three ANA domains. EF measures were response inhibition, short-term memory, inferential reasoning, task switching, mental rotation, attention, metacognition, and interoception. NE measures were distress tolerance, ostracism, amotivation, anhedonia, resilience, affect and alexithymia. IS measures were approach-avoidance bias, implicit alcohol associations, and alcohol demand. Ancillary measures assessed in the Natural History Protocol pertinent to the three domains were included in the analyses (alcohol sensitivity, anxiety, depression, aggression, impulsivity, craving, personality, delay discounting). CT was measured using the Childhood Trauma Questionnaire (CTQ). Psychiatric diagnoses were assessed using the Structured Clinical Interview for DSM-5 Disorders. Participants were classified based on their history of AUD and mood disorder: Healthy controls (HC; $n = 68$, 23.9%), AUD only ($n = 108$, 36.0%), and AUD with comorbid MD (AUD + MD; $n = 113$, 37.7%). Those with MD only (i.e., without comorbid AUD) were excluded due to the small group size ($n = 8$, 2.7%). Factor analyses were used to identify the latent factors underlying each domain. Analysis of variance were used to compare CTQ scores and factor scores across the three diagnostic groupings. Structural equation models (SEM) were used to evaluate the relationships between CT, domain factors, and psychiatric diagnoses. Age, sex and race were included as covariates. Bonferroni correction was used to correct for multiple testing.

Results: Five factors of EF were identified: Response Inhibition, Working Memory, Interoception, Rumination, and Impulsivity (TLI/CFI > 0.91, RMSEA = 0.05). Two factors of IS were found: Alcohol Sensitivity and Alcohol Motivation (TLI/CFI > 0.99, RMSEA = 0.03). Three factors of NE were elucidated: Internalizing, Externalizing, and Resilience (TLI/CFI > 0.94, RMSEA = 0.07). CTQ scores were associated with all factors (standardized estimates = 0.11 to 0.57, p's < 0.02), except for alcohol sensitivity (p = 0.10) and response inhibition (p = 0.052). Compared to HC, individuals with a history of AUD (with and without comorbid MD) showed elevated dysfunction in all domain factors (Cohen's d = 0.09 to 3.34; p's < 0.01) except for resilience and response inhibition (p's > 0.17), and endorsed greater levels of CT (Cohen's d = 0.61, $p < 0.001$). Those with AUD + MD also showed greater levels of dysfunction in all domain factors (Cohen's d = 0.17 to 3.53; p's < 0.01) except for response inhibition and working memory (p's > 0.82), and exhibited greater CT compared to those with AUD only (Cohen's d = 0.46; $p < 0.01$). After controlling for all identified factors and covariates, only alcohol motivation mediated the relationship between CT and membership to the AUD only group (indirect effect = 0.31, $p < 0.001$), but not the AUD + MD group (indirect effect = 0.10, p > 0.20).

Conclusions: We identified unique factors underlying each ANA domain. Individuals with AUD with and without comorbid MD showed elevated levels of dysfunction on most of these domain factors relative to HC, and individuals with AUD + MD showed additional levels of dysfunction compared to AUD only. CT was associated with most of these identified factors, but only alcohol motivation was a significant mediator between CT and risk of developing AUD without MD. This suggests that addressing heightened alcohol motivation in individuals with a history of CT may be especially pertinent in improving AUD treatment outcomes. Future analysis will focus on subtypes of CT (e.g., abuse, neglect) as well as additional psychiatric comorbidities commonly associated with AUD.

Keywords: Childhood Trauma, Alcohol Use Disorder, Mood Disorder, Addictions Neuroclinical Assessment, RDoC

Disclosure: Nothing to disclose.

P782. Transdiagnostic Neural Correlates of Fear and Anxiety Sensitivity in a Focal Fear Sample

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Background: Fear and anxiety sensitivity (the belief that anxiety symptoms or arousal can be harmful/"fear of anxiety-related sensations"), are transdiagnostic constructs that may help parse heterogeneous diagnostic categories into more homogeneous, neurobiologically-based constituents, laying the groundwork for more targeted classification of the anxiety disorders. Both constructs have both been linked to aberrant processing of negative stimuli; as distinct contributors to psychopathology, fear and anxiety sensitivity were expected to show specific associations with neurocircuit response.

Methods: Fifty-two adults (37 female; M = 23.65 years, SD = 9.69) who all shared a common "focal fear" diagnosis (i.e., specific phobia or performance-only social anxiety disorder), but varied in extent of additional comorbid anxiety and mood disorders, passively viewed negative and neutral pictures while fMRI BOLD was recorded. Analyses focused on identifying the unique neural correlates of fear and anxiety sensitivity, above and beyond the other dimension.

Results: Greater fear was associated with reduced negative > neutral fMRI BOLD in the thalamus (t = 3.85, $p < 0.05$ FWE), suggesting avoidant processing of negative stimuli. On the other hand, higher levels of anxiety sensitivity were associated with increased negative > neutral fMRI BOLD in the insula (t = 3.93, $p < 0.05$ FWE), a brain region implicated in the representation of interoceptive information.

Conclusions: Fear and anxiety sensitivity show unique associations with threat neurocircuitry, suggesting distinct means of responding to negative stimuli in the environment. These transdiagnostic constructs could serve as candidates for a more fine-grained means of understanding pathological anxiety.

Keywords: Transdiagnostic, Negative Emotionality, fMRI, Adult Clinical Anxiety

Disclosure: Nothing to disclose.

P783. Race, Ethnicity, Education, Sex and Gender Effects on Neuropsychological Test Scores: Limitations of Current Evidence and Impact on Clinical Trials and Clinical Practice

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Background: Interpretation of neuropsychological (NP) tests depends on the quality of the normative standards available for the tests. The precision of measurement for each test variable depends on the psychometric properties of the test and how many people were used to standardize that test. Co-norming across tests is necessary when interpreting differences between scores on different tests at one time point (i.e., profile or discrepancy score analysis), or differences between scores on the same test repeated over time. The relevance of specific norms for an individual examinee further depends on multiple design features of the standardization studies, including: when the studies were conducted, sampling strategy, inclusion/exclusion criteria, age, sex/gender, education, race and ethnicity, socioeconomic status, and region. This paper examines the standardization studies of the most widely used NP tests, identifies their strengths and weaknesses, and makes recommendations for interpretive caveats based on these analyses.

Methods: We reviewed the standardization strategies and coded information about the sampling frames, inclusion/exclusion criteria, stratification methods, sample sizes overall and within each stratum where relevant, methods for representing or

analyzing race, ethnicity and other demographic characteristics. These methods were applied to the WAIS-IV, WMS-IV, CVLT3, D-KEFS, Pearson Advanced Clinical Solutions (ACS), Rey Complex Figure Test, WCST, Symbol Digit Modalities Test, RBANS, BVMT-R, HVLT, Halstead-Reitan ("Heaton et al.") Norms for Boston Naming, Finger Tapping, Grooved Pegboard), MOANS, and MOAANS (Boston Naming, Trail Making Test, Judgement of Line Orientation). We calculated multiple indexes for each test, including standard errors and confidence intervals for scaled scores, and standard errors of measurement for repeated measures based on reported test reliabilities.

Results: Most tests used age only as a stratification factor, providing "age corrected" scores for selected age bands. The sample sizes for the age strata range from 1 to ~200 but are usually less than 100 participants/stratum. Sex differences were rarely reported, and while larger studies estimated sex distributions from census statistics, some studies had markedly uneven distributions of sex. Education was not used as a stratification factor in any study, and only the ACS, Heaton and MOANS/MOAANS norms attempt corrections for education. The possible interactions of age and education on test scores are seldom reported and cell sizes for combinations of age and education may be too small to enable robust estimates of scores especially at lower levels of education and older ages. The possible impact of race and ethnicity are rarely interrogated except in ACS, Heaton and MOAANS norms, which all focus on "African American" participants. Discrepancies in scores across ACS, Heaton and MOAANS suggest marked sampling differences, and show the same raw scores may yield clinically meaningful differences in scaled scores depending on which norms are used. Most of the norms studied are at least 15 years old, and poorly represent current racial and ethnic characteristics of the United States.

Conclusions: Existing norms have major limitations and may impact the clinical assessment of individuals and result in inappropriate treatment recommendations as well as inappropriate classification in clinical trials, which may include score "cutoffs" based on widely used normative standards. Particularly, race and ethnicity are poorly represented and existing norms present major conflicts for African American groups, with the same raw scores differing by a full standard deviation depending only on the source of normative data. Furthermore, these norms often fail to reflect demographic shifts in the United States, making underrepresentation of racial and ethnic minority groups more marked than before and leading to questions about whether results from these measures can be generalized. Additionally, sex differences are examined infrequently and it remains unclear to what extent sex or gender differences may affect some scores. Co-norming was done for only selected measures and those sample sizes are smaller so the precision of measurement of difference scores is often low; this is unfortunate because interpretation of clinical results and findings from clinical trials often involves examining differences between tests. Most norms use only age as a stratification factor, despite robust impacts of education on scores. Lack of standardization by educational background and selection of "representative" samples means that those of higher education will be given inappropriately higher standard scores and those of lower educational opportunity will be given inappropriately lower standard scores relative to their true abilities. There is an urgent need for new, preferably "dynamic" normative standards, that include sampling by socially and demographically meaningful metrics, to provide greater precision in assessment of neuropsychological scores and score discrepancies, and for evaluating the inclusion/exclusion criteria, and criteria for efficacy in clinical trials that use neurocognitive endpoints

Keywords: Neuropsychology, Neurocognitive Assessment, Psychometric Properties, CNS Clinical Trials

Disclosure: Atai Life Sciences: Honoraria (Self), Verasci: Honoraria (Self).

P784. Tonic and Phasic Neurophysiological Relationships With Adverse Posttraumatic Outcomes Vary by Racial/Ethnic Group

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Background: Racial and ethnic groups experience differing levels of socioeconomic stress that can affect responses to traumatic stress. Emergent work demonstrates that both structural inequities and individual racism-related stressors underlie race-related differences in neural and physiological responses. In particular, core threat neurocircuitry such as the amygdala may be a key region impact by structural racism. Greater levels of negative life events throughout development appear to contribute to both lowered threat-elicited amygdala responses and subsequent skin conductance responses (SCRs) in racially minoritized individuals. Disparate levels of stressor exposure between groups may also partially explain race-related differences in posttraumatic symptoms after trauma exposure. However, limited research to date has investigated brain and physiological responses that may predict posttraumatic outcomes and whether these may differ by racial/ethnic group as a result of structural racial inequities. Understanding potential heterogeneity in brain-behavior relationships is crucial for the development of generalizable neural treatments and interventions for trauma and stress-related disorders.

Methods: Participants ($n = 283$) were recruited as part of the AURORA Study, a multisite, longitudinal study of trauma and posttraumatic outcomes. Briefly, trauma-exposed participants were recruited from 22 Emergency Departments (EDs) from across the United States. Initial participant demographic and psychometric data were collected after admission to the ED which included trauma exposure type, participant marital status, income, education level, and employment. Participants' home address was geocoded to derive an area deprivation index (ADI) to reflect neighborhood disadvantage. PTSD, depression, and anxiety symptoms were assessed with the PTSD Symptom Checklist for DSM-5 (PCL-5) and the PROMIS. Participants completed psychophysiological recording and functional magnetic resonance imaging (fMRI) approximately 2-weeks after trauma exposure. Skin conductance level (SCL) and SCR were assessed during a Pavlovian conditioning task. Amygdala reactivity to threat was assessed during passive viewing of fearful and neutral faces during fMRI and was indexed as the BOLD response for the fearful > neutral contrast. Amygdala functional connectivity was assessed using resting-state fMRI using a seed to voxel approach. Multiple comparisons at the voxel level were corrected using a clustering approach (alpha = 0.05) and Benjamini-Hochberg False Discovery Rate adjustments were made for other statistical tests.

Results: Demographic data by racial/ethnic group are reported in Table 1. We observed significant differences in education level [$X2 = 9.90$, $p = 0.007$], income [$X2 = 7.47$. $p = 0.023$], and marital status [$X2 = 6.46$, $p = 0.040$]. No significant difference was observed in employment within the sample [$X2 = 0.59$, $p = 0.745$]. A significant difference in ADI was observed between the groups [$F(2,280) = 31.73$, $p < 0.001$]. There were significant racial/ethnic differences in tonic SCLs [$F(2,126) = 6.41$, $p = 0.002$] with Black participants showing significantly lower tonic SCL than White participants [$t(61.40) = 3.25$, $p = 0.002$, variance inequality adjusted]. Similarly, there were significant racial/ethnic differences in amygdala connectivity to dorsal anterior cingulate cortex, dorsolateral prefrontal cortex (PFC), insula, and cerebellum. However, there was no main effect of racial/ethnic group