3 receptor availability in patients with depression is associated with pro-inflammatory activation and greater apathy scores.

**Significance:** Understanding the neurobiology of core symptoms of depression, such as anhedonia, is key for the development of symptom-specific therapeutics for depression.

**Funding Source(s):** R01 MH086858 (PI: Jon-Kar Zubieta)
Presenters: Eliese N. Pergi

Education: University of Pittsburgh, Dietrich School of Arts and Sciences

Current Position: Undergraduate Student

Principal Area of Research Interest: Schizophrenia, Psychophysiology

Current Research Support: Not applicable

Mentor(s): Leslie Horton, PhD and Gretchen Haas, PhD

Investigating real-life stress reactivity in adolescence: A novel approach

Author(s): Pergi E\(^1\), St. John J\(^1\), Nuutinen M\(^2\), and Horton L\(^1\)

Affiliation(s): \(^1\)Department of Psychiatry, University of Pittsburgh School of Medicine

Study: Ambulatory monitoring through recent technology provides an innovative approach to investigating stress reactivity in real-life settings. Given that stress sensitivity may increase risk for psychosis, this methodology may be well-suited for examining stress in vulnerable populations. The Zephyr BioHarness 3.0, a physiological module worn around the chest, demonstrates reliable heart-rate variability (HRV) monitoring in field-based settings. Thus, we propose this device will provide a feasible and valid method for studying HRV and stress beyond the lab. Further, we hypothesize that (1) we will detect physiologically stressful experiences in daily life, which will correspond to ecological momentary assessment (EMA) reports of stress and (2) familial high risk (FHR) adolescent offspring of individuals with schizophrenia will report higher stress on EMA questionnaires as compared to healthy controls (CTR).

Methods: Participants (FHR=10; CTR=40) were recruited for the Adolescent’s Social Stresses, Emotions, and Thoughts (ASSET) study, which investigates the influence of daily stressors on FHR adolescents. Participants completed EMA subjective reporting on daily stress, emotions, and activities over three weekends via smartphone, as well as HRV measures of laboratory stress during the Trier Social Stress task, a social evaluative task which reliably induces moderate physiological stress. A subset of pilot participants (n=4) completed the ambulatory psychophysiology protocol, in which the BioHarness module was worn during EMA procedures.

Results: Findings suggest good compliance and feasibility of pilot procedures. We found significant group differences on a measure of HRV, Respiratory Sinus Arrhythmia (RSA), when participants were reporting low perceived stress in daily life ($M=7.67, SD=1.43$) compared to occasions of high perceived stress ($M= 84.18, SD=11.73$), $t(61)= 6.07, p< .001$. By visual inspection, ambulatory pilot data corresponded to laboratory stress responses. FHR participants also reported overall higher perceived stress compared to controls; $t(38) =-2.33, p=.025$.

Conclusion: Results favor this novel methodology as a viable and valid approach to monitoring stress reactivity beyond the lab. Higher experienced stress in FHR adolescents in preliminary analyses support differences in ambulatory physiological stress response compared to controls.

Significance: It is clinically relevant to study dysregulated stress reactivity observed in FHR individuals as this may contribute to development of schizophrenia. The implications of ambulatory psychophysiological monitoring may extend to early detection and intervention.

Funding Source(s): NIMH grant K23 MH100187 (PI: Leslie Horton, PhD)
Identifying cellular mechanisms underlying the anti-compulsive properties of fluoxetine

Author(s): Piantadosi SC\textsuperscript{1,2}, Hyde J\textsuperscript{2}, and Ahmari SE\textsuperscript{1,2}
Affiliation(s): \textsuperscript{1}Center for Neuroscience, University of Pittsburgh and \textsuperscript{2}Department of Psychiatry, University of Pittsburgh School of Medicine

Study: Serotonin reuptake inhibitors (SRIs) are the first-line and most efficacious pharmacotherapeutic treatment for obsessive compulsive disorder (OCD). However, complete remission following SRI treatment is rare (< 20%), and only 40-60% of patients report improvement in symptoms following monotherapy. It is therefore important to determine the neural changes that underlie responsiveness vs resistance to treatment. Aberrant striatal activity may underlie OCD symptoms, evidenced by functional imaging studies in OCD patients that demonstrate hyperactivity within the striatum. Notably, successful treatment of OCD symptoms with SRIs reduces hyperactivity in the striatum of treatment-responsive patients, suggesting a potential mechanism for treatment response. In addition, a recent meta-analysis suggests that the therapeutic effects of SRIs in treatment-responsive OCD patients may occur much sooner than previously believed, suggesting that short term changes in neural activity may be important.

Methods: Sapap3 knockout (KO) mice, which have both a hyperactive striatum and compulsive OCD-like grooming phenotype, were injected with AAV-GCaMP6m and implanted with a GRIN lens in the centromedial striatum (CMS) to visualize striatal calcium activity during spontaneous grooming behavior. All mice received 7 days of treatment with the SRI fluoxetine, and underwent imaging and grooming assessments on days 3, 5, and 7 of treatment.

Results: Sapap3-KO mice displayed elevated grooming behavior at baseline, and treatment with fluoxetine decreased grooming. Interestingly, in contrast to published studies, this reduction in compulsive grooming occurred more rapidly than expected, after just 3 days of treatment. At baseline, Sapap3-KO mice also had elevated striatal activity as measured by calcium events relative to WT animals. This increase in calcium activity during grooming behavior was reduced by successful fluoxetine treatment. Preliminary studies selectively examining D1-medium spiny neurons (MSN) in Sapap3-KO mice also suggest increased baseline activity, which may be decreased following treatment. Ex vivo data suggest that fluoxetine may be modulating the activity of striatal fast spiking interneurons (FSIs) in order to normalize striatal activity.

Conclusion: Hyperactivity of the striatum and compulsive grooming behavior can be reversed with successful SRI treatment in a valid mouse model of OCD-like behaviors.

Significance: Understanding cell-type specific effects of successful and unsuccessful SRI treatment may help us develop treatments for patients that have better efficacy and fewer side effects.

Funding Source(s): NIMH R01 MH104255
Temporal learning dynamics of age-related reward processing

Author(s): Pongibove M\(^1\), Calabro F\(^2,3\), and Luna B\(^2,4\)
Affiliation(s): Departments of \(^1\)Neuroscience, \(^2\)Psychiatry, \(^3\)Bioengineering, and \(^4\)Psychology, University of Pittsburgh

Study: By analyzing Functional Magnetic Resonance Imaging data from a reward learning task, this study aimed to understand the normative temporal dynamics of reward processing systems as subjects learn the task’s reward contingencies. Additionally, this study investigated possible age effects to determine whether adolescents and adults demonstrate different patterns of neuronal responses as they learn.

Methods: Participants included 120 healthy individuals ages 12-30. Functional Magnetic Resonance Imaging data was collected as participants performed a reward learning task in a combined PET/MR scanner. During the task, participants explored a map, uncovering rewards and learning underlying reward probabilities.

Results: Temporal activation patterns were recorded as responses to either a high reward, low reward, or null reward. This study focused on the high and low reward responses. Subjects showed strong effects of trial number in the high reward condition across many striatal regions: RH Caudate p=8.551e-10, RL Caudate p= < 2.2e-16, RH NAcc p=0.01521, RL NAcc p= 3.934e-05. Overall, the shape of the recorded activations peaked early on through the trials. This is seen most clearly under the high reward condition. Ae effects were observed under the low reward conditions in the nucleus accumbens: RH NAcc p=0.00484, RL NAcc p=0.022 and caudate: RH Caudate p= 0.00405, RL Caudate p= 0.01292.

Conclusion: Our results showed that sub-cortical reward responses exhibit strong temporal dynamics, reflecting prior observation and reward learning. Additionally, results showed that adolescents tend to exhibit higher activations in the subcortical region early on in the reward learning task.

Significance: These results suggest that differences between how adolescents and adults learn from rewards may arise from differences in how low reward outcomes are valued and learned from, relative to high reward outcomes. Future work will incorporate behavioral data, including accuracy and memory recall, to uncover the implications of these age-dependent temporal response patterns on reward learning systems.

Funding Source(s): This work is supported by NIMH grant 5R01 MH080243 (PI: Beatriz Luna, PhD) and the Staunton Farm Foundation.
**Neurocognitive development of response inhibition and risk for substance use**

*Author(s):* Quach A\(^1\), Tervo-Clemmens B\(^1\), Chung, T\(^2\), Luna B\(^1,2\), and Clark DB\(^2\)

*Affiliation(s):* \(^1\)Department of Psychology, University of Pittsburgh and \(^2\)Department of Psychiatry, University of Pittsburgh School of Medicine

**Study:** Previous research indicates that poor response inhibition and lower levels of brain activity supporting cognitive control are risk factors for substance use. In normative development, inhibitory control functions undergo progressive refinement through adolescence into adulthood. However, the relationship between neurocognitive development of response inhibition and risk factors for substance use has not been definitively determined.

**Methods:** As part of the National Consortium on Adolescent Neurodevelopment and Alcohol (NCANDA) study, an fMRI antisaccade task was administered at baseline (N= 125) and at one year follow up (N = 99) to both healthy controls (n = 61, CON) and adolescents at risk for problematic alcohol use (n = 64), based on at least one of the following: family substance use disorder history (FH; n = 23), externalizing symptoms (EXT, n = 34), or internalizing symptoms (INT, n = 28). The sample spanned adolescence and into early adulthood (mean age =16.94, sd = 2.61).

**Results:** Consistent with previous studies, age showed a significant, positive relationship with antisaccade performance \((X^2(1) = 32.94, z = 5.74, p < .001)\). There was a significant main effect of EXT, where those at risk performed worse than CON \((X^2 (1) = 4.04, z = -2.10, p = .044)\). The effect of EXT did not differ by visit \((z = 1.15, p = .252)\). A trend towards an interaction between age and group indicated that younger subjects in the EXT group performed worse but approached equivalence to CON for older subjects \((X^2 (1) = 3.14, z = 1.77, p = 0.076)\). In contrast, INT and FH shows equivalent performance CON at both baseline and follow up. Preliminary fMRI analysis showed reduced BOLD activation in anterior cingulate cortex (ACC) for EXT at baseline \((p < .05, \text{ voxelwise correction})\).

**Conclusion:** Results suggest that inhibitory control impairments may be uniquely associated with externalizing risk. Specifically, externalizing psychopathology in early adolescence may confer limitations in inhibitory control due to abnormalities in engaging brain systems that support cognitive control, including the ACC. However, inhibitory control is normalized in later adolescence by maturation and/or compensatory mechanisms.

**Significance:** The present findings suggest deficits in response inhibition to be a possible cognitive marker for predicting externalizing psychopathology that may increase risk for substance use disorders.

**Funding Source(s):** NIAAA grants U0AA1021690 (PI: Beatriz Luna, PhD)
Study: Over recent years, pediatric depression has been increasingly shown to be bidirectionally associated with autoimmune disorders, although without a clear etiology for this association. Similarly, pediatric depression has been linked to elevations in inflammatory markers such as interleukin-6, in addition to abnormalities in the inflammatory-mediated kynurenine pathway, part of the tryptophan metabolic pathway. Tryptophan is metabolized into kynurenine, which is ultimately metabolized into quinolinic acid, which has potential depressive effects mediated by the NMDA-glutamate receptor. In this post-hoc secondary analysis, we sought to assess the associations of peripheral interleukin-6, kynurenine, tryptophan, and depression severity in a cohort of adolescents with inflammatory bowel disease (IBD).

Methods: Participants included youth aged 9-18, with 44 subjects with gastroenterologist-diagnosed inflammatory bowel disease. Peripheral kynurenine, tryptophan and interleukin-6 were assessed via blood draw. To assess depression severity of the child, research staff administered the child-rated Childhood Depression Inventory (CDI), a self-report measure.

Results: Interleukin-6 levels were significantly positively associated with the kynurenine/tryptophan ratio, a proxy for peripheral kynurenine pathway activation (n=19, r=0.818, p<0.001). When subjects were dichotomized by depression severity, we found a trend for elevated kynurenine/tryptophan ratios in subjects with higher depression severity (M=0.0489, SE= 0.0076) compared to subjects with lower depression severity (M=0.0330, SE=0.0027), t(43) = 2.010, p<0.10. However, kynurenine, tryptophan, and interleukin-6 were not independently correlated with child-rated Child Depression Inventory scores.

Conclusion: On an exploratory basis, tryptophan metabolic pathway markers in depressive symptoms in IBD subjects. Specifically, elevated activation of the kynurenine pathway may be associated with worse depression severity. Additionally, elevated inflammation cytokines, such as interleukin-6, may be associated with activation of the kynurenine pathway, which may ultimately contribute to depressive symptomatology.

Significance: Our findings emphasize the interaction of inflammatory pathways, the tryptophan metabolic pathway, and depressive symptomatology in a cohort of adolescent IBD subjects, indicating a direction for future research to better address depressive symptomatology in the IBD population.

Funding Source(s): NIMH (R01 MH077770) and NIH Director’s Innovator Award (1DP2OD001210).
Calcineurin regulates cocaine-cue neuroplastic changes in the amygdala to alter relapse-like behavior

Author(s): Rich MT\textsuperscript{1,2,3}, Cahanap TC\textsuperscript{1}, Huang Y\textsuperscript{1,2}, and Torregrossa MT\textsuperscript{1,2,3}

Affiliation(s): \textsuperscript{1}Department of Psychiatry, \textsuperscript{2}Center for Neuroscience, \textsuperscript{3}Center for the Neural Basis of Cognition, University of Pittsburgh

Study: Evidence suggests that interfering with memory reconsolidation or inducing memory extinction within the lateral amygdala (LA) may serve to weaken maladaptive memories. Previous studies have identified thalamic and/or cortical excitatory synapses within the LA as potential loci for cue-mediated learning, as they are strengthened by associating a cue with either a fearful or rewarding stimulus. The extinction of a fear-associated memory correlates with a weakening of synaptic strength; however, these mechanisms have not been well studied in the context of drug-associated learning. Both extinction and reconsolidation are regulated by various protein kinases and phosphatases, such as CaMKII and calcineurin. We have recently shown that inhibiting CaMKII enhances the extinction of and interferes with the reconsolidation of drug-associated memories. The aims of the current study were to further investigate the synaptic mechanisms within the LA that regulate drug-cue memories, and to examine a potential pharmaco-behavioral strategy to reduce drug-seeking behavior.

Methods: We utilized an approach that combined cocaine self-administration with \textit{ex vivo} electrophysiology in male Sprague-Dawley rats (n = 8-12 rats/group). We examined the effect of cocaine-cue learning on both thalamic and cortical synapses in the LA, and whether these synapses were altered by cue extinction and reconsolidation, respectively. Additionally, we tested the effects of LA administration of chlorogenic acid (CGA), an activator of calcineurin, on both the behavioral and physiological effects of cue extinction and reconsolidation.

Results: We found that cocaine training potentiated thalamo-amygdala but not cortico-amygdala synapses relative to saline-trained controls (p < 0.05). This potentiation was unaltered by either instrumental extinction training or context exposure alone, and was not potentiated significantly more by drug-cue memory reconsolidation. Conversely, synaptic strength was progressively reduced by increasing levels of cue extinction. Finally, CGA infusions in the LA following cue extinction or reconsolidation caused a significant reduction in both EPSC amplitude and cue-induced reinstatement relative to vehicle-infused controls (p < 0.05).

Conclusion: Together, our results suggest that inducing drug-cue memory extinction or inhibiting reconsolidation reverses cocaine-induced potentiation at thalamo-amygdala synapses in a calcineurinindependent manner, and this activity is important for reducing drug-seeking behavior.

Significance: Drugs of abuse induce neuroplastic changes within brain reward circuits. Over time, these synaptic events form strong drug-associated memories that become a trigger for drug-seeking behaviors. Disrupting these memories in individuals struggling with addiction may maintain long-term abstinence.

Funding Source(s): R01DA042029, F31DA039646, T32DA031111
The clinical utility of depression and weight-related subtypes among weight-concerned women smokers

Author(s): Salk RH, Kolko RP, Germeroth LJ, Emery RL, Cheng Y, and Levine MD

Affiliation(s): 1Department of Psychiatry, University of Pittsburgh School of Medicine and 2Department of Statistics, University of Pittsburgh

Study: Weight concerns and depression symptoms are barriers to quitting smoking among women. Extant research has not examined subtypes of women who may have different symptom profiles that are amenable to more specialized intervention. Thus, we examined whether a group-based analysis could meaningfully capture individual differences on symptom measures of depression, body esteem, and eating behaviors, and demonstrate clinical utility.

Methods: Weight-concerned women (N = 349; 86% white) received smoking cessation counseling and were randomized in a double-blind, placebo-controlled trial to one of two adjunctive counseling components and one of two medication conditions. At baseline, women completed measures of depression, body esteem, and eating behaviors. Women also completed measures to assess BMI, nicotine dependence, number of cigarettes smoked per day, age, and education. Latent profile analysis (LPA) was used to identify subtypes of weight-concerned women. ANOVA was used to characterize baseline differences among identified subtypes.

Results: Results supported a three-profile model: LP1 (15% of the sample; high depression, low body esteem, low disinhibition), LP2 (51%; moderate on all measures), and LP3 (34%; low depression, high body esteem). Entropy for the model was .77 and average latent class probabilities ranged from 89% to 91%. Groups did not differ on age, education, or nicotine dependence. All groups differed significantly on BMI: LP1 (M = 30.55); LP2 = (M = 28.08); and LP3 (M = 24.56). Women in LP1 smoking significantly more cigarettes (M = 24.08) than the other two groups: LP2 (M = 20.34) and LP3 (M = 19.79).

Conclusion: Among weight-concerned women smokers, heterogeneity in the symptom presentation of depression, body esteem, and eating behaviors was captured by three distinct groups. The group with the highest depression and lowest body esteem symptoms (15% of the sample) consisted of obese women who smoked over a pack of cigarettes a day, demonstrating clinical utility. These women may need more specialized, intensive intervention.

Significance: Identifying groups with distinct symptom profiles can lead to more personalized medicine strategies to improve smoking cessation outcomes among weight-concerned women.

Funding Source(s): R01 DA04174 (Marsha D. Marcus, PhD)
Introducing peer navigators: Improving patient engagement by embedding enhanced peer support services in acute care settings

Author(s): Sapra M1, Lucas A2, Parham K3, Gopalan K3 and, Shanahan A3
Affiliation(s): 1Department of Psychiatry, University of Pittsburgh School of Medicine; 2Allegheny HealthChoices, Inc.; and 3Western Psychiatric Institute and Clinic of University of Pittsburgh Medical Center

Study: Peer Recovery Support Services (PRSS) are now well-recognized as part of continuum of services for Substance Use Disorders (SUD). There is limited research on use of PRSS in acute care medical settings. We studied results of a quality improvement project set-up to use peer support to engage patients and facilitate referrals to SUD treatment centers.

Methods: Peer Recovery Specialists were trained in engagement strategies, such as Motivational Interviewing, tools of Screening & Brief Interventions, as well as conducting level-of-care assessments using the Pennsylvania Client Placement Criteria (PCPC). The specialists were referred to as “Peer Navigators” (PNs) and deployed at three community hospitals: UPMC Mercy, UPMC McKeensport, and UPMC East. PNs engaged patients in Emergency Departments (ED) and inpatient medical units. PNs provided education, support and facilitated referrals to appropriate SUD and other treatment settings. Utilization rates of acute care visits were studied for all patients seen by PNs between 5/1/2015 and 4/30/2016. Patient satisfaction and staff feedback were collected.

Results: On average, patients found their time with peers to be very beneficial. They reported that they were very/somewhat likely to seek follow-up services after their PN encounter. Staff satisfaction was high with most of them reporting high likelihood of consulting PNs in the future. Of the 892 patients seen in the study period, a “high utilization” group was identified (n=157) of individuals using either ED services or inpatient services more than 3 times in a period of 9 months. In this group, there was a 42% decrease in total inpatient discharges and 18% decrease in the use of ED services in the period of 9 months following the index PN visit.

Conclusion: The interventions provided by the PNs were well-received by the patients and the hospital staff. There was significant decline in the utilization of inpatient hospital and ED visits, particularly in the high utilization group.

Significance: The acceptance and growth of PRSS will depend on further research and cost-benefit analysis. Present findings demonstrate that PN services can be integrated well in acute care settings and lead to significant decline in utilization rates of acute care services.

Funding Source(s): Pennsylvania Department of Human Services and five Managed Care Organizations
Relationship between duration of untreated psychosis and intrinsic corticostriatal connectivity in patients with early phase schizophrenia

Author(s): Sarpal DK1, Robinson DG2,3,4, Fales C2, Lencz T2,3,4, Argyelan M2,3,4, Karlgodt KH5, Gallego JA6, John M2,4, Kane JM2,3,4, Szesko PR7,8, and Malhotra AK2,3,4

Affiliation(s): 1Department of Psychiatry, University of Pittsburgh School of Medicine; 2Department of Psychiatry, Zucker Hillside Hospital; 3Center for Psychiatric Neuroscience, Feinstein Institute for Medical Research; 4Department of Psychiatry, Hofstra Northwell School of Medicine; 5Department of Psychology, University of California, Los Angeles; 6Department of Psychiatry, Weill Cornell Medical College; 7Department of Psychiatry, Icahn School of Medicine at Mount Sinai; and 8James J. Peters VA Medical Center

Study: Patients with first-episode psychosis experience psychotic symptoms for a mean of up to two years prior to initiation of treatment, and long duration of untreated psychosis (DUP) is associated with poor clinical outcomes. Meanwhile, evidence compiled from numerous studies suggests that longer DUP is not associated with structural brain abnormalities. To date, few studies have examined the relationship between DUP and functional neuroimaging measures. In the present study, we used seed-based resting-state functional connectivity to examine the relationship between DUP and corticostriatal circuitry.

Methods: We examined patients with early phase schizophrenia who underwent resting state scanning prior to entering 12 weeks of prospective treatment with second-generation antipsychotic drugs. DUP was quantified based on interviews with patients and their families. Patients were followed during treatment and response to treatment was defined, a priori, based on minimal psychotic symptom items of the Brief Psychiatric Rating Scale. We generated functional connectivity maps from 6 regions of interest (ROIs) within the striatum in each hemisphere. Group level analyses were performed for each ROI, independently, with log transformed DUP as a covariate. Significance was defined at p<0.05, cluster corrected. Post-hoc mediation analyses were performed on a composite measure of corticostriatal connectivity derived from the significant results of our DUP analysis.

Results: We included 83 patients in our analyses (mean age 21; 61 males, 24 females), who had a mean DUP of 102 weeks (SD=77; median=35 weeks). We found that longer DUP correlated with decreased functional connectivity between striatal nodes and frontal and parietal regions, some of which are within the central executive network. In post-hoc analyses, a primary explanatory factor within these significant connections showed a mediation effect between DUP and treatment response.

Conclusion: Our results indicate that variation in corticostriatal circuitry may play a role in the relationship between longer DUP and worsened response to treatment.

Significance: This study suggests the possibility for causal links between DUP, striatal circuitry and clinical outcomes. Future, prospective, studies are necessary to further characterize consequences of longer DUP.

Funding Source(s): NIMH grants P50MH080173, P30MH090590; R01MH060004; R21MH101746; K23MH100264; R01MH076995 and R21MH101746
**Mental health elective for pediatric residents**

*Author(s): Schreiber J1,2, Reis E1, and Schlesinger A2*

*Affiliation(s): 1Department of Pediatrics, University of Pittsburgh School of Medicine and 2Department of Psychiatry, University of Pittsburgh School of Medicine*

**Study:** Twenty Percent of youth ages 13-18 years old live with a mental health condition. There is a shortage of child psychiatrists, making pediatricians often the first line of identification and treatment for children. Due to this need the American Academy of Pediatrics recommends pediatricians “preform appropriate learning practices” around behavioral health. One way to accomplish this is through direct clinical contact and participation in behavioral health clinics, which lead to the development of the mental health elective for pediatric residents.

**Methods:** Pediatric residents attend clinic visits with psychiatrists and therapists at various outpatient settings. Overall the objectives of the rotation are for trainees to be able to evaluate and treat depression, anxiety and ADHD, evaluate for suicidality, how to refer to child psychiatry, and prepare participants for mental health questions on the pediatrics boards. To assess these objectives a pre and post test is done which has questions assessing level of comfort in diagnosing and treating psychiatric conditions and pediatric board style questions.

**Results:** Compared to the start of the rotation all five participants had increased comfort in assessing for suicidality and self harm. Three of the five participants in the post-test compared to zero out of five in the pre-test had increased comfort in diagnosing depression and anxiety. In the post test all five participants felt comfortable asking patients about psychiatric concerns compared to three on the pre-test. For the sixteen board style questions the average score went from a 10.6 to a 10.8.

**Conclusion:** This study does show that there is a clinical benefit for pediatric residents to do a mental health elective, as it increases comfort to ask about psychiatric conditions, suicidality and diagnosis depression and anxiety. The post-test showed no improvement in board question response, so this will be an area for further study.

**Significance:** This study is limited in the participants, but hopefully this leads to increased interest in pursuing the rotation allowing for further evaluation of how this kind of exposure to psychiatry can better prepare pediatric residents to take care of these patients upon graduation.

**Funding Source(s):** None
Stuck on a feeling: Spontaneous recall of daily events among children at high vs. low familial risk for depression

Author(s): Scott L¹, Vine V¹, Ladouceur CD¹, and Bylsma LM¹
Affiliation(s): ¹Department of Psychiatry, University of Pittsburgh School of Medicine

Study: Offspring are at a 3-4 times higher risk to develop depression if a biological parent has a history of depression. Depression risk has been associated with difficulties in the ability to repair one’s sad moods or engage in adaptive emotion regulation responses. A regulation technique that is seldom studied is the practice of spontaneously recalling positive autobiographical memories to repair one’s mood. Depressed people tend to have deficits in recalling these memories to repair their sad mood. It is important to better understand the potential role of daily event recall in the etiology of depression by examining patterns of daily event recall in high- (vs. low-) risk offspring.

Methods: Participants were youth (aged 9-13) at high (n = 38) and low (n = 47) familial risk for depression with no personal history of a depressive disorder. Youth completed a 9-day Ecological Momentary Assessment (EMA) protocol, where they identified their most positive and most negative events since the previous prompt, their event appraisals, and whether they had spontaneously recalled (i.e., whether they had thought about the event again or not) these recent positive or negative daily life events since they occurred.

Results: Across the sample, stronger positive or negative appraisals of daily events predicted a higher frequency of spontaneous recall (negative events, $r = .33, p < .005$; positive events, $r = .35, p < .003$). We also found that for negative daily events, low- and high-risk likelihood of recall was significantly related to negative event appraisals ($p < .04$), and this effect did not depend on depression risk group ($p > .23$). For positive events, however, spontaneous recall among high- and low-risk groups was differentially related to positive appraisals—a marginally significant interaction emerged ($p < .08$), such that more positively appraised events were likelier to be recalled, but only among low-risk children ($p < 0.02$), whereas among high-risk children rates of recall were unrelated to the positivity of the event ($p > .30$).

Conclusion: High risk youth were less likely to think about positive events that happened throughout their day, which may contribute to risk for the onset of future depression.

Significance: These results can contribute to the understanding of affective familial risk factors for depression and may have implications for mechanism of depression risk and prevention related to the formation and recall of positive memories.

Funding Source(s): NIH K01MH104325
**Presenter:** Gina Sequeira, MD  
**Education:** Tulane University School of Medicine  
**Current Position:** Pediatric Resident, Children’s Hospital of Pittsburgh  
**Principal Area of Research Interest:** Transgender Health  
**Current Research Support:** Beckwith Foundation (PI: Dana Rofey)  
**Mentor(s):** Dana Rofey, PhD and Elizabeth Miller, MD, PhD

**Impact of gender expression on disordered eating, body dissatisfaction and BMI in a cohort of transgender youth**  
**Author(s):** Sequeira G, Miller E, McCauley H, Eckstrand K, Rofey D  
**Affiliation(s):** 1Children’s Hospital of Pittsburgh, 2Michigan State University, 3Western Psychiatric Institute and Clinic, 4University of Pittsburgh

**Study:** Transgender and gender nonconforming (TGNC) youth report higher rates of body dissatisfaction and disordered eating than their cisgender peers. Despite this, systematic screening tools and evidence-based treatment for disordered eating have not yet been developed for TGNC youth. Gender affirming care may impact body dissatisfaction and disordered eating, which arise in the context of gender dysphoria; however, the extent to which gender affirming care affects body dissatisfaction and disordered eating remains unclear. The objectives of this study were to evaluate the association between gender identity, body mass index (BMI), disordered eating behaviors, and body image in transgender adolescents and investigate the impact gender affirming hormone therapy has on body dissatisfaction and disordered eating.

**Methods:** The sample included patients participating in a TGNC support group, who self-identified as transgender. Participants were classified as either transwomen (n=18 [M=15.7 yrs]) or transmen (n=32 [M=14.3 yrs]). Data were collected over a 6-month period. All participants completed measures of body dissatisfaction and disordered eating behaviors using the Stunkard Figure Rating Scales and Eating Attitudes Tests. Gender affirming care was measured based on whether participants initiated pubertal blockers or cross sex hormones. Data were analyzed using ANOVA and paired T-tests.

**Results:** Transmen had greater overall body dissatisfaction F(1,2)=2.13, p < .05 than transwomen and cisgender controls. Both transwomen and transmen had more symptoms of disordered eating than controls (F(1,2)=1.99 and F(1,2)=1.67, p < .05 respectively). At six months, 11% of participants were receiving pubertal blockers and 28% cross sex hormones. Individuals that initiated hormone therapy (n=18), had lower levels of body dissatisfaction (t(31)=2.31, p < .05) and disordered eating (t(31)=1.78, p < .05). Transwomen had 1.20 kg/m2 lower and transmen 1.31 kg/m2 higher BMIs than cisgender controls.

**Conclusion:** TGNC identity is associated with body dissatisfaction and puts youth at high risk for disordered eating behaviors. Initiation of gender affirming hormone therapy is beneficial in alleviating body dissatisfaction and disordered eating, though, larger studies are needed.

**Significance:** Assessment for unhealthy body-related thoughts and behaviors is important to the clinical care of TGNC adolescents.

**Funding Source(s):** Beckwith Foundation (PI: Dana Rofey)
**Presenter:** Anna Shafer  
**Education:** University of Pittsburgh  
**Current Position:** Student  
**Principal Area of Research Interest:** Schizophrenia  
**Current Research Support:** NIH MH094328, NIH R01 MH108568, NIH P50 MH103204  
**Mentor(s):** Brian A. Coffman, PhD and Dean F. Salisbury, PhD

**Reduced mismatch negativity is associated with decreased Heschl’s gyrus volume in first episode schizophrenia**  
**Author(s):** Shafer A\(^1\), Coffman BA\(^1\), Murphy TK\(^1\), Haigh SM\(^1\), Luna B\(^1\), and Salisbury DF\(^1\)  
**Affiliation(s):** \(^1\)Department of Psychiatry, University of Pittsburgh School of Medicine

**Study:** Primary auditory cortex (Heschl’s gyrus) pathophysiology is linked to auditory deficits and auditory verbal hallucinations in schizophrenia. In an earlier study, Dr. Salisbury and colleagues found a correlation between reductions in the magnitude of the pitch-deviant mismatch negativity (MMN) response during a passive auditory task and reductions in gray matter volume in Heschl’s gyrus in subjects with first-episode schizophrenia (FESz). The aim of this study was to replicate these findings in a larger sample, and to expand the findings to include duration-deviant MMN.

**Methods:** Participants included 28 FESz and 28 healthy control subjects matched for age, parental socioeconomic status, IQ, sex, race, and handedness. High-resolution T1-weighted structural MRI data (3T) were acquired for each subject. Freesurfer was used to segment white matter, gray matter, and pial surfaces on the structural MRI image. The boundary between gray and white matter in Heschl’s gyrus was then hand-traced following the method of Barta et al. (1995). For MMN, standard tones were presented repeatedly (1kHz, 75 dB, 50 ms pips, 5 ms rise/fall times, 330 ms SOA), with occasional pitch-deviants (1.2 kHz, 10% of trials) and duration-deviants (100 ms, 10% of trials) interspersed. Pitch and duration MMN (pMMN, dMMN, respectively) were measured as the averaged amplitude within a 100-ms window at Fz.

**Results:** In FESz, there was a significant correlation between the magnitude of pMMN and total gray matter volume in Heschl’s gyrus (TGMV, \(r = -0.38, p < .05\)), and between dMMN and TGMV (\(r = -0.44, p < .05\)). There were no significant correlations within the healthy control group, and the pathological correlation between pMMN and TGMV in FESz was significantly different from healthy controls (Fisher’s Z =1.9, \(p < .05\)), while dMMN showed marginally significant difference (Fisher’s Z =1.6, \(p = .06\)).

**Conclusion:** Smaller Heschl’s gyrus in FESz is related to a smaller magnitude MMN for both pitch- and duration-deviants.

**Significance:** The relationship between MMN amplitude and Heschl’s gyrus volume in FESz suggests the presence of pre-psychosis gray matter loss in a subset of patients, and may be useful for tracking disease progression and as an outcome measure of clinical interventions.

**Funding Source(s):** NIH R01 MH108568, NIH P50 MH103204, NIH MH094328
Postpartum psychological distress associated with systematized emergency team response during labor and delivery

Author(s): Silverstein RG, Centore M, Pollack A, and Lim G
Affiliation(s): 1Department of Anesthesiology, University of Pittsburgh School of Medicine

Study: Post-traumatic stress disorder (PTSD) and acute stress disorder (ASD) can occur after perceived traumatic childbirth. Utilization of an emergency team response (ETR) during labor and delivery has not been extensively studied as a potential risk factor for postpartum ASD and PTSD. The purpose of this pilot study was to evaluate the feasibility and acceptability of a study protocol aimed at determining the relationship between ETR and ASD and PTSD symptoms.

Methods: For this IRB-approved prospective observational study, participants undergoing childbirth between June 6 and July 1, 2016 were approached. Participants filled out validated questionnaires within 72 hours and at six weeks postpartum, including: ASD screening (Stanford Acute Stress Reaction Questionnaire, SASRQ); PTSD screening (Post-Traumatic Stress Disorder Checklist for Civilians, PCL, and Impact of Events Scale, IES); and measures of anxiety, social support, and pain. The primary outcome was PTSD (IES and PCL scores) at six weeks. The secondary outcome was ASD (SASRQ score) within 72 hours. Recruitment, retention rates and sample size for a fully powered study were calculated. ETR and non-ETR groups were compared by the Mann-Whitney U Test. A P-value of <0.05 was required to reject the null hypothesis.

Results: Of 564 eligible women, 369 sought more information and 249 were enrolled (67.5% recruitment rate). Of enrollees, 207 completed the 72-hour questionnaires, and 125 participants completed all the study procedures (50.2% retention). Twenty women experienced an ETR (3.5% event rate). Of these, 12 enrolled in the study (60.0% recruitment rate), nine completed the 72-hour questionnaires, and eight completed the study (66.7% retention). The ETR group had higher PTSD scores in both the PCL (medians = 16, 2; U = 305.5; P = 0.08) and the IES (medians = 22.5, 20; U = 298.5; P = 0.08). ASD scores were not different between groups. A sample size of 88 (44 in each group) is needed to detect an effect of ETR on postpartum PTSD as measured by IES, and a sample size of 360 (180 in each group) is required if the primary outcome is assessed by PCL (power = 80%, significance level α=0.05).

Conclusion: This study methodology investigating the effect of ETR on postpartum psychological distress is feasible and acceptable to patients and providers. A trend toward a relationship between ETR and PTSD symptoms is demonstrated.

Significance: The effect of ETR on postpartum psychological distress is a significant question because it could inform health care providers’ ability to target high-risk women for support.

Funding Source(s): NIH UL1-TR-001857 (Clinical and Translational Science Institute)
Pseudophosphorylation of MAP2c increases MAP2 protein accumulation

Author(s): Sun X\textsuperscript{1}, Salsovic JJ\textsuperscript{2}, and Sweet RA\textsuperscript{3,4,5*}

Affiliation(s): \textsuperscript{1}Tsinghua University; \textsuperscript{2}University of Pittsburgh; \textsuperscript{3}Translational Neuroscience Program, Department of Psychiatry, University of Pittsburgh; \textsuperscript{4}Department of Neurology, University of Pittsburgh; and \textsuperscript{5}VISN4 Mental Illness Research, Education and Clinical Centre (MIRECC), VA Pittsburgh Healthcare System

Study: Microtubule-associate protein 2 (MAP2) is a neuronal phosphoprotein that regulates microtubule dynamics and plays an important role in neurite outgrowth and dendrite development. Alterations in MAP2 expression and phosphorylation has been implicated in multiple human diseases, particularly in schizophrenia. A specific phosphorylated site (S426) in MAP2c was shown to be significantly altered in schizophrenia. However, the mechanism by which MAP2 phosphorylation contributes to neuronal pathology in neurodegenerative and psychiatric diseases is not known.

Methods: Human MAP2c- IRES-EGFP Plasmids are used to overexpress MAP2c protein in HEK293 cells through transfection. S426E/A mutation were introduced into the WT MAP2c plasmid to mimic the presence (E) or lack of (A) phosphorylation at this site. Detection of relative MAP2c expression was achieved using Western Blot. RT-qPCR was used to detect initial mRNA level of overexpressed MAP2. Cycloheximide (CHX) treatment was used to detect the half-life of different MAP2 mutants.

Results: Pseudophosphorylation at S426 site of MAP2c results in increased protein levels compared to WT and S426A mutant in transient transfected HEK293 cells. Data indicating whether the mechanism underlying this accumulation results from transcriptional changes or alteration in protein half-life will also be presented.

Conclusion: Pseudophosphorylation at MAP2c S426 site leads to increased protein levels.

Significance: The present findings indicate that pseudophosphorylation of MAP2c results in its accumulation in cells and provide us a new perspective of potential pathological mechanisms of phosphorylated MAP2 in neurodegenerative and psychiatric diseases.

Funding Source(s): R01 MH071533 (PI: Robert Sweet, MD)
Personality and vulnerability to suicide in the elderly

Author(s): Szücs A\textsuperscript{1}, Szanto K\textsuperscript{2}, Kenneally L\textsuperscript{2}, Aubry J-M\textsuperscript{1}, and Dombrovski AY\textsuperscript{2}

Affiliation(s): \textsuperscript{1}University of Geneva, Faculty of Medicine and \textsuperscript{2}Department of Psychiatry, University of Pittsburgh School of Medicine

Study: In younger adults, Cluster B traits, particularly borderline and impulsive-aggressive, are thought to predispose to suicide. These factors appear to play a smaller role in older adults, but there is no consensus regarding the personality profile that predisposes an individual to suicide in old age. The present work addresses this gap in knowledge by integrating existing evidence in a systematic literature review.

Methods: A systematic literature search has been conducted on PubMed, Google Scholar and PsychInfo using key words grouped in three descriptor fields: personality (33 key words); suicide (6 key words); elderly (7 key words). Criteria for exclusion were: different subject, not a data paper, foreign language, euthanasia, no mapping onto DSM criteria or Five-Factor Model (857 articles). Twenty-three articles were retained, and 6 more were found by reference tracking.

Results: Prevalence of personality disorders as primary diagnoses (0-0.7% for all disorders, 0.05% for borderline) in elderly suicide victims were significantly lower than in younger victims (8.6-11% for all disorders, 1.79% for borderline). In studies where all comorbid diagnoses were considered, personality disorders were present in 14-16% of elderly suicides versus 34% of younger victims. Anankastic (obsessive-compulsive) personality was over-represented among older suicide victims. In addition, elderly victims displayed lower extraversion and higher conscientiousness than healthy controls. One qualitative study of older suicide victims described an introverted and controlling personality profile. The elderly who attempted suicide had higher levels of neuroticism and lower levels of conscientiousness than those who succeeded. The personality profile of older adults who contemplated suicide without ever attempting included high neuroticism as well as borderline and narcissistic personality disorders.

Conclusion: While suicidal ideation in the elderly is associated with Cluster B personality disorders and high neuroticism, obsessional-compulsive traits, low extraversion and high conscientiousness may distinguish the personality profile of older adults who die by suicide.

Significance: Older people who contemplate but do not attempt suicide display externalizing traits, like younger suicidal people. By contrast, rigid personalities are overrepresented among older people who die by suicide. While based on a small body of evidence, these findings suggest that inability to adapt to the social and health changes of aging is a key vulnerability factor in late-life suicide.

Funding Source(s): None
Gamma oscillations in auditory steady-state stimulation among adolescents with psychosis

Author(s): Tarcijonas G, Nuutinen MR, and Bachman P

Affiliation(s): 1Department of Psychiatry, University of Pittsburgh School of Medicine

Study: Schizophrenia is associated with a variety of neurocognitive deficits which are thought to be caused by dysfunctional neuronal connectivity. Evoked auditory steady-state responses (ASSRs) in the gamma (30-50 Hz) range of frequencies are thought to reflect synchronization mediated by rhythm-generating parvalbumin γ-aminobutyric (GABA) interneurons and N-methyl-D-aspartate (NMDA) receptors, and are abnormal in schizophrenia. Adult patients have been shown to exhibit a reduction in both spectral power and phase synchronization ability during 40-Hz stimulation, but it has yet to be found whether patients with psychosis exhibit similar deficits.

Methods: Participants included 35 adolescents with early course psychosis and 32 healthy controls, all ages 12-21. Electroencephalography (EEG) was used to detect 20-, 30-, and 40-Hz ASSRs.

Results: Our results indicate significant abnormalities in gamma power at multiple electrode locations over the right hemisphere in the psychosis group when compared to controls. Surprisingly, our results show both an expected 40-Hz ASSR power decrease as well as a power increase early after stimulus onset.

Conclusion: Gamma power abnormalities between the early course psychosis group and healthy controls suggest differences in local cortical circuit activity associated with psychosis. The observed power decrease may be indicative of delayed gamma amplitude development in adolescents with psychosis.

Significance: The present study begins the characterization of ASSRs in psychotic adolescents in hopes of better understanding the development of neuronal connectivity in schizophrenia.

Funding Source(s): NIMH grant K23 MH097040 (PI: Peter Bachman, PhD), and Department of Psychiatry, University of Pittsburgh School of Medicine
Early cannabis use and neurocognitive risk: A prospective cohort fMRI study

Author(s): Tervo-Clemmens B\textsuperscript{1}, Calabro F\textsuperscript{2}, and Luna B\textsuperscript{1,2}
Affiliation(s): \textsuperscript{1}Department of Psychology, University of Pittsburgh and \textsuperscript{2}Department of Psychiatry, \textsuperscript{3}University of Pittsburgh School of Medicine

Study: Previous research suggests cannabis onset during early adolescence (prior to 16-years-old) may increase the risk for later working memory impairment. However, to-date, the majority of functional neuroimaging research examining this relationship has been retrospective and cross-sectional. Therefore, it is unknown whether neurocognitive function prior to cannabis use predicts onset, partially explaining effects reported in retrospective studies.

Methods: A high-risk prospective cohort neuroimaging study was conducted where participants (N = 90) were initially assessed at age twelve, prior to any reported cannabis use (baseline), and then again at age fifteen (follow up). By follow up, approximately 25% (n=24) of the sample reported using cannabis. At both visits, subjects performed a visuospatial working memory (WM) task during fMRI acquisition.

Results: Participants who would go onto use cannabis by age 15 had lower WM accuracy at baseline and follow up (p’s < .05). WM differences between the cannabis group and non-users did not change between visits (p = .734). At baseline, those who would go onto use cannabis by 15 displayed increased BOLD activation in the inferior parietal lobule (IPL) and dorsolateral prefrontal cortex (DLPFC) and decreased activation in the precuneus and visual association cortices (BA 18) (p’s < .05. voxelwise correction) during correct trials. At follow up, only the IPL and BA 18 continued to show group differences. Activation in the posterior cingulate, which did not differ between groups at baseline, was significantly greater in the cannabis group at follow up (p < .05, voxelwise correction). However, activation in the posterior cingulate was not related to WM performance (p = .997).

Conclusion: At baseline, results show poorer WM performance and limitations in frontoparietal cognitive control systems in 12-year-old subjects who would go onto initiate cannabis use by 15. At follow up, results show 15-year-old users maintain poorer WM performance and the difference between users and non-users does not increase following cannabis initiation.

Significance: Purported WM effects of early cannabis onset may not be causally related to cannabis initiation but instead driven by inherent limitations or immaturities in WM systems predictive of substance use.

Funding Source(s): PA-HEAL Program Sap #4100055579 (PIs: David Lewis, MD, Beatriz Luna, PhD)
Health behaviors by adolescents with ADHD: Associations with ADHD symptoms and symptom subtype

Author(s): Tiani A\textsuperscript{1}, Pedersen S\textsuperscript{1}, White S\textsuperscript{1}, Dawkins M\textsuperscript{1}, Engster S\textsuperscript{1}, Green C\textsuperscript{1}, Hunter D\textsuperscript{1}, Joseph H\textsuperscript{1}, Kipp H\textsuperscript{1}, Kolko D\textsuperscript{1,2}, and Molina BSG\textsuperscript{1,2}

Affiliation(s): \textsuperscript{1}Department of Psychiatry, University of Pittsburgh School of Medicine and \textsuperscript{2}Department of Psychology, University of Pittsburgh

Study: Research findings support a link between Attention Deficit Hyperactivity Disorder (ADHD) and elevated BMI (Waring & Lapane, 2008). ADHD is also associated with health risk behaviors (less sports and physical activity participation and more substance use) (Kim et al., 2011). Little is known about ADHD symptoms and health behaviors within treated adolescents. We hypothesized that increased ADHD symptom count will be associated with increased BMI, decreased physical activity and sports engagement, reduced sleep, and increased substance use.

Methods: Participants included 169 adolescents (boys n=132, 78%; girls n = 37, 22%) aged 13-18, and treated for ADHD with stimulant medication by a primary care provider. Participants were recruited for a study of management of ADHD treatment and completed a survey which included items about height, weight, sleep, substance use, and ADHD symptoms.

Results: After controlling for age, gender, and race, hyperactive symptoms were significantly associated with cigarette smoking frequency ($r = .231, p =.003$) and marginally associated with number of cigarettes smoked per day ($r = .135, p =.088$). Inattentive symptoms were marginally associated with lifetime marijuana use ($r = .149, p =.059$), as well as marijuana use in the past 6 months ($r = .131, p =.096$). ADHD symptoms were not significantly related to BMI, exercise, sports engagement, or sleep. Future analyses will examine parent report of teen ADHD symptoms and prescribed stimulant use in relation to these same variables.

Conclusion: Hyperactive and inattentive symptoms showed differential associations with cigarette and marijuana use, which may suggest that ADHD symptom type influences substance choice. No association was found between number of self-reported ADHD symptoms and decreased health behaviors. Our health behavior questions did not assess diet, sport type, or amount of physical exertion. Better measurement may yield different results.

Significance: These findings highlight the potential value of adolescent self-reported ADHD symptoms in relation to substance use. Additionally, these findings suggest that among treated adolescents, conversations with doctors and parents about how ADHD may put them at an increased risk for substance use may be beneficial.

Funding Source(s): DA040213 (PI: Brooke Molina, PhD)
Clustering emotion dysregulation in autism spectrum disorders

Author(s): Transue E\(^1\) and Mazefsky C\(^1\)
Affiliation(s): \(^1\)Department of Psychiatry, University of Pittsburgh School of Medicine

Study: In addition to the diagnostic features of Autism Spectrum Disorders (ASD), many children with ASD have prominent emotional problems or challenging behaviors, such as anxiety, depression, frequent tantrums, self-injury, or aggression. Studies have begun investigating the relevance of emotion regulation to understanding clinical presentation in ASD. Cluster analysis is a method to reveal phenotypic groupings of emotion dysregulation and the subsequent associations between this dysregulation, core ASD symptoms, and other symptoms.

Methods: Subjects included 1053 patients aged (6-18) with ASD from two combined samples (patients from six specialized child psychiatry hospital units via the Autism Inpatient Collection and a national online registry via the Interactive Autism Network). Primary measures included the Child Behavioral Checklist (CBCL), Emotion Dysregulation Inventory (EDI), Social Communication Questionnaire (SCQ), and Aberrant Behavior Checklist (ABC).

Results: Cluster analysis of CBCL items from the anxious/depressed, withdrawn/depressed, rule-breaking behavior, and aggressive behavior scales revealed three clusters. Clusters were stratified by emotional and behavioral symptom severity, such that one cluster had the least impairment, another had moderate impairment, and the final cluster had the most severe impairment. Clusters significantly differed on both CBCL and ABC subscales indicative of a range of concerns, in the same severity order. The least impaired cluster had fewer inpatient participants, fewer females, and more minimally verbal youth. The severe cluster had slightly but significantly more severe ASD symptoms than the other two clusters. The groups were equivalent in age. Logistic regression demonstrated that EDI Reactivity scores were strongly predictive of group membership.

Conclusion: Contrary to emotional and behavioral symptoms falling along internalizing versus externalizing or traditional psychiatric diagnostic lines, cluster analysis revealed three groups with different degrees of severity across a broad range of emotional and behavioral problems. This pattern suggests that a shared underlying mechanism such as poor emotion regulation may contribute to maladaptive emotional and behavioral functioning in ASD.

Significance: The identification of ASD subgroups based on emotional and behavioral patterns may aid in the identification of underlying mechanisms and potential treatment targets.

Funding Source(s): NICD R01HD079512 (PI: Carla Mazefsky, PhD); Simons Foundation Autism Research Initiative and the Nancy Lurie Marks Family Foundation, (SFARI #296318 to M. Siegel)
Study: Circadian rhythm disruptions commonly occur in mood disorders. Recent clinical findings suggest that phase delayed rhythms more commonly occur during depressive episodes, whereas phase advanced rhythms more frequently occur during manic episodes. The suprachiasmatic nucleus (SCN) synchronizes bodily rhythms with the environment, and may underlie the misaligned rhythms observed in mood disorders. Recently, disrupting molecular rhythms in the SCN was shown to cause mood-like disturbances in mice, suggesting that disrupting SCN neural activity rhythms may affect mood. Thus, here our goal was to develop a model system to determine if phase-delaying and phase-advancing manipulations of SCN neural activity have differential effects on mood-like behaviors.

Methods: Channelrhodopsin-2 (ChR2) was genetically introduced into the SCN by crossing mice expressing Cre recombinase in GABAergic neurons with mice expressing Cre-dependent ChR2. Optic fibers were implanted above the SCN and mice were housed in cages equipped with piezoelectric floor sensors to monitor circadian rhythms and sleep. Mice were then placed in constant darkness (DD) to observe their SCN-driven rhythms. Mice subsequently received stimulations (1 h, 10 ms pulse width, 8 Hz) every three days at times early or late into their active phase to induce phase delays or phase advances, respectively. After six stimulation sessions, mood-like behaviors were assessed.

Results: Stimulating the SCN early in the active phase induced phase delays, increasing the period of activity rhythms (24.40 ± 0.06 hr) relative to control mice (24.13 ± 0.06 hr). Stimulating the SCN late in the active phase induced phase advances, decreasing the period of activity rhythms (23.55 ± 0.07 hr) relative to controls (23.95 ± 0.02 hr). We did not find effects of the stimulation paradigms on mood-like behaviors in these small cohorts (n = 5-8 per group).

Conclusion: Optogenetic stimulation of GABAergic neurons in the SCN induced phase shifts in circadian activity rhythms, resembling the known effects of light pulses applied in DD.

Significance: We developed a model system to determine the role of SCN-mediated phase shifts in circadian rhythms on mood-like behaviors.

Funding Source(s): NIMH R01 MH106460 (PI: Colleen McClung, PhD) and NIMH R01 MH077159 (PI: Colleen McClung, PhD)
Global probabilistic tractography and symptom dimensions in a prospectively characterized sample of adults with a childhood diagnosis of ADHD

Authors: Versace A, Allen B, Jones N, Pelham W, Molina B, and Ladouceur C
Affiliation(s): 1Department of Psychiatry, University of Pittsburgh School of Medicine

Study: White matter abnormalities have been shown to play an important role in the pathophysiology of Attention Deficit-Hyperactivity Disorder (ADHD). However, little is known about the extent to which ADHD symptom severity is associated with abnormalities in white matter tracts known to be involved in attention and emotional control processes.

Methods: In the present study, we aimed to determine if abnormalities in fronto-temporal white matter tracts involved in attention (superior longitudinal fasciculus, SLF) and emotional control processes (uncinate fasciculus, UF) relate to clinically relevant symptom-dimensions in 46 adults with or without ADHD (32 ADHD, 14 non-ADHD; mean age[SD]=33[3] years, 44 males), recruited from an ongoing longitudinal study in 347 children with ADHD prospectively characterized from youth-to-adulthood. Symptom-dimensions of inattention, hyperactivity/impulsivity (H/I), and anger-irritability (A/I) were used. Global probabilistic tractography was used to reconstruct SLF and UF. Volume, length, and diffusivity metrics were extracted for each participant.

Results: ADHD, vs non-ADHD, adults showed higher volume in the right UF (p=.05) and right SLF (p=.06). In ADHD adults, H/I symptoms were negatively correlated with length in the SLF (left: r=-.40, p=0.01; right: r=-.40, p=0.03) and A/I symptoms were positively correlated with volume of the right UF (r=0.40,p=0.04).

Conclusion: Findings suggest that higher volumes in fibers connecting medial-temporal and orbitofrontal regions might be associated with higher severity of A/I symptoms. Abnormal reorganization of the fibers connecting the DLPFC and tempo-parietal regions, as evidenced by a shorter length in the SLF, may represent a neurobiological substrate of higher levels of H/I symptoms, possibly associated with inability of modulating thoughts and actions in goal-directed behaviors reported in ADHD.

Significance: In the present study, diffusivity measures did not correlate significantly with symptom-dimensions of interest; however, diffusivity measures in a given tract reflect the average coherence of the fibers across this entire tract. On the other hand, structural (higher volume and shorter length of the fibers) abnormalities are usually associated with lower coherences of the fibers in proximity of the cortex (i.e., fibers that fan-out into the cortex occupy a larger volume and the reconstruction of the fiber terminates prematurely due to the drop-off of fractional anisotropy) and might be more sensitive indexes of structural connectivity.

Funding Source(s): MH101096-03 (MPI: Brooke Molina, PhD; Cecile Ladouceur, PhD)
Paternal age at birth of child with ASD and its association with symptom severity

Author(s): Vezzoli J, Santangelo S, Mazefsky C, and the Autism Inpatient Collection (AIC)
Affiliation(s): 1Department of Psychiatry, University of Pittsburgh School of Medicine and 2Maine Medical Center Research Institute

Study: Research suggests that paternal age at time of a child’s birth is associated with prevalence of Autism Spectrum Disorder (ASD). Fathers aged 40 and above are 2.2-6 times more likely to father a child with ASD than fathers younger than 40. Although ASD presentation is markedly heterogeneous, no previous research has been conducted to determine if paternal age is related to the severity of symptoms of ASD. We hypothesized that higher paternal age at time of child’s birth would be positively correlated with more severe behaviors and symptoms in their affected children.

Methods: Subjects included fathers (n=403) aged 17 to 61 at time of birth of ADOS-2 confirmed ASD patients (age 4-21) who participated in the Autism Inpatient Collection study. Parent report data were collected on their child’s emotion dysregulation, self-injurious behavior, adaptive behavior, and on family demographic and psychiatric history, aberrant behavior, and ethnicity. Assessments included the ADOS-2 and nonverbal IQ. Psychiatric comorbidities were recorded by the attending psychiatrist and unit clinician. Paternal age was evaluated for statistical correlation with the child’s behavioral, demographic, and psychiatric data.

Results: Paternal age at child’s birth was not significantly correlated with severity of scores on the EDI (reactive, dysphoria), ADOS-2 comparison score, Nonverbal IQ, SIB (RBS-R), Adaptive Behavior Composite (VABS), or number of full or half siblings with ASD diagnoses. Psychiatric comorbidities and ABC subscale scores did not significantly differ between fathers of different age brackets at the time of the child’s birth (<24, 25-29, 30-35, 35-40, 40+).

Conclusion: Paternal age at child’s birth was not associated with the severity of behavior and functioning of psychiatric inpatients with ASD. Comparisons of pertinent child characteristics and family factors also did not differ between fathers who were in different age categories at their child’s birth.

Significance: Although greater paternal age at child’s birth has been shown to increase the risk of having a child with ASD, our findings suggest that it does not influence the child’s severity or behavioral presentation. Given that the entire sample were psychiatrically hospitalized, future efforts will incorporate ASD community and outpatient samples to increase sample representativeness.

Funding Source(s): Simons Foundation Autism Research Initiative and the Nancy Lurie Marks Family Foundation, (SFARI #296318; PI: M. Siegel.), NIH R01HD079512 (PI: Carla Mazefsky, PhD)
Predicting self-injurious thoughts and behaviors over time: The roles of self-conscious emotions and interpersonal stress

Author(s): Victor SE\textsuperscript{1,2}, Stepp SD\textsuperscript{1}, and Scott LN\textsuperscript{1}
Affiliation(s): \textsuperscript{1}Department of Psychiatry, University of Pittsburgh School of Medicine; \textsuperscript{2}Department of Psychology, University of British Columbia

Study: Self-injurious thoughts and behaviors (SITB) are strongly associated with self-conscious emotions (SCE), including self-criticism and shame. However, existing research has not addressed how these constructs function at the state and trait levels to predict SITB in daily life, as well as how interpersonal stress, such as perceived rejection or criticism (PRC), may moderate the relationship between SCE and SITB. In this study, we examined main and interactive effects of SCE and PRC on SITB during a 21-day ecological momentary assessment (EMA) protocol.

Methods: Young adult (18-24) women enrolled in the Pittsburgh Girls Study who reported recent SITB or aggression were recruited to complete questionnaires, semi-structured interviews, and an EMA protocol, which included 7 assessments (“beeps”) per day for 21 days. Measures included depression, past year SITB, EMA compliance, EMA SITB, EMA SCE, and EMA PRC. We used multilevel modeling to estimate fixed effects of within-persons and between-persons predictors on SITB; within-persons predictors were lagged so beep \( t-1 \) predicted SITB at beep \( t \).

Results: SCE was associated with higher odds of SITB during the EMA for both mean SCE (between-persons) predicting any SITB during the EMA and for beep \( t-1 \) SCE (within-persons) predicting SITB at beep \( t \). These results were statistically significant when controlling for relevant covariates such as depression, past year SITB, and EMA compliance. Similarly, PRC was associated with EMA SITB for both mean PRC (between-persons) and beep \( t-1 \) PRC (within-persons) above and beyond known covariates. When SCE, PRC, and their interaction were modeled jointly, mean SCE and PRC were no longer associated with SITB; however, higher beep \( t-1 \) SCE was significantly associated with beep \( t \) SITB. Higher beep \( t-1 \) PRC was associated with higher odds of beep \( t \) SITB, although this relationship was not statistically significant. The interaction between SCE and PRC was not a significant predictor of SITB.

Conclusion: State SCE is associated with increased likelihood of later SITB in an at-risk sample of young adult women, above and beyond known correlates of SITB, including depression, past SITB, and interpersonal stress.

Significance: These results highlight the importance of understanding momentary affect and its potentially causal role in the development of SITB, with implications for development of prevention and intervention strategies targeting SITB in daily life.

Funding Source(s): NIMH K01 MH101289 (PI: Lori Scott, PhD), AFSP Young Investigator Grant (PI: Lori Scott, PhD)
Presenter: Monica Walker Payne, MA  
Education: Duquesne University  
Current Position: Evaluation Director, Youth and Family Training Institute  
Principal Area of Research Interest: High Fidelity Wraparound  
Current Research Support: OMHSAS / Community Care Behavioral Health Organization  
Mentor(s): Kenneth C. Nash, MD, MMM

Evaluating youth peer support within high fidelity wraparound: Defining roles, tracking progress, and exploring preliminary outcomes  
Author(s): Payne MW, Owens C, Nash K, Dan D, Jones L  
Affiliation(s): ¹ Department of Psychiatry, University of Pittsburgh School of Medicine; ² Youth and Family Training Institute; and ³ Community Care Behavioral Health Organization

Study: High Fidelity Wraparound (HFW) is a youth-guided and family-driven planning process that follows a series of phases, principles, and activities to help youth with complex mental health issues and multi-system involvement. The Youth and Family Training Institute has a standardized training and coaching model for the Youth Peer Support Partner role in HFW, and thus has been able to evaluate peer support and show positive outcomes as a result of HFW.

Methods: The HFW Chart Form Evaluation is implemented in 15 counties state-wide and has a total of 30 Youth Peer Support Partners in the workforce. 986 youth (age range 0-26) and their families in HFW have been evaluated through contact notes and a pre-post evaluation.

Results: Youth Peer Support Partners spend 91% of their time in face-to-face contact with youth/families that they work with. 49% of their time is spent in the youth/family home, 23% is spent in community locations, 11% is spent in schools, 11% is spent in office locations, 3% is spent in court, and 3% is spent in other locations. Youth Peer Support Partners utilize the following 5 skills the most in their contact notes. Providing support for the youth (59%), providing support for the family (23%), identifying new areas of need (28%), identifying new strengths (22%), and brainstorming new ideas (22%). Youth Peer Support Partners begin with 38.1% of contacts “Doing For” and only 3.9% of contacts “Cheering On.” By the end of the process, this is shifted to only 5.9% of contacts “Doing For” and 44.8% of contacts “Cheering On.” Family Vision ratings (on a scale of 1/low – 10/high) at the start of the process average a 1.82 and increase to an average of 7.86 by transition/graduation. High-level Behavioral Health Services decrease utilization from 56.0% of youth at Intake to 17.2% of youth at Discharge.

Conclusion: HFW (including standardized youth peer support) is associated with an increase in Family Vision ratings, a decrease in High-level Behavioral Health Services and in the teaching and transferring of skills to youth and families.

Significance: Findings indicate the importance of utilizing the HFW process for those who are the hardest to reach and result in the highest cost to the child-serving systems.

Funding Source(s): Pennsylvania Office of Mental Health and Substance Abuse Services (PI: Kenneth Nash, MD, MMM); Community Care Behavioral Health Organization; and the Department of Psychiatry, University of Pittsburgh School of Medicine
Role of genetically-influenced 5-HT functioning in a bifactor model of psychopathology

Author(s): Wang F¹, Chung T², Vanyukov M¹,², Maher B³, and Ye F⁴

Affiliation(s): ¹Department of Psychiatry, University of Pittsburgh School of Medicine; ²Department of Pharmaceutical Sciences and Human Genetics, University of Pittsburgh; ³Department of Mental Health, Johns Hopkins Bloomberg School of Public Health; ⁴Department of Psychology in Education, University of Pittsburgh School of Education

Study: Models of psychopathology propose unique etiological factors that differentiate disorders lying on internalizing and externalizing spectra of psychopathology, and general risk to develop mental illness (general psychopathology factor). The serotonergic (5-HT) system might contribute to variation in risk for multiple psychiatric conditions, influencing general liability towards psychopathology. This study examined a polygenic score indexing 5-HT functioning as a predictor of a general psychopathology factor, and of internalizing and externalizing sub-factors in the Center for Education and Drug Abuse Research (CEDAR) project.

Methods: CEDAR participants (N=227; 72.7% male) were assessed at three waves (T1: 17-20 years; T2: 20-23 years; T3: 24-26 years). Analyses included non-Hispanic Caucasian (to control for population stratification) offspring, whose fathers had substance use disorders (high average risk, HAR; N=112) or no psychiatric disorder (low average risk, LAR; N =115). At T1-T3, participants reported internalizing and externalizing symptoms on the Achenbach Self Report Form. The polygenic score was computed using results from an independent genome-wide association study of 5-HIAA concentrations in the cerebrospinal fluid (Luykx et al., 2014). Structural equation modeling tested associations of the polygenic score with a bifactor model that included 3 waves of data, with correlated uniquenesses to model time-specific variance.

Results: The bifactor model was comprised of a general psychopathology factor on which all T1-T3 subscales loaded (attentional problems, aggression, delinquency, anxiety, somatic problems, and social withdrawal), and specific fear (T1-T3 anxiety and somatic problems), distress (T1-T3 social withdrawal symptoms), and externalizing (T1-T3 aggression, delinquency) factors. The bifactor model fit the data adequately (RMSEA=0.08, CFI=0.93, SRMR=0.06). For the LAR group only, lower polygenic scores (i.e., lower 5-HT functioning) were associated with higher general psychopathology (β = -0.29, p = 0.01). Polygenic score did not predict any other factor.

Conclusion: Among LAR, 5-HT functioning might increase the risk for multiple psychiatric conditions because it influences individuals' general liability towards psychopathology.

Significance: 5-HT functioning, indexed by the polygenic score, might help to explain the etiology underlying psychiatric comorbidity through the general psychopathology factor.

Funding Source(s): National Institute on Drug Abuse P50DA005605 (PI: Ralph Tarter, PhD)
Transcallosal auditory connectivity in first episode schizophrenia

Author(s): Wang Y1, Coffman BA1, Murphy TK1, Luna B1, Yeh F-C1, and Salisbury DF1
Affiliation(s): 1Department of Psychiatry, University of Pittsburgh School of Medicine

Study: Auditory verbal hallucinations (AVH) are one of the most common symptoms in schizophrenia. Connectivity between left and right auditory cortices may be related to AVH. The aim of this study was to examine transcallosal auditory cortex connectivity in first-episode schizophrenia patients (FESz) with and without AVH by contrast with healthy comparison individuals.

Methods: Diffusion spectrum imaging (DSI) data were obtained from 23 healthy controls (HCs) and 29 FESz, 14 of which were AVH+ with a score of at least a 2 on auditory hallucinations, voices commenting, or voices conversing measured with the Scale for the Assessment of Positive Symptoms (SAPS); 15 were AVH-. The three groups (AVH+, AVH-, and healthy controls) were matched for age, parental socioeconomic status, years of education, IQ, gender, and handedness. A deterministic fiber tracking algorithm was used to identify the transcallosal auditory white matter tract, which was defined as 1000 fibers passing through the posterior third of the corpus callosum and ending bilaterally in Brodmann’s area 22, Heschl’s gyrus, or planum temporale.

Results: MANOVA revealed a difference in transcallosal auditory cortex connectivity between groups (F(6, 94) = 2.34, p = .038) driven by tract volume (F(2, 49) = 3.46, p = .039) and generalized functional anisotropy (gFA, F(2, 49) = 4.77, p = .013). Pairwise t-tests indicated lower gFA and greater tract volume for AVH+ vs AVH- (p’s < .05). HCs trended towards greater gFA (p = .068) vs AVH+ and tract volume (p = .063) vs AVH-. All other comparisons were nonsignificant (p > .1).

Conclusion: AVH+ FESz have less efficient transcallosal auditory connectivity as reflected in reduced directionality in fiber tracts. By contrast, AVH- individuals may have reduced structural connectivity between auditory cortices as reflected in smaller tract volume.

Significance: These findings suggest interhemispheric auditory cortex functional connectivity abnormalities may underlie AVH in schizophrenia even early in disease course, while overall structural connectivity differences may play a role in AVH- individuals. Thus, symptom-level phenotypes may be related to differences in white matter interhemispheric connectivity.

Funding Source(s): NIH R01 MH108568, NIH P50 MH103204
Increased cerebral blood flow in middle and posterior cingulate is associated with improvement in depression severity in a longitudinal treatment trial of late-life depression

Affiliation(s): 1Central South University Xiangya Medical School; 2Department of Bioengineering, University of Pittsburgh; 3Keelung Chang Cung Memorial Hospital; and 4Department of Psychiatry, University of Pittsburgh School of Medicine

Study: Treatment of late-life depression (LLD) often requires long trials, which increases the risk of negative health outcomes. Understanding neural changes following treatment may reveal important insights. Low regional cerebral blood flow (CBF) has been shown to be associated with depression; however, post-treatment change trajectories are unclear.

Methods: We used pseudo-continuous arterial spin labeling (pCASL) to investigate CBF changes in a sample of LLD subjects (N=46, 29 female). Participants were enrolled into treatment trial and underwent five magnetic resonance imaging (MRI) scans [baseline (day 1), following a placebo (day 2), following a single dose of venlafaxine (day 3), a week after starting venlafaxine (week 1), and end of trial (week 12)]. Montgomery-Åsberg Depression Rating Scale (MADRS) was used to evaluate depression and treatment outcome.

Results: Increased CBF in the middle and posterior cingulate between baseline and end of the trial was significantly associated with percent decrease of MADRS, and this change was independent of gender and mini-mental status exam (MMSE) score. No significant effects were detected between baseline and other scans.

Conclusion: We showed that regional CBF increase post-treatment is associated with depression improvement. Though we did not detect any significant acute/sub-acute effects, we did observe a trend of early CBF change which requires larger sample size to confirm or reject.

Significance: This supports the vascular depression hypothesis in late-life populations that cerebrovascular disease may predispose, precipitate or perpetuate some geriatric depressive syndromes. Importantly, this may serve as an early marker of treatment response.

Funding Source(s): NIMH R01 MH076079 (PI: Howard Aizenstein, MD, PhD), SR01 MH083660 (PI: Charles Reynolds III, MD), T32 MH019986 (PI: Charles Reynolds III, MD), Educational grant from Central South University Xiangya School of Medicine, Research grant from Keelung Chang Cung Memorial Hospital
**Presenter:** Maribeth Wesesky, BPS  
**Education:** Geneva College/The Pennsylvania State University  
**Current Position:** Research Project Coordinator  
**Principal Area of Research Interest:** Comorbid Alcohol Use Disorders and Major Depressive Disorder  
**Current Research Support:** NIAAA (R21 AA022123) and NIAAA (R21 AA022863)  
**Mentor(s):** Jack R. Cornelius, MD, MPH

---

**Combined young and older adult mirtazapine pilot trials in AUD/MDD**  
**Author(s):** Wesesky MA\(^1\), Cornelius JR\(^1\), Chung TA\(^1\), Douaihy A\(^1\), Fitzgerald D\(^1\), Kirisci L\(^1\), and Salloum I\(^2\)  
**Affiliation(s):** \(^1\)Department of Psychiatry, University of Pittsburgh School of Medicine and \(^2\)University of Miami

**Study:** Results from our recent open label study suggested robust within-group acute phase efficacy for mirtazapine for decreasing both the depression and the drinking of that population.

**Methods:** We now present outcome findings from a combined sample involving two small double-blind placebo-controlled pilot trials (R21AA022123 and R21AA022863) of mirtazapine in AUD/MDD subjects that differed only in the age of the participants (young adult vs. middle-aged adult), including 11 who received mirtazapine and 10 subjects who received placebo. All subjects also received MET therapy.

**Results:** Within-group t tests in the mirtazapine group showed a significant decrease in BDI depressive symptoms by week 2, also noted at all subsequent assessments (wks 3, 4, 6, 8 10 and 12) during the 12-week study. In contrast, no significant decrease in depressive symptoms was noted in the placebo group until week 6, and the magnitude of that improvement was smaller than that seen in the mirtazapine group (11.0 vs. 15.3 points, p=.03 vs p=0<0.0005). Both treatment groups showed significant decreases in both depression and drinking by week 12 of the study, but no significant between-group differences or age effects were noted.

**Conclusion:** These findings suggest acute phase efficacy for mirtazapine for decreasing the depressive symptoms of depressed alcoholics, and suggest that the improvement may occur earlier with mirtazapine, though effects on drinking are less clear.

**Significance:** Large double-blind, placebo-controlled studies are warranted to clarify the efficacy of mirtazapine in depressed alcoholics.

**Funding Source(s):** Supported by NIAAA R21 AA022123 and R21 AA022863 grants.
Rostral-caudal effects of kalirin reduction on dendritic spines in APPSWE/PSEN1dE9 transgenic mice

Author(s): Westbrook KJ\textsuperscript{1}, Erickson SL\textsuperscript{1}, and Sweet RA\textsuperscript{1,2,3}

Affiliation(s): \textsuperscript{1}Department of Psychiatry, University of Pittsburgh School of Medicine; \textsuperscript{2}Department of Neurology, University of Pittsburgh School of Medicine; \textsuperscript{3}Mental Illness Research, Education, and Clinical Care, VA Pittsburgh Healthcare System

Study: Psychotic symptoms, delusions, and hallucinations are common in Alzheimer disease (AD) with patients suffering from this condition showing limited response to existing treatments. Currently, the mechanism by which AD with psychosis (AD+P) advances is unknown. Research suggests that a reduction in kalirin, a guanine nucleotide exchange factor with critical roles in dendritic spine maintenance and growth, in the prefrontal cortices of AD+P patients may play a role in its development.

Methods: Presenilin and amyloid precursor protein transgenic mice (PSAPP) were used as mouse model of AD. Kalirin under-expressers (Kal +/-) were used as a model of kalirin reduction. Eight subjects were used, one to three mice in each genotype: PSAPP + Kal (+/+), PSAPP + Kal (+/-), WT + Kal (+/+), and WT + Kal (+/-). Image stacks of beta-amyloid plaques were collected from rostral and caudal cortical tissue samples from each subject and comparatively analyzed for spine morphology and structural protein content.

Results: Preliminary results indicate that numerous measures of spine size and supporting proteins are elevated in PSAPP + Kal (+/-) subjects compared to PSAPP + Kal (+/+). This effect of genotype was consistent across the two regions studied. In both genotypes, these measures appeared lower in the rostral sections compared to caudal.

Conclusion: These preliminary analyses are consistent with our recently published behavioral findings on the same subjects showing that kalirin reduction rescues behavioral deficits associated with plaque accumulation in the PSAPP + Kal (+/+) model.

Significance: These preliminary findings highlight the importance of future work on establishing a mechanism for the development of AD+P to one day better the lives of patients suffering from the condition.

Funding Source(s): This work was funded by the Veteran’s Health Administration, BX000452.
Contributions of distinct ventral prefrontal subregions to value-based decision-making

Author(s): Wilson J and Dombrovski A
Affiliation(s): ¹Department of Psychiatry, University of Pittsburgh

Study: Signals according with expected value, or the relative worth of available or obtained options, have been mapped to the ventral prefrontal cortex (vPFC) in animal electrophysiological and lesion studies as well as human imaging studies. However, while rodent and primate studies map value signals to the central orbitofrontal cortex (cOFC), human imaging studies consistently uncover value signals in the ventromedial prefrontal cortex (vmPFC). One possible explanation for this seeming discrepancy is the difference in the nature of value representations, i.e. learned value (associative strengths) in human experiments vs. the magnitude of anticipated or obtained reward in animal studies. We hypothesized that, in humans, learned value would be represented in the vmPFC and obtained reward magnitude will be represented in the cOFC.

Methods: Functional magnetic resonance imaging (fMRI) data were collected on 25 healthy individuals. In the scanner participants completed 300 trials of a modified 3-armed bandit task. Reward probabilities changed gradually and independently of one another unbeknownst to the subject. The magnitude of the reward at stake was announced before the subject made a choice, manipulated orthogonally to the learned value (here, estimated reward probability) of the best option. We used a reinforcement learning model to estimate expected value. Parametric regressors corresponding to expected value and reward magnitude signals were inputted to the single-subject GLM predicting voxelwise blood oxygenation level dependent (BOLD). Voxelwise t-tests were performed (p<.0001) and cluster-thresholded at 23 voxels.

Results: Even though reward magnitude was not predictive of future payoffs for a given option, it elicited a behavioral approach tendency. Learned value signals were mapped to the vmPFC and a network of paralimbic cortical regions. By contrast, reward magnitude recruited responses in an associative neocortical network including the cOFC, the anterior cingulate cortex and the frontoparietal network. We will explore the differential effects of these responses on behavior and their relationships with individual differences in impulsivity.

Conclusion: In humans, the central OFC responds to the present characteristics of the reinforcing stimulus, such as magnitude. The vmPFC, on the other hand, integrates reinforcement over time, tracking expected value.

Significance: The contributions of the ventral prefrontal cortex in behavioral adaptation were poorly understood until recently. Computational models of learning and choice help us uncover abstract signals represented in the distinct subregions of the vPFC, and their distinct functional roles.

Funding Source(s): NIMH R01 MH1000095-01A1 (PI: Alexandre Dombrovski, MD)
Stimulation of medial orbitofrontal cortex terminals in ventromedial striatum causes neuroplastic changes in cortical networks

Author(s): Wood J1, Snyder RK1, and Ahmari SE1
Affiliation(s): 1Department of Psychiatry, University of Pittsburgh School of Medicine

Study: Optogenetic stimulation of specific neuronal projections is a powerful tool for dissecting neural circuit function, but the network effects of axon terminal stimulation have not been thoroughly explored. To study these effects, we optogenetically stimulated medial orbitofrontal cortex (mOFC) projections in ventromedial striatum (VMS) while recording electrophysiological activity in mOFC networks during 10 days of repeated ChR2 stimulation.

Methods: mOFC neurons were infected with AAV5-EF1α-FLEX-ChR2-EYFP (channelrhodopsin 2, ChR2) or control in EMX-cre mice, restricting optogenetic expression to mOFC excitatory neurons. 1 month later we implanted tetrode arrays in VMS and mOFC and an optic fiber in VMS. This approach allowed us to record neuronal activity in VMS and mOFC while selectively activating mOFC projections to VMS.

Results: We measured pairwise cross correlations between mOFC neurons in 15-minute periods before and following stimulation. Prior to stimulation, there was no mOFC synchrony in ChR2 animals (0/66 pairs of simultaneously recorded mOFC neurons). Immediately following stimulation, 3% of mOFC neuron pairs had significant cross correlations. Synchrony continued to emerge in mOFC networks. Prior to the final day of optogenetic stimulation (pre-stimulation period in session ten), 6.6% of mOFC pairs fired in synchronous fashion. Optogenetic stimulation induced even greater levels of synchrony, such that 14.3% (13/91 pairs) of mOFC pairs fired synchronously. Significant pairwise synchrony was never detected in control mice.

Conclusion: Terminal stimulation of corticostriatal projections causes antidromic activation and entrainment of mOFC, and induces neuroplastic changes in mOFC networks. Furthermore, because increased cortical synchrony is reflective of increased shared connections between neurons, these data raise the possibility that antidromic activation of corticostriatal projections induces a long-lasting change in connectivity within the cortex.

Significance: Taken together, these findings provide evidence for a novel mechanism through which optogenetic stimulation of specific projections can alter circuit activity and plasticity in a broader manner than previously suspected.

Funding Source(s): NIMH
**Presenter:** Mary L. Woody, MS  
**Education:** Binghamton University (SUNY)  
**Current Position:** Clinical Psychology Predoctoral Intern  
**Principal Area of Research Interest:** Major Depressive Disorder  
**Current Research Support:** Not applicable  
**Mentor(s):** Rebecca Price, PhD and Jennifer Silk, PhD

**Competition effects in visual cortex between emotional distractors and a primary task in remitted depression**

**Author(s):** Woody M\(^{1,2}\), Miskovic V\(^{1}\), Owens M \(^{3}\), James K\(^{1}\), Feurer C\(^{1}\), Sosoo E\(^{4}\), and Gibb B\(^{1}\)

**Affiliation(s):**  
\(^{1}\)Department of Psychiatry, University of Pittsburgh School of Medicine;  
\(^{2}\)Center for Affective Science, Binghamton University (SUNY);  
\(^{3}\)University of South Florida, St. Petersburg;  
\(^{4}\)University of North Carolina, Chapel Hill

**Study**: Attentional biases, particularly difficulty inhibiting attention to negative stimuli, are implicated in risk for major depressive disorder (MDD). The current study examined a neural measure of attentional inhibition by using a continuous index of visuocortical engagement (steady-state visual evoked potentials [SSVEPs]) before and after a negative mood induction in a population at high-risk for MDD recurrence due to a recently remitted MDD (rMDD) episode. Working memory (WM) capacity was examined as a potential moderator of the link between rMDD and visuocortical responses.

**Methods**: The sample consisted of 27 women with rMDD and 28 never-depressed women. To assess attentional inhibition to emotional distractors, we measured frequency-tagged SSVEPs evoked from spatially superimposed task-relevant stimuli and emotional distractors (facial displays of emotion) oscillating at distinct frequencies. WM capacity was assessed during a visuospatial memory task.

**Results**: Women with rMDD, relative to never-depressed women, displayed difficulty inhibiting attention to all emotional distractors before a negative mood induction, with the strongest effect for negative distractors (sad faces). Following the mood induction, rMDD women’s attention to emotional distractors remained largely unchanged. Among women with rMDD, lower WM capacity predicted greater difficulty inhibiting attention to negative and neutral distractors.

**Conclusion**: By exploiting the phenomenon of oscillatory resonance in the visual cortex, we were able to track competition in neural responses for spatially superimposed stimuli differing in valence. Women with rMDD displayed impaired attentional inhibition of emotional distractors independent of state mood and this bias was strongest among those with lower WM capacity.

**Significance**: This study provides a more nuanced and precise understanding of how attentional biases to emotional stimuli may play a role in MDD recurrence and for whom, which is key for individualized models of risk essential for next-generation intervention efforts.

**Funding Source(s):** American Psychological Foundation Ruth G. and Joseph Matarazzo scholarship (PI: Mary Woody, MS), Sigma Xi grant G20141015665524 (PI: Mary Woody, MS), Society for a Science of Clinical Psychology Dissertation grant (PI: Mary Woody, MS), NIMH grant MH098060 (PI: Brandon Gibb, PhD)
Presenter: Eric C. Zimmerman, BS
Education: University of Washington
Current Position: MD/PhD Student
Principal Area of Research Interest: Preclinical circuits relevant to schizophrenia
Current Research Support: NIMH F30 MH109199 and NIMH R01 MH57440
Mentor(s): Anthony A. Grace, PhD

The nucleus reuniens of the midline thalamus gates prefrontal-hippocampal modulation of ventral tegmental area dopamine neuron activity

Author(s): Zimmerman EC\(^1\) and Grace AA\(^{1,2,3}\)
Affiliation(s): Departments of \(^1\)Neuroscience, \(^2\)Psychiatry, and \(^3\)Psychology, University of Pittsburgh

Study: In schizophrenia there is a strong association between exaggerated presynaptic dopamine signaling and psychotic symptoms. However, the afferent regions controlling the activity of ventral tegmental area (VTA) dopamine neurons are not completely characterized. Here, we utilized electrophysiological and behavioral approaches in rodents to investigate the role of a corticothalamic circuit comprised of the infralimbic subdivision of the medial prefrontal cortex (iLPFC), the nucleus reuniens of the midline thalamus (RE), and the ventral subiculum of the hippocampus (vSub), in controlling the activity of VTA dopamine neurons.

Methods: Following pharmacological stimulation of RE, we: 1) performed single-unit recordings of VTA dopamine neurons in anesthetized rats, measuring population activity (number of spontaneously firing neurons), firing rate, and burst firing, and 2) measured amphetamine-induced locomotion, a behavioral correlate of VTA dopamine neuron responsivity. Next, we pharmacologically inhibited iLPFC and measured VTA dopamine neuron activity as above. Finally, we assessed the impact of pharmacological inhibition/electrical stimulation of iLPFC, or projection-specific inhibition (via DREADDs) of iLPFC-RE axons, on firing in RE neurons.

Results: Pharmacological stimulation of RE enhanced VTA dopamine neuron population activity and amphetamine-induced locomotion. The effect of RE stimulation on population activity was prevented if vSub was also inhibited. In addition, pharmacological inhibition of iLPFC enhanced VTA dopamine neuron population activity, but this effect did not occur if RE was also inhibited. Pharmacological inhibition of iLPFC had no effect on overall firing rate, but reduced burst firing in RE neurons. Electrical stimulation of iLPFC enhanced burst firing and attenuated tonic firing in RE neurons. Finally, DREADD-mediated, projection-specific inhibition of the direct iLPFC-RE pathway enhanced burst firing in RE neurons.

Conclusion: These findings suggest that elevated dopamine neuron activity following inhibition of iLPFC occurs via disinhibition of thalamo-hippocampal communication.

Significance: These data suggest that loss of top-down prefrontal regulation via disruption of corticothalamic communication could contribute to a hyperdopaminergic state and dysregulated cortico-hippocampal interactions, both of which may play a role in psychotic disorders.

Funding Source(s): NIMH grants F30 MH109199 (PI: Eric Zimmerman, BS), NIMH R01 MH57440 (PI: Anthony Grace, PhD)