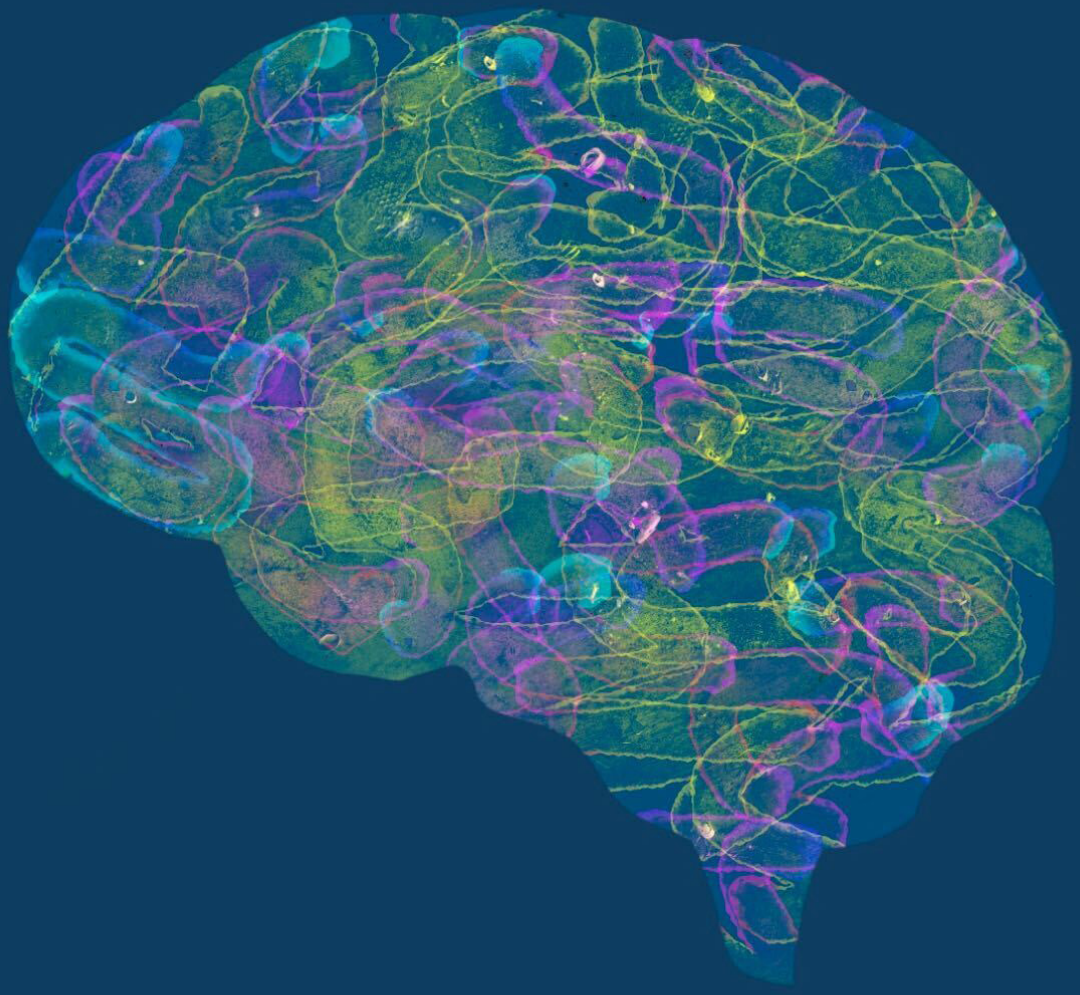
THE UNDERGRADUATE RESEARCH JOURNAL OF

PSYCHOLOGY

AT UCLA



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Special thanks to our founders and past members, Dr. Aaron P. Blaisdell, Dylan Sarnowski and the rest of the University of California, Los Angeles, Department of Psychology, and all of the faculty, staff, and graduate students who have supported us throughout the years.

NOTE FROM THE EDITORS-IN-CHIEF

Dear readers,

With great pride and pleasure, we present to you the seventh volume of The Undergraduate Research Journal of Psychology at UCLA—the first-ever volume to be published in the summer. This journal is not only a culmination of the finest current undergraduate psychology research, but it is also a testament to the patience, perseverance, and persistence of our editors, staff, graduate student mentors, and readers throughout this academic year.

There are many adversities that presented themselves on the journey to this publication. In terms of public health, the coronavirus took the lives of over 170,000 Americans thus far and shut down colleges, research laboratories, and the economy across the nation. Protests for racial and social equity across the United States sparked deep reflection about what it means to be American among younger and older people alike. Disasters such as the explosion in Beirut, Lebanon, became evidence for the necessity of a reliable government and the gravity of voting for proper leadership during the upcoming November presidential election.

Although we were shadowed by sorrows and setbacks, we refused to surrender. Our authors displayed the most determination in editing their manuscripts upon every request to do so (and there were many requests). Our editors and staff showed the most tenacity in their eagerness to publish a tangible, beautifully designed journal, regardless of the delay to do so. Our graduate student mentors and faculty advisor, Dr. Aaron Blaisdell, were most generous in their everlasting wisdom and kindness in the fine crafting of this publication. Our readers showed the most support in their relentless confidence in our ability to have a final masterpiece published. For the abundant faith in and care for our organization, we are most grateful.

The publication before you features the articles of eight budding researchers, each from a unique personal and educational background. Their contributions to the current literature provide momentous foundation and insight that will influence the future of psychology research. With a heart full of pride and conviction, we hope that the Undergraduate Research Journal of Psychology at UCLA continues to serve as a platform to empower undergraduates.

Sincerely,

Vanessa Hilo and Vivian Nguyen

Editor-in-Chief and Associate Editor-in-Chief

AARON P. BLAISDELL, PH.D.

Professor

University of California, Los Angeles

Department of Psychology

The Brain Research Institute

Neuroscience Interdepartmental Program

It's once again time for me to step up to the pitcher's mound and deliver the honorary first pitch of the season, or in my case, the opening remarks to this year's annual issue of The Undergraduate Research Journal of Psychology, published at UCLA by a stellar team of UCLA Undergraduate Student Editors.

But, wait! Where are the fans? Where is the wall of noise crashing down from the cacophonous and riotous stadium—screening out the players' grunts and expletives? Ah, right. We're in the middle of a pandemic caused by SARS-COV-2, and while the masked warriors are finally allowed back on the field, the spectators must stay home and watch online.

Since this time last year, American society has been rocketed by pandemic and social uprisings. This has dramatically altered both the fabric of society and our day-to-day living experience. We've added new words to our lexicon, such as "Zoom fatigue". And the NASDAQ has hit an all-time high, riding the wave of success of the big tech firms (and Walmart). Nevertheless, despite all of these unpredicted changes, the editorial board has steered this journal with a steady hand, and student authors have continued to write up their engaging research for publication in this journal.

In these virtual pages, you will find 8 new papers that span the field of psychology. Half of these papers cover issues of mental health, such as "Transcranial direct current stimulation and major depressive disorder," "Is poor engagement in treatment associated with lower likelihood to participate in research? A study of families in school-based mental health," "The association between early life adversity and anxiety sensitivity," and "The relationship between early life stress and VTA-Hippocampal functional connectivity." Note that the latter two are concerned with early life events, for which there is growing awareness in psychology of its importance.

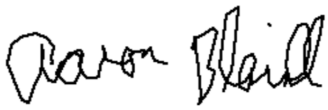
Two papers cover topics in clinical psychology and psychopathology, such as "Life happens: Relationship between provider response to emergent life events and client attendance" and "Atypical relationship of functional connectivity among youth with autism spectrum disorder to genetic risk".

One paper focuses on minority psychology "Subjective sexual well-being among LGBTQIA+ students: An exploration of role of social networking sites and applications." With identity politics gaining traction in our society, this paper is quite relevant to the times.

Perhaps most presciently, there is one paper that is relevant to the ongoing pandemic "Contagious or not contagious: Is that the question? Evaluating the effects of disease contagion on memory for word lists." This last paper unmasks the role of perceived contagiousness of a speaker on the listener's memory for word lists spoken by the speaker. In it participants are asked to listen to a list of words being read by a speaker who is described as having an infectious disease (influenza) or a non-infectious disease (cancer). No differences in recall was found for either group of participants. I wonder, though, if the results would have been different if this study were conducted now, in the midst of the coronavirus pandemic, and with the speaker in the infectious-disease condition infected with coronavirus rather than influenza?

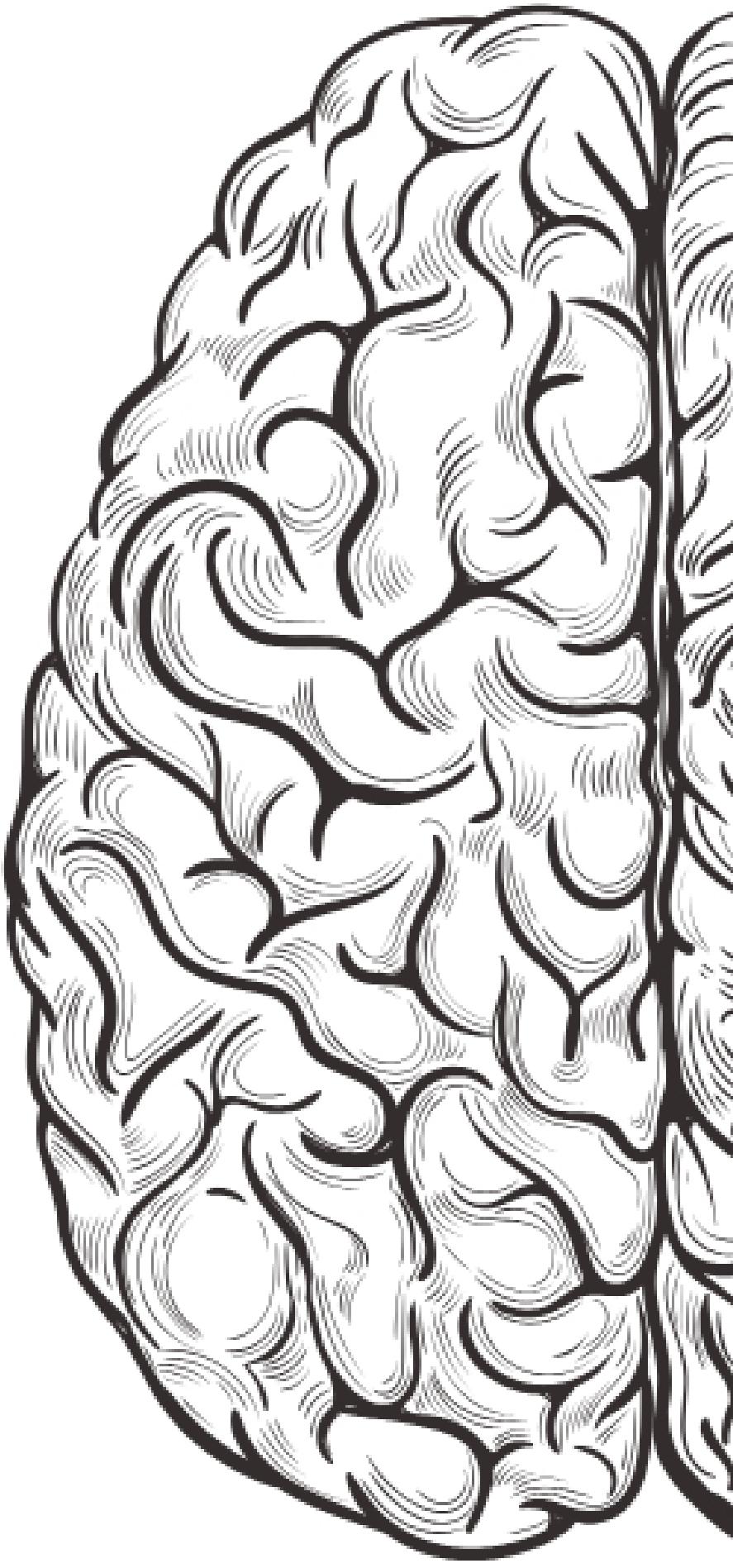
The success of this year's efforts in bringing the publication to fruition stands as a testament to the enduring human spirit that cannot be crushed by volatile world events. Rather, to paraphrase Dr. Ian Malcom from Jurassic Park, "Scholarship finds a way!"

To Scholarship!



Professor Aaron Blaisdell

August, 2020



Nadeen Eltoukhy, BA
University of Pennsylvania

Nadeen Eltoukhy is a Summa Cum Laude 2019 graduate of the University of Pennsylvania, where she studied Psychology and Healthcare Management. While pursuing her Bachelor's degree at Penn, Nadeen got a headstart on her medical education at Cairo University, Egypt. She is currently a 4th year student. She hopes to combine the knowledge she has obtained on healthcare-related fields to advocate for and provide high-quality comprehensive patient care internationally In her free time, she enjoys dancing, traveling, watching musicals and Broadway shows as well as hosting game nights with friends and family.

Contact: nelt@sas.upenn.edu

Was there a particular experience that sparked your research interests?

I've always found neuropsychological development very interesting, so I sought out the Changing Brain Lab, because I knew that their mentorship would be an incredible learning experience. Once I joined the lab, I started focusing on which topics within neuropsychological development I would find most intriguing. At that time, I was taking a class on the effect of trauma on different cognitive abilities, so I found it fitting to explore that in my research project as well.

Who has been an influential person in your life?

My Mom has always encouraged me to explore my interests and to enjoy every day to the fullest. She has supported me without adding any pressure and has made me laugh every step of the way. Watching her navigate life with kindness and grace, witnessing her intelligence and humility as a pediatric cardiologist as well as understanding the sacrifices she's made as a mother as I grow older, inspires me every day. I couldn't be more grateful to have her as my role model and best friend!

A special shoutout to my sister, whose support, jokes and stories will always hold a special place in my heart.

When and where are you the most productive?

Although it is not related to academia, I consider my greatest accomplishment to be the personal growth and strength that I have gained throughout the past decade, through the adversities and opportunities life has thrown my way. I consider the relationships I have with my family and friends to be the pillars that have helped through it all. I'm still a work in progress, but I wouldn't have gotten this far without them.

Where do you see yourself in 10 years?

In 10 years, I hope to be a have started my medical practice. Volunteering with the Castleman Disease Collaborative Network has inspired my to start my own non-profit organization one day, focused on providing mental health support to children with chronic illnesses and their loved ones. I hope that within the next decade, I get to start my own family and that throughout the journey, I keep dancing.

The Relationship Between Early Life Stress and VTA-Hippocampal Functional Connectivity

Nadeen Eltoukhy[1]
Supervisors: Anne T. Park[1], and Allyson P. Mackey[1], PhD

Studies have shown that early life stress affects components of the brain's reward circuitry, including the direct dopaminergic projections between the ventral tegmental area (VTA) and the hippocampus (Marusak et al., 2017). Episodic memory relies on the synchronized activity of the VTA-Hippocampal loop. The role of this loop is to prevent overwhelming humans' limited memory capacity by regulating and incorporating novel memories (Lisman & Grace, 2005). Recent data has demonstrated a decrease in the resting-state functional connectivity between the VTA and hippocampus in children exposed to chronic stress (Marusak et al., 2017). Because the dopaminergic projections from VTA to hippocampus regulate the entry of novel information into long-term memory, we hypothesize that atypical attenuation of this circuitry could result in the pathological inability to detect and retain novel episodic memories. The dataset examined was provided by the Healthy Brain Network Initiative. We focused on three specific measures: Parent reported Negative Life Events Scale (NLES) as a measure of stress, Resting state fMRI (rs-fMRI) as a measure of connectivity and the NIH Toolbox Picture Sequence Memory Test (TPSMT) as a measure of Episodic Memory abilities. We expected to find statistically significant correlations between the three variables. However, our analysis indicated statistical insignificance between VTA-Hippocampal connectivity and both NLES scores and Picture Sequence Memory scores. We suggest altering the eligibility criteria and utilizing more specific assessment measures for future studies.

Early life stress (i.e., stress experienced during childhood) has been shown to impact learning and memory abilities (Pechtel & Pizzagalli, 2011; Anacker et al., 2016; Teicher et al., 2003). It has also been linked to the development of psychiatric disorders later in life, such as mood, personality and anxiety disorders (Carr et al., 2013). Attempting to understand how stress relates to the changes in cognitive functioning and what mechanisms underlie these changes could provide necessary insight into developing effective interventions to aid children experiencing stress. Previous research has shown that early life stress has an impact on episodic memory, which is important for everyday functioning (Anacker et al., 2016; Teicher et al., 2003; Schwabe et al., 2012). There are various inconsistencies in the literature regarding the conditions under which the effects of stress emerge as well as the mechanism underlying stress' impact on different types of memory (Shields et al., 2017). Therefore, we decided to focus our research on the effects of early life stress on episodic memory abilities specifically, and how this might be related to changes in brain regions that are important for memory and goal-directed learning.

Episodic Memory

Episodic memory is defined as the capacity to form and retrieve conscious memories of specific past events. This form of long-term memory is acquired rapidly after a

1 University of Pennsylvania

single experience, is rich in contextual details, and is in reference to a specific time and place (Lisman et al., 2011). Episodic memories are also assumed to be relational, meaning they encode the various relationships between multiple elements of a single event (Ghetti & Bunge, 2012). It supports a variety of abilities essential to the human experience, including providing the foundation for autobiographical memory and contributing to humans' sense of self-continuity over time as well as supporting independence, education, and success in individuals' personal and professional lives (Buckner & Carroll, 2007). Episodic memory abilities continue to develop throughout childhood and into adolescence, possibly due to the substantial postnatal developmental changes in brain regions and neuronal connections associated with episodic memory. For example, there are gradual increases in hippocampal volume and myelination which could have functional consequences. Indeed, studies have demonstrated age-related changes to humans' episodic memory abilities (Grady & Craik, 2000).

Studies have suggested that communication between the Ventral Tegmental Area (VTA) and the hippocampus plays a crucial role in episodic memory (Wittmann et al., 2007; Marusak et al., 2017; Murty et al., 2016). The VTA is part of the brain's reward system and is considered to be one of the main sites of dopamine synthesis in the brain. The hippocampus is a region of the medial temporal lobe primarily associated with memory-related processes. Episodic memory functioning relies on the intricate communication between these two brain areas (Lisman & Grace, 2005).

The VTA-Hippocampal Loop

The VTA-hippocampal loop is thought to control the entry of novel information into long-term memory, thus protecting previously stored memories. The loop is formed of two arcs, each believed to relay critical information for the formation of new episodic memories: a downward glutamatergic arc and an upward dopaminergic arc. The downward glutamatergic arc carries information signaling novelty from the hippocampus to the VTA, thereby activating novelty-dependent dopaminergic neurons in the VTA (Marusak et al., 2017). Animal studies have also provided further evidence to support the hippocampal role in novelty detection (Diamond et al., 1994; Lisman & Grace, 2005). Stimulating the hippocampal region elicits an increase in exploratory behavior in a manner akin to that produced by novelty itself. Furthermore, interfering with hippocampal function has been shown to inhibit the orienting of rabbits to novel stimuli and attenuate the novelty-initiated skin conductance response in humans (Lisman & Grace, 2005).

The VTA dopaminergic neurons form the upward arc which projects from the VTA back to the hippocampus (Lisman & Grace, 2005). Activation of these novelty-dependent neurons based in the VTA enhances and stabilizes long-term potentiation and long-term memory. These connections are believed to play a crucial role in memory modulation in response to novel information and thus allow experience-dependent modification of previously stored memories. The fMRI study by Wittman et al. (2007) demonstrated that VTA activation in humans was stronger in response to the unexpected presentation compared to the expected presentation of novel items, highlighting the VTA's role in experience-dependent alteration of memories. According to a different study, electrical recordings from the VTA-dopaminergic cells in awake monkeys and cats reveal that these cells respond rapidly with bursts of spikes to novel stimuli. However, as the stimuli become familiar, the dopaminergic neurons no longer show this change in activity (Lisman & Grace, 2005).

Accordingly, dopamine agonists lead to memory improvements, while dopamine depletion has been shown to impair memory both in humans and animals (Wittmann, Schiltz, Boehler & Düzel, 2008). Increasing dopamine concentrations, whether through L-DOPA administration to healthy human participants or through decreasing COMT activity, an enzyme which metabolizes dopamine, have been associated with improvements in episodic memory (Lisman & Grace, 2005). Rodent studies have provided further evidence of the role of dopamine in episodic memory. Although rats are normally able to update memories quickly if reward locations are changed in a maze, hippocampal infusion of SCH23390, a dopaminergic antagonist, before encoding impairs rats' ability to recall the new reward locations after 24 hours (Lisman et al., 2011). These findings all highlight the role of dopamine release from the VTA to the hippocampus

in episodic memory formation. The synchronized activity of both structures in this loop is therefore crucial for the formation of episodic memory.

The mechanisms supporting novelty detection for episodic memory formation are likely to be intricate and complex because not all novel events may be of sufficient importance to enter into long-term memory. There is so much novelty in the environment that if we were to incorporate all of it into memory, it could overwhelm our limited memory capacity and theoretically overwrite pre-existing information. The role of the novelty-dependent VTA-hippocampal loop may be to ensure that entry and long-term encoding does not occur unless the information is behaviorally advantageous (Lisman & Grace, 2005). The novelty detection process itself is thus important to determine whether the incoming information is truly new or just a varied representation of a previously stored memory. The complexity of the loop may be designed to precisely determine novelty and allow long-term memory modifications to occur only when the experiences are indeed novel. However, as we emphasized before, even if the information is new, activation of the VTA appears to be contingent on additional criteria, such as relevance to goals and salience. In this way, the system only allows encoding of specific occurrences and elements, thereby minimizing the possibility of overwriting previously stored information (Lisman & Grace, 2005).

Because of their relational component, episodic memories are considered flexible. This means that they are constructed in a manner that allows relevant elements of a past event to be recalled as needed to direct future behavior. It is therefore plausible for episodic memory to be influenced by parts of the brain's reward system, such as the VTA, because it is advantageous for an individual to remember circumstances which led to rewards, resulting in adaptive behaviors (Shohamy & Adcock, 2010). In fact, activating the VTA by a reward should enhance hippocampal-dependent episodic memory of information present at the time of reward. A prior fMRI study corroborated this in humans, by indirectly activating the VTA by giving participants a monetary reward at the time of encoding, which improved their long-term episodic memory for novel stimuli even 24 hours later. Importantly, this reward-related memory enhancement was correlated with simultaneous activation of the VTA, striatum, and hippocampus (Lisman, Grace, & Duzel, 2011).

The Impact of Stress on VTA-Hippocampal Connectivity

The present study is one of few to take a three-pronged, Recent data has demonstrated a decrease in the resting-state functional connectivity between the VTA and hippocampus in children exposed to stress (e.g., abuse or violence) (Marusak et al., 2017). Functional connectivity refers to the functionally integrated relationship between different brain regions that could be spatially separated. Functional connectivity can be measured using resting state fMRI and is typically analyzed in terms of correlation, coherence, and spatial grouping based on temporal similarities. During resting state fMRI scans, participants are asked to stay still in the MRI machine and are not asked to perform any task, therefore they are considered to be resting (Hutchison et al., 2013).

Chronic childhood stress, which is associated with a decrease in the resting-state functional connectivity between the VTA and hippocampus, results primarily due to childhood maltreatment, which is linked to psychiatric illnesses and behavioral dysfunction (Clayton & Russell, 2009; Marusak et al., 2017). Childhood stress is considered to be any experience that would likely require notable psychological, social, or neurobiological adaptation by the average child and that represents a deviation from the expected, safe, and nurturing rearing environment. Examples include loss of a significant relationship, death of a close family member, sleep or food deprivation, or social exclusion by peers (McLaughlin, 2016). It transitions to a chronic state if the stressor is associated with increased intensity or persistence, heightened uncontrollability and unpredictability of distress, or lowered sense of adaptability, thus augmenting the magnitude of the stress response (Sinha, 2008). Stress experiences can be emotionally, psychologically, and physiologically challenging, resulting in the activation of the body's stress responses and adaptive processes to avert the negative effects of the stressor. This is primarily mediated by the release of central catecholamines, particularly noradrenaline and dopamine, which are also involved in modulating brain motivational centers including the VTA (Sinha, 2008). The central catecholamines target brain

motivational pathways to critically affect adaptive and homeostatic processes. When children are chronically stressed, the risk for persistent homeostatic dysregulation due to the negative effects of the catecholamines increases (Teicher et al., 2003).

Previous cognitive and electrophysiological studies on animals have supported the hypothesis that stress diminishes hippocampal functioning (Diamond et al., 1994; Marusak et al., 2017; Teicher et al., 2006). For instance, exposing rats to a stressor such as an unfamiliar environment or a predator has been shown to impair hippocampus-dependent memory. Furthermore, rats exposed to decreased or fragmented maternal care during the early postnatal period displayed significant changes in hippocampal structure and synaptic plasticity later in life, indicating the lasting effects of early stress (Schwabe et al., 2012). These changes were accompanied by impairments in various hippocampus-dependent tasks when tested under normal conditions.

Several studies have shown that stress can also impact VTA functioning. In a recent study by Pena et al. (2017), early life stress has been shown to affect the VTA through long-lasting transcriptional changes in the Otx2 gene transcription factor. Interestingly, this study found that these transcriptional changes were related to important depression-like symptoms, which could include altered memory abilities. Other studies have shown that trauma-exposed children show diminished resting-state connectivity between the VTA and hippocampus, but no group differences in Substantia Nigra (SN) connectivity with VTA or hippocampal regions (Marusak et al., 2017). However, there were overall age-related decreases in both VTA and SN connectivity with the hippocampus, regardless of trauma. These findings suggest that age-related attenuations in VTA-hippocampal circuitry may be exacerbated in trauma-exposed participants (Marusak et al. 2017). Because the dopaminergic projections from VTA to hippocampus regulate the entry of novel information into long-term memory, atypical changes within this circuitry could result in pathological overwriting or persistence of stored memory. It is hypothesized that attenuated connectivity may serve to adaptively prevent the overwriting of a previously stored trauma memory to retain the learned environmental contingencies caused by the stress (Lisman et al., 2005). Alterations in this loop may therefore contribute to the broad range of cognitive and emotional disturbances associated with early stress exposure. However, it is important to note that functional connectivity analyses do not determine directionality or eliminate the possibility of indirect pathways contributing to observed changes in connectivity. Additionally, the group differences in connectivity were observed during rest without relating the findings to behavioral and ability changes.

Based on the aforementioned findings, we hypothesize that early life stress is associated with connectivity alterations in the VTA-Hippocampal loop which are associated with a decrease in episodic memory abilities. This requires establishing a correlation between childhood stress, VTA-hippocampal functional connectivity and episodic memory in a developmental population. Understanding the relationships between these variables could contribute to the study of children's wellbeing and potentially help us combat the effect of stress on cognitive abilities.

Method

The dataset examined for this paper was provided by the Healthy Brain Network (HBN) Initiative, which is the signature scientific initiative of the Child Mind Institute. The Child Mind Institute is an independent national nonprofit. This community-centered program aims to collect data from 10,000 children and adolescents in New York City to allow further study of child and adolescent mental illnesses and provide participants with diagnostic consultations. The goal of this initiative is to identify biological markers such as neuroimaging and physiological data that will improve our understanding, diagnosis, and treatment of mental health and learning disorders from an objective biological perspective (Alexander et al., 2017). The HBN Biobank therefore includes behavioral and cognitive phenotyping, as well as multimodal brain imaging, and an extensive phenotyping protocol that includes comprehensive psychiatric and learning assessments, instruments probing a range of familial, environmental and lifestyle variables. The comprehensive evaluation takes approximately 12 hours to complete. Data collection was approved by the Chesapeake Institutional Review Board. The Healthy Brain Network is committed to sharing

data on a pre-publication basis to allow researchers around the world to address rich and clinically relevant questions. All participants provide informed consent for their data to be shared via IRB-approved protocols and all personal identifiers are removed according to the Health Insurance Portability and Accountability Act (HIPAA), with the exception of zip code (O'Connor et al., 2017).

Participants

To generate a dataset that captures the broad range of heterogeneity in developmental psychopathology, the HBN participants included in the full dataset consisted of children ages 5-21 years who live in the New York City metropolitan area. Participants are referred by community members through advertisements and announcements released to educators, local care providers and parents via email lists and events. To determine eligibility, participants are required to complete an initial screening questionnaire over the phone to rule out anything that might disqualify them from participating. Reasons for exclusion include but aren't limited to the presence of acute safety concerns (e.g., danger to self or others), cognitive or behavioral impairments that could interfere with testing (e.g., being nonverbal, IQ less than 66), or medical concerns that are expected to affect brain-related findings. However, it is important to note that participants taking stimulants are enrolled even if the medication is taken on the day of testing (Alexander et al., 2017). These participants were included under the assumption that stimulants allowed them to function similarly to neurotypical peers. Stimulants increase alertness, attention, and energy by increasing dopamine availability in synapses (Rawson, 1999).

Once eligibility is determined, participants or their legal guardians are asked to provide written informed consent. Upon completing the evaluation, participants are offered referrals to psychology and neurology specialists and three in-person feedback sessions. They are also provided with up to $150 in monetary compensation for their time and transportation expenses.

For the purpose of this paper, we focused on a subsample of the HBN data. Our subsample initially consisted of 224 participants who had structural MRI (T1) and resting state fMRI data, as well as Negative Life Events Scale (NLES) data. This subsample was reduced to 112 participants who had usable T1 data after subjecting it to quality checks. This was done through visual checks, and structural images were deemed unusable if motion artifacts substantially obscured the boundaries between gray and white matter. The final subsample consists of 107 who have usable resting state data, which was defined as <10% motion outliers. An outlier was defined as any time point where the participant had moved more than 2 mm. The data available thus limits our participant group to 107 individuals between the ages of 11-18 years (Figure 1). The mean age of our sample is 12.59 years with a standard deviation of 3.44 years. Previous studies have focused on younger participants between the ages of 5-8 years. Regarding gender, 19.6% of participants identified as male, 43.9% as female, and 36.5% chose not to specify (Figure 2).

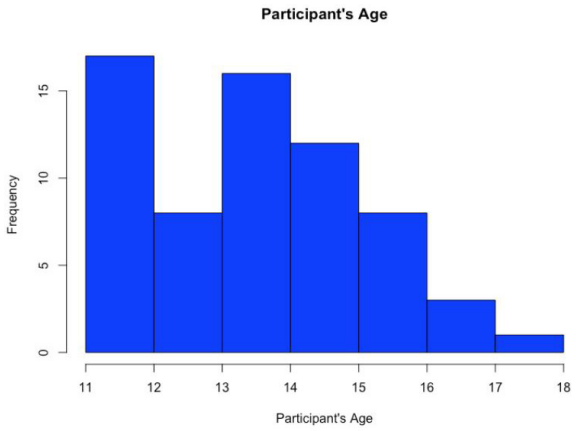


Figure 1: Age distribution of our sample population (Mean: 12.59 years ± 3.44 years)

Demographics	
N	107
Imaging N	66
Age (mean ± SD) Age range	12.59 ± 3.44 11-18
Gender	19.6% male 43.9% female 36.5% unspecified

Figure 2: Demographic distribution of our sample population, including age, gender and sample size.

The Negative Life Events Scale (NLES)

The accompanying parent of the HBN study participant is asked to fill out several online questionnaires on site about the participant's emotions, behaviors, social experiences, and academic performance. These structured questionnaires evaluate behavior, family structure, and exposure to normative life stressors, giving researchers additional details and a well-rounded picture of the participant's overall functioning and quality of life. Our questionnaire of interest is the NLESe. Respondents answer 'yes/no' about whether their child has experienced a particular negative event, and provide a subjective rating of the event impact on a 0-4 scale, with 0 indicating "no impact" and 4 indicating "very impacted" (Appendix). To score this questionnaire, a "yes" response is ascribed 1 point, and "no" is ascribed 0 points. The NLES score is obtained by summing together the negative life event items, weighted by how stressful they were for the child. Within our sample, scores ranged between 0-50 with a mean of 16.51 ± 11.15 (Figure 3).

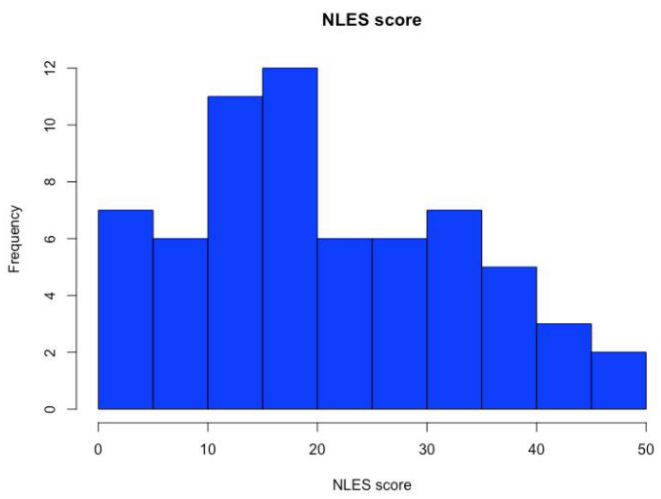


Figure 3: Negative Life Events Scale (NLES) score distribution of our sample population (Mean: 16.51 ± 11.15).

Neuroimaging data

Study participants completed MRI imaging to examine their overall brain structure and function. The imaging data collected was used for research purposes and participants did not receive their scans as part of their feedback report, unless an abnormality was detected. The HBN collected both structural MRI and resting state fMRI data in three phases. The initial test phase utilized a 1.5 T Siemens Avanto system in a mobile trailer to assess the feasibility of using a mobile MRI platform. However, because the data collected during this phase was of lower quality because of the lower magnetic field strength of 1.5 T, it was excluded from our dataset and analyses.

The subsequent deployment phase relied on a Siemens 3 T Tim Trio MRI scanner located at the Rutgers University Brain Imaging Center (RUBIC), which is equipped with a Siemens 32-channel head coil and the CMRR simultaneous multi-slice echo planar imaging sequence. The third stage used Prisma scanners located at the CitiGroup Cornell Brain Imaging Center and the CUNY Advanced Science Research Center. Participants had either 5 or 10 minutes of resting state data due to changes to the HBN MRI scan protocol over time. All imaging datasets are openly shared with users according to the HBN data generation and sharing initiatives, regardless of data quality. The reasoning behind releasing imaging data of varying quality is the lack of agreement within the imaging community on the parameters of 'good' or 'poor' quality data. Furthermore, because this dataset is being openly shared with scholars in various fields, it is plausible to assume that the lower quality data could be used to develop artifact correction techniques and enhance reliability and reproducibility techniques.

Behavioral data

The study requires participants to complete a battery of computerized tests. Specialists administered the NIH Toolbox Cognition Battery (NIHTB-CB), which is designed to provide a brief (30-min), widely accessible, and easily administered cognitive screener capturing the lifespan (3–85 years). The battery consists of seven tests which measure five neurocognitive domains, namely executive functions, episodic memory, processing speed, working memory, and language.

The most significant domain of cognition for this paper is episodic memory. The nonverbal NIH Toolbox Picture Sequence Memory Test (PSM), which is standardized by age, evaluates participants' episodic memory abilities by asking them to reproduce the order of an arbitrarily ordered sequence of pictures presented on a screen. Administration time is approximately 10 minutes. The

pictures presented are thematically related but with no inherent order. The general themes are "Working on the farm," "Playing at the park," and "Going to the fair." Color-illustrated pictures appear one at a time on the computer monitor in a fixed order that the participant must remember and then reproduce. Each picture is presented for 2.2 seconds and is accompanied by a brief recording describing the content of each picture. The picture then moves to the side of the screen and is automatically placed in its position in the sequence. The sequence of images then disappears and after a few minutes. The images then reappear in a random order. The participant is asked to reproduce the initial sequence. The task is explained to participants verbally as well as through practice sequences. For all ages, participants are asked to complete practice sequences prior to administration of the first test trial to help orient them to the PSM task and to allow them to experience moving the pictures to the correct position in the sequence.

With development, children's memory becomes more deliberate and strategic, resulting in increases in their ability to organize memorable material. Thus, older children typically remember longer lists of items relative to younger children, making list length a prime target for exploitation in tests of episodic memory designed for wide age ranges. The picture memory sequences in the PSM vary in length from 6 to 15 pictures to adjust for ability. The level of difficulty of the task for different age ranges was determined during pilot testing of the NIH toolbox tasks. Thus, for ages 3 to 4 years, 6 pictures are administered; 5 to 6 year olds are presented with 9 pictures; 9 years or older are presented with 15 pictures. To increase reliability, researchers administer multiple trials. The task has been shown to have high test – retest reliability and promising construct validity.

The child's score on the PSM is acquired from the cumulative number of adjacent pairs of pictures remembered correctly over three learning trials. Adjacent pairs are two adjacent pictures placed in consecutive, ascending order. For example, pictures placed in the correct order such as 1–2 and 2–3 would receive credit, but pictures placed in the incorrect orders such as 1–3 and 3–15 would not receive credit. In a 6-picture sequence, a child presenting the sequence 1–2–3–5–4–6, would receive a score of 2: one point would be awarded for each of the correct pairs 1–2 and 2–3. However, no points would be earned for the incorrectly ordered pairs 3–5 and 4–6. The maximum score for each trial is one less than the number of pictures in the sequence. Within our sample, scores ranged between 0-15 with a mean of 12.88 ± 2.76 (Figure 4).

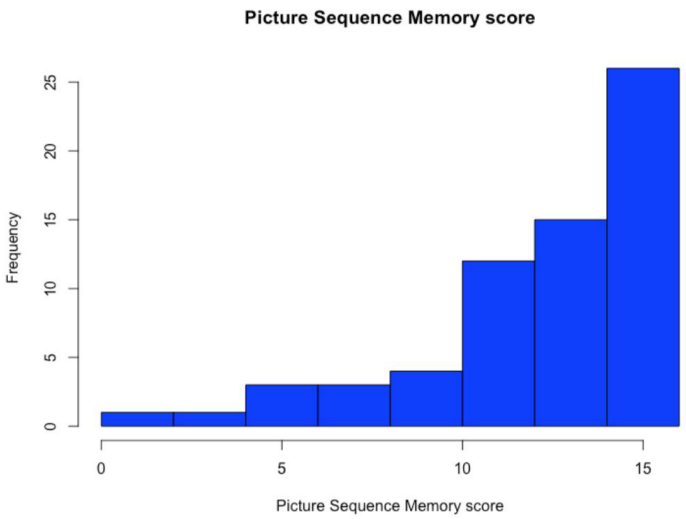


Figure 4: Picture Sequence Memory (PSM) score distribution of our sample population (Mean: 12.88 ± 2.76).

Analysis

For the purpose of this paper we aimed to examine the correlations between children's NLES score and the resting state connectivity between their hippocampi and VTA. Resting state connectivity is often used to reflect stable individual differences in connectivity. Moreover, we assessed the associations between the connectivity and their PSM scores, aiming to ultimately establish whether the NLES scores and PSM scores are significantly correlated. If the NLES scores and PSM scores are indeed significantly correlated in our sample, we then could formally test whether this relationship is mediated by VTA-hippocampal connectivity.

Prior to submitting the raw resting state fMRI data to any type of statistical analysis, the appropriate preprocessing steps were taken. Preprocessing involves numerous steps to clean and standardize the data. It is meant to detect and account for potential artifacts in the data that may be caused by the scanner itself or the participant (Gavrilescu

et al., 2008). For example, preprocessing involves motion correction, which accounts for participant motion during the resting state scan by realigning each functional volume to a reference point. Outlier volumes in the functional data were defined using a tool called ART based on composite motion (>2 mm of head displacement between volumes) and global signal intensity (>3 s.d.s from the mean). Motion-related and physiological-related confounds, such as heart rate and respiration, were regressed out of the data. We proceeded to check for T1 quality and the correctness of the functional-to-structural coregistration step (i.e., that the resting state fMRI data is aligned with the T1 structural image). The functional data were bandpass filtered (0.01–0.1 Hz), spatially smoothed with an isotropic 6 mm Gaussian kernel (FWHM), and normalized to MNI152 2 mm space. Preprocessing and group analyses were conducted with FSL and FreeSurfer. The VTA and bilateral hippocampi were chosen as seeds, and defined according to anatomical atlases. Subject-level connectivity maps for each of the VTA and hippocampi seeds were created.

We controlled for age, gender, motion outliers, and neurological and psychological diagnoses in our group-level whole-brain analyses. In addition to the group-level whole brain analyses, we also conducted an ROI to ROI analysis between the VTA and the hippocampi to examine the correlation between our three variables of interest. In other words, we extracted the average time series within the VTA, and correlated this with the average time series within the hippocampus, and related these VTA-hippocampus correlation values to our NLES and PSM variables of interest.

Results

We first examined for correlations between participant age and NLES as well as PSM scores. Our analysis demonstrated a statistically significant correlation between NLES scores and age ($r = 0.39$, $p < 0.05$), suggesting that older participants have experienced a higher number of negative life events (Figure 5). Upon examining the correlation between age and PSM scores, our results were statistically insignificant ($r = 0.43$, $p > 0.05$) (Figure 6). The scores for this task seem to plateau at age 14 years, indicating that episodic memory development may also plateau beyond a particular level of development. However, this could also indicate that the task was relatively easy for participants older than 14 years of age.

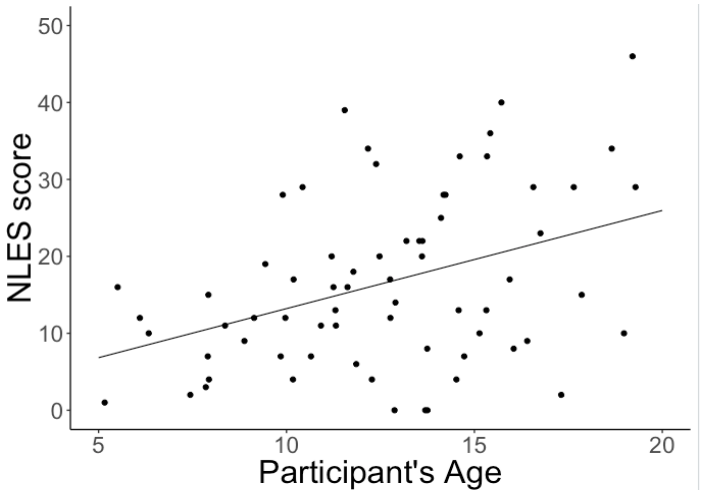


Figure 5: Relationship between participant age and Negative Life Events Scale (NLES) Score. The relationship is statistically significant ($r = 0.393$; $p<0.05$).

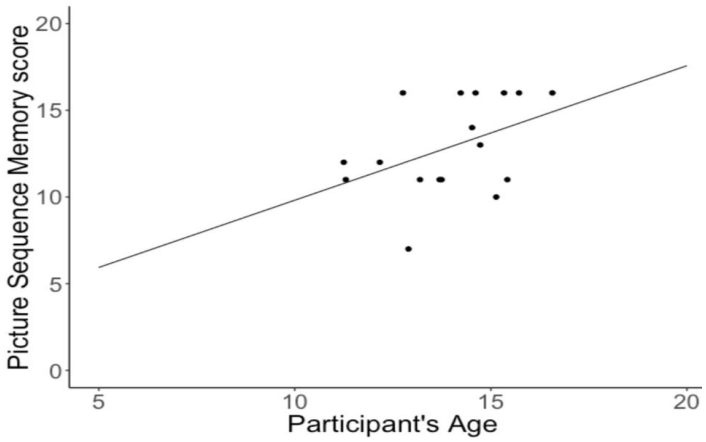


Figure 6: Relationship between participant age and Picture Sequence Memory Score. The relationship is statistically insignificant ($r = 0.431$; $p>0.05$).

Next, we examined the group average functional connectivity maps in our sample and compared them to those of another dataset sample, namely Neurosynth, as a helpful quality check. As mentioned above, we relied on resting state connectivity because resting state has previously been used to indicate stable individual differences in connectivity. Because the connectivity results from the right and left hippocampi are fairly similar,

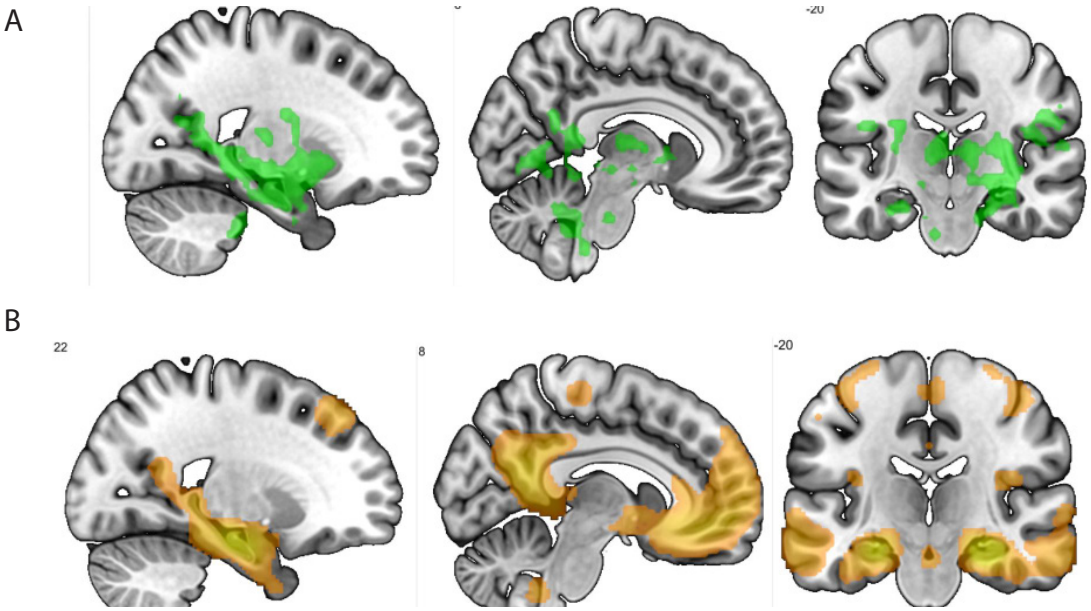


Figure 7: (A) Functional coupling between right hippocampus and associated brain region in our HBN sample; thresholded at p< 0.001 to correct for multiple comparisons. (B) Functional coupling between right hippocampus and associated brain regions in the Neurosynth meta-analysis sample; thresholded at p< 0.001 to correct for multiple comparisons.

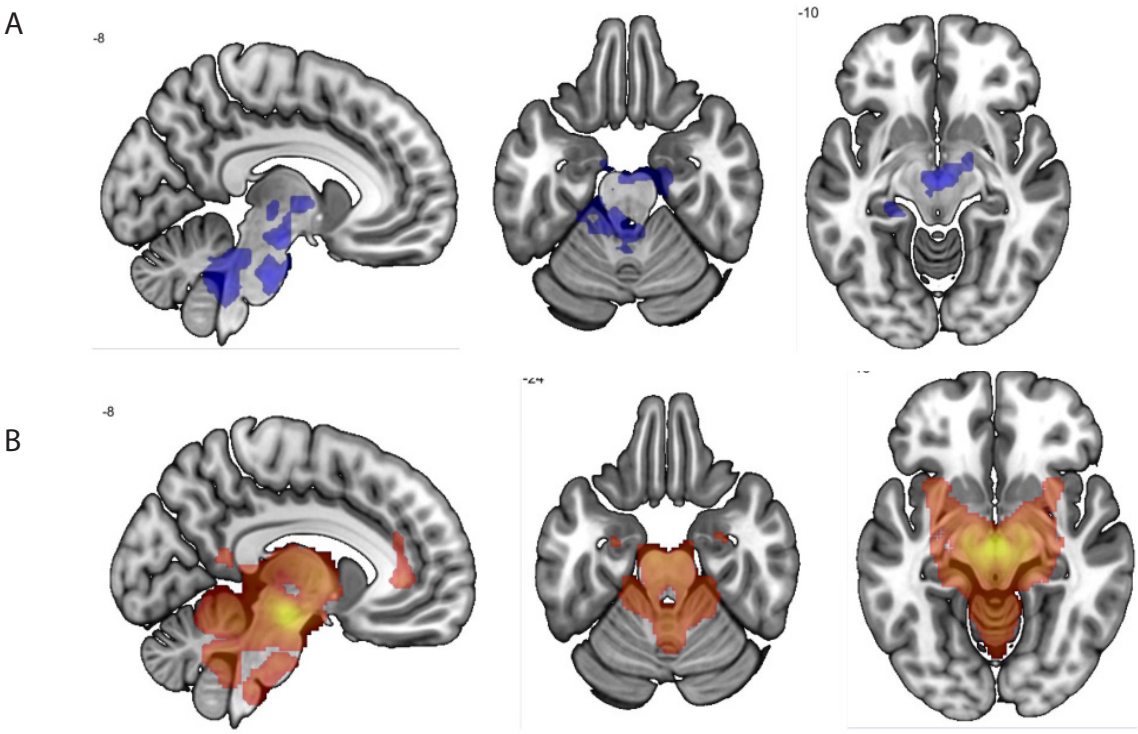


Figure 8: (A) Functional coupling between the Ventral Tegmental Area and associated brain regions in our HBN sample; thresholded at p< 0.01 to correct for multiple comparisons. (B) Functional coupling between the Ventral Tegmental Area and associated brain regions in the Neurosynth meta-analysis sample; thresholded at p < 0.001 to correct for multiple comparisons.

showed connectivity patterns with typical brain regions such as the Amygdala, Medial Temporal Lobe, Posterior Cingulate Cortex and the VTA. To correct for multiple comparisons, we relied on a threshold of $p < 0.001$ (Figure 7A). We proceeded to compare the connectivity group average images of our sample to those of participants in the Neurosynth meta-analysis (N = 1000). The resulting images were fairly similar to ours, with the exception of increased connectivity between the Hippocampus and Prefrontal Cortex in the Neurosynth sample (Figure 7B). Despite this exception, these results strengthen the validity of the connectivity patterns presented by our sample, given that Neurosynth is a large dataset.

We followed the same protocol to examine the Ventral Tegmental Area. This area demonstrated connections with the Ventral Striatum, Orbitofrontal Cortex, Anterior Cingulate Cortex, Thalamus and Hippocampi. However, when correcting for multiple comparisons for the VTA images, we relied on a more lenient threshold of $p < 0.01$ (Figure 8A). This is because the connectivity to the above mentioned brain regions would not have been evident otherwise, possibly due to the smaller size of our sample. The smaller sample size may have also contributed to the decreased size of connected areas relative to the Neurosynth sample group average images (Figure 8B).

To test our hypothesis, we evaluated the relationships between NLES scores, VTA-Right Hippocampal connectivity, and PSM scores. VTA-Right Hippocampal connectivity was quantified using an ROI-to-ROI approach. Firstly, the correlation between NLES scores and VTA-Right Hippocampal connectivity was statistically insignificant in our sample ($r = 0.10$, $p = 0.86$) (Figure 9). An insignificant result was obtained for the relationship between VTA-Right Hippocampal connectivity and PSM scores as well ($r = 0.32$, $p = 0.29$) (Figure 10). Upon examining the data further, it became evident that the correlation between NLES scores and PSM scores was also statistically insignificant ($r = 0.26$; $p = 0.34$) (Figure 11). A significant correlation between these two variables was expected, given that many previous studies have highlighted the effect of stress on memory abilities (Schwabe et al., 2012; Shields et al., 2017; Pechtel & Pizzagalli, 2011). Therefore, we could not test for a possible mediation effect because the relationship between environment (i.e., stress exposure measured through NLES) and behavio

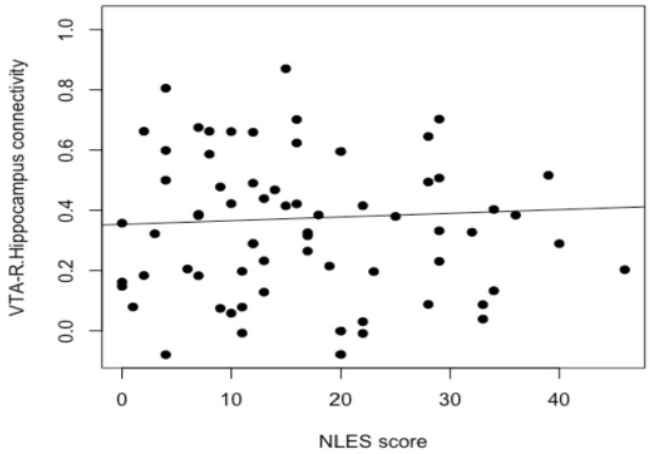


Figure 9: Relationship between NLES score and VTA-Right Hippocampal Connectivity. The relationship was statistically insignificant ($r = 0.097$; $p = 0.861$).

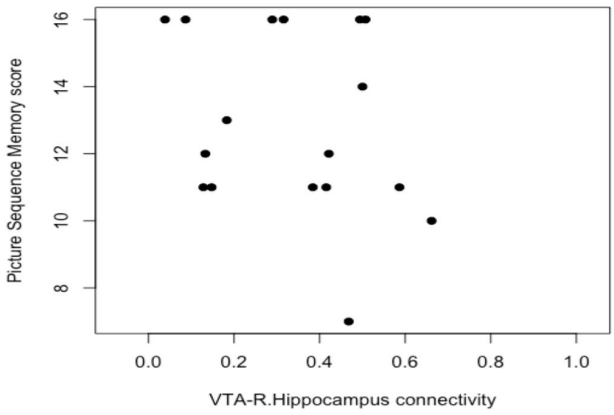


Figure 10: Relationship between VTA-Right Hippocampal Connectivity and Picture Sequence Memory score. The relationship is statistically insignificant ($r = 0.327$; $p = 0.289$).

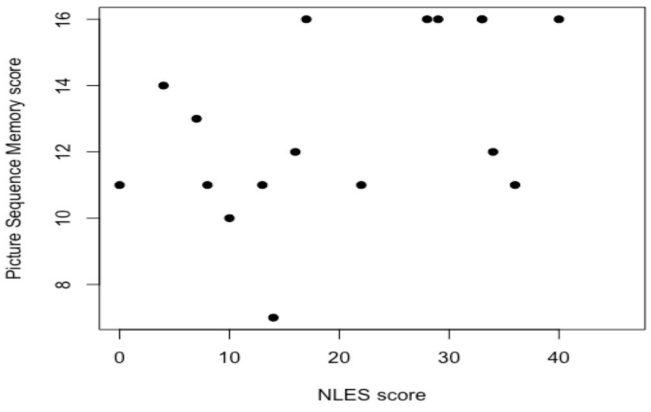


Figure 11: Relationship between NLES score and Picture Sequence Memory score. The relationship is statistically insignificant ($r = 0.259$; $p = 0.341$).

(i.e., episodic memory measured through PSM), were not correlated in this particular sample.

Discussion

The goal of our study was to establish correlations between childhood stress, VTA-hippocampal functional connectivity and episodic memory abilities. We hoped that such correlations could help us better understand how childhood stress exposure is linked to episodic memory abilities. However, our analyses resulted in statistically insignificant correlations. The lack of a significant relationship between Negative Life Events Scale and Picture Sequence Memory scores may be related to the sample size and quality of the data. The participants that were included were only those who had usable data related to our variables of interest available, reducing the sample size significantly. A further disadvantage of relying on secondary data is that the measures lacked sufficient details about the timing of the negative life events, which may relate to connectivity patterns.

It is also worth mentioning that the majority of our participants had at least one psychological or neurological diagnosis. Although we corrected for these diagnoses, it is unclear what their impact on functional connectivity or the PSM scores entails. Thus, future studies should examine the effect of various diagnoses on the VTA-Hippocampal connectivity and PSM scores, and whether these diagnoses may be linked to children's stress response.

Another possible underlying cause for the insignificant relationship between NLES scores and VTA-hippocampal functional connectivity is the fact that previously conducted studies focused primarily on younger children. They had found significant correlations in participants generally younger than 10 years. Thus, it is unclear whether the relationship is insignificant in older children due to the brain's plasticity and ability to readjust and adapt over time or whether it is in some sense related to the timing of the negative life event. Perhaps a significant relationship emerges in younger children because the negative events occurred relatively recently, whereas older children may have had years to deal with the events and their brains could have readjusted. Therefore, as previously mentioned, it would have been interesting to record the timing of the negative life events to investigate whether a 13-year old who experienced a negative event within the past couple of years displayed similar connectivity patterns to a 13-year old who had experienced a negative life event at age 5.

Perhaps general episodic memory abilities are not the right behavioral outcomes to examine in association with stress's effect on VTA-Hippocampal connectivity. It may be more informative to look at episodic memory tasks with more of a reward or goal-focused component, or tasks that look at exploratory novelty-related behaviors such as learning and curiosity levels (Gruber et al., 2014).

Future Directions

To conclude, it would be interesting to conduct further studies on older children to determine the effects of early life stress on brain connectivity and episodic memory abilities. This would allow us to better understand whether the effects of stress persist long term. If the effect does not last, then it would be intriguing to examine how the brain readjusts and what coping mechanisms the children develop. However, as researchers delve deeper into this topic, they should reconsider the different measures utilized and attempt to collect more detailed information about their participants and their experiences. For example, the NLES-scale could include more questions on the timing of the events, what coping mechanisms, if any, the child attempted to rely on, and duration of these events. It is important to note that although events such as a divorce occur over a short period of time, the ramifications extend over varying amounts of time depending on each family's circumstances. Thus, each child experiencing their parents' divorce may be impacted differently. Furthermore, it may be useful to use an episodic memory measure that primarily evaluates novelty detection and not just overall episodic memory abilities, given the specific role of the VTA-hippocampal loop. It would also be interesting to delve into the effects of psychological and neurological diagnoses on VTA-hippocampal connectivity. This could be further examined to conclude whether these diagnoses hinder the development of episodic memory abilities after stress exposure.

Lastly, recent studies have implicated the role of

we decided to report specifically on right hippocampal findings in this report. The right hippocampal images VTA-Hippocampal connectivity in goal-directed behaviors with novelty nuances. Perhaps changes in the connectivity between these two brain regions have larger effects on human curiosity and intrinsic motivation to learn about unexplored concepts and ideas. In a study by Gruber and colleagues (2014), fMRI results revealed that activity in the midbrain and the nucleus accumbens was enhanced during states of high curiosity. Moreover, participants showed improved memory for information that they were curious about, and also for incidental material learned during states of high curiosity (Gruber et al., 2014). Researchers have also attempted to explain why humans constantly learn in the absence of explicit rewards and found that participants who completed a task in which no external reward was provided, exhibited enhanced fMRI-signals within the dopaminergic midbrain, hippocampus, and ventral striatum (i.e., the VTA-Hippocampal loop) when successfully grasping the meaning of new-words. Importantly, new-words that were better remembered showed increased activation and enhanced functional connectivity between the midbrain, hippocampus, and ventral striatum (Ripollés et al., 2016). Therefore, researchers should explore the link between VTA-Hippocampal connectivity, curiosity, and memory further. Understanding the brain mechanisms through which early life stress affects various behavioral outcomes could help us provide appropriate support measures to children and adolescents exposed to stressful situations.

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Appendix

Negative Life Events Scale (NLES)									
Question	**Variable Name**	**Variable Type**	**Values**	**Value Labels**					
1a. The child's brother/sister was in serious trouble (such as trouble with the law, school, or drugs)	NLES_P_01a	Numeric	0-1	0=No, 1=Yes					
1b. If yes, the child was aware that his/her brother/sister was in serious trouble	NLES_P_01b	Numeric	0-1	0=No, 1=Yes					
1c. If yes, how upset was the child that his/her brother/sister was in serious trouble	NLES_P_01c	Numeric	0-4	0=Not at all upset, 1=A tiny bit upset, 2=A little upset, 3=Pretty upset, 4=Very upset					
2a. The child's close friend had serious troubles, problems, illness, or injury	NLES_P_02a	Numeric	0-1	0=No, 1=Yes					
2b. If yes, the child was aware that his/her close friend has serious troubles	NLES_P_02b	Numeric	0-1	0=No, 1=Yes					
2c. If yes, how upset was the child that his/her close friend had serious troubles	NLES_P_02c	Numeric	0-4	0=Not at all upset, 1=A tiny bit upset, 2=A little upset, 3=Pretty upset, 4=Very upset					
3a. The child suffered from a serious physical illness, injury, or extreme pain (something that required rest of	NLES_P_03a	Numeric	0-1	0=No, 1=Yes					
3b. If yes, the child was aware he/she suffered from a serious illness or injury	NLES_P_03b	Numeric	0-1	0=No, 1=Yes					
3c. If yes, how upset was the child that he/she suffered from a serious illness or injury	NLES_P_03c	Numeric	0-4	0=Not at all upset, 1=A tiny bit upset, 2=A little upset, 3=Pretty upset, 4=Very upset					
4a. The child's brother or sister suffered from serious physical illenss, injury, or extreme pain (something that	NLES_P_04a	Numeric	0-1	0=No, 1=Yes					
4b. If yes, the child was aware his/her brother/sister suffered from a serious illness or injury	NLES_P_04b	Numeric	0-1	0=No, 1=Yes					
4c. If yes, how upset was the child that his/her brother/sister suffered from a serious illness or injury	NLES_P_04c	Numeric	0-4	0=Not at all upset, 1=A tiny bit upset, 2=A little upset, 3=Pretty upset, 4=Very upset					
5a. One of the child's brothers or sisters was very angry or upset.	NLES_P_05a	Numeric	0-1	0=No, 1=Yes					
5b. If yes, the child was aware that his/her brother/sister was very angry or upset	NLES_P_05b	Numeric	0-1	0=No, 1=Yes					
5c. If yes, how upset was the child that his/her brother/sister was very angry or upset	NLES_P_05c	Numeric	0-4	0=Not at all upset, 1=A tiny bit upset, 2=A little upset, 3=Pretty upset, 4=Very upset					
6a. People in the child's family (such as his/her parents, brothers or sisters) physically hit each other hard or	NLES_P_06a	Numeric	0-1	0=No, 1=Yes					
6b. If yes, the child was aware that people in his/her family hurt each other	NLES_P_06b	Numeric	0-1	0=No, 1=Yes					
6c. If yes, how upset was the child that people in his/her family hurt each other	NLES_P_06c	Numeric	0-4	0=Not at all upset, 1=A tiny bit upset, 2=A little upset, 3=Pretty upset, 4=Very upset					
7a. The child's parent suffered from serious illness, injury, or extreme pain, something that required rest for	NLES_P_07a	Numeric	0-1	0=No, 1=Yes					
7b. If yes, the child was aware that his/her parent suffered from serious or injury	NLES_P_07b	Numeric	0-1	0=No, 1=Yes					
7c. If yes, how upset was the child that his/her parent suffered from serious illness or injury	NLES_P_07c	Numeric	0-4	0=Not at all upset, 1=A tiny bit upset, 2=A little upset, 3=Pretty upset, 4=Very upset					
8a. The child's mother or father talked about having serious money troubles (being worried about bills for or	NLES_P_08a	Numeric	0-1	0=No, 1=Yes					
8b. If yes, the child was aware that his/her mother or father talked about having serious money troubles	NLES_P_08b	Numeric	0-1	0=No, 1=Yes					
8c. If yes, how upset was the child that his/her mother or father talked about having serious money troubles	NLES_P_08c	Numeric	0-4	0=Not at all upset, 1=A tiny bit upset, 2=A little upset, 3=Pretty upset, 4=Very upset					
9a. The child's relatives such as aunts, uncles, grandparents said bad things about his/her mother or father.	NLES_P_09a	Numeric	0-1	0=No, 1=Yes					
9b. If yes, the child was aware that his/her relatives said bad things about his/her mother or father	NLES_P_09b	Numeric	0-1	0=No, 1=Yes					
9c. If yes, how upset was the child that his/her relatives said bad things about his/her mother or father	NLES_P_09c	Numeric	0-4	0=Not at all upset, 1=A tiny bit upset, 2=A little upset, 3=Pretty upset, 4=Very upset					
10a. The child's mother or father fought or argued with his/her relatives such as aunts, uncles, grandparents	NLES_P_10a	Numeric	0-1	0=No, 1=Yes					
10b. The child's If yes, the child was aware that his/her mother or father fought or argued with his/her relati	NLES_P_10b	Numeric	0-1	0=No, 1=Yes					
10c. If yes, how upset was the child that his/her mother or father fought or argued with his/her relatives	NLES_P_10c	Numeric	0-4	0=Not at all upset, 1=A tiny bit upset, 2=A little upset, 3=Pretty upset, 4=Very upset					
11a. The child's mother or father acted badly in front of the child's friends (did things like yelled at them or c	NLES_P_11a	Numeric	0-1	0=No, 1=Yes					
11b. If yes, the child was aware that his/her mother or father acted badly in front of the child's friends	NLES_P_11b	Numeric	0-1	0=No, 1=Yes					
11c. If yes, how upset was the child that his.her mother or father acted badly in fron of the child's friends?	NLES_P_11c	Numeric	0-4	0=Not at all upset, 1=A tiny bit upset, 2=A little upset, 3=Pretty upset, 4=Very upset					
12a. The child's mother or father was intoxicated in the child's presence	NLES_P_12a	Numeric	0-1	0=No, 1=Yes					
12b. If yes, the child was aware his/her parents were intoxicated	NLES_P_12b	Numeric	0-1	0=No, 1=Yes					
12c. If yes, how upset was the child that his/her parents were intoxicated	NLES_P_12c	Numeric	0-4	0=Not at all upset, 1=A tiny bit upset, 2=A little upset, 3=Pretty upset, 4=Very upset					
13a. The child's mother or father forgot to do important things for him/her that they promised they would d	NLES_P_13a	Numeric	0-1	0=No, 1=Yes					
13b. If yes, the child was aware his/her mother or father forgot to do important things for him/her	NLES_P_13b	Numeric	0-1	0=No, 1=Yes					
13c. If yes, how upset was the child that his/her mother or father forgot to do important things for him/her	NLES_P_13c	Numeric	0-4	0=Not at all upset, 1=A tiny bit upset, 2=A little upset, 3=Pretty upset, 4=Very upset					
14a. The child's mother or father was arrested or sent to jail.	NLES_P_14a	Numeric	0-1	0=No, 1=Yes					
14b. If yes, the child was aware his/her mother or father was arrested or sent to jail	NLES_P_14b	Numeric	0-1	0=No, 1=Yes					
14c. If yes, how upset was the child that his/her mother or father was arrested or sent to jail	NLES_P_14c	Numeric	0-4	0=Not at all upset, 1=A tiny bit upset, 2=A little upset, 3=Pretty upset, 4=Very upset					
15a. The child's mother or father lost a job	NLES_P_15a	Numeric	0-1	0=No, 1=Yes					
15b. If yes, the child was aware her/her mother or father lost a job	NLES_P_15b	Numeric	0-1	0=No, 1=Yes					
15c. If yes, how upset was the child that his/her mother or father lost a job	NLES_P_15c	Numeric	0-4	0=Not at all upset, 1=A tiny bit upset, 2=A little upset, 3=Pretty upset, 4=Very upset					
16a. A close family member to the child died such as a parent, close uncle, grandparent, or some other relati	NLES_P_16a	Numeric	0-1	0=No, 1=Yes					
16b. If yes, the child was aware that a close family member to the child died	NLES_P_16b	Numeric	0-1	0=No, 1=Yes					
16c. If yes, how upset was the child that a close family member to the child died	NLES_P_16c	Numeric	0-4	0=Not at all upset, 1=A tiny bit upset, 2=A little upset, 3=Pretty upset, 4=Very upset					
17a. A close friend of the child died	NLES_P_17a	Numeric	0-1	0=No, 1=Yes					
17b. If yes, the child was aware that a close friend of the child died	NLES_P_17b	Numeric	0-1	0=No, 1=Yes					
17c. If yes, how upset was the child that a close friend of the child died	NLES_P_17c	Numeric	0-4	0=Not at all upset, 1=A tiny bit upset, 2=A little upset, 3=Pretty upset, 4=Very upset					
18a. A close friend of the child moved away	NLES_P_18a	Numeric	0-1	0=No, 1=Yes					

Alexander Farquhar-Leicester, BA
University of Nebraska-Lincoln

Alex Farquhar-Leicester is currently a PhD student at the University of Nebraska-Lincoln in the Counseling Psychology program. Alex is currently interested in the intersection of neurodiversity and gender identity and the myriad ways in which distal and proximal stressors impact the mental health and academic success of undergraduate college students. Alex is a recent graduate of the University of California, Davis, where they completed a bachelor's degree in Psychology and a minor in Sexuality Studies. In addition to completing an honors thesis under the guidance of Nicole Polen-Petit, PhD, Alex worked at the UC Davis MIND Institute, under the supervision of Dr. Sally Ozonoff and Dr. Meghan Miller, during their undergraduate education. As a Research Assistant and eventually Junior Specialist, they assisted Dr. Ozonoff and Dr. Miller with various NIH-funded projects that examined the early behavioral manifestations of autism spectrum disorder (ASD) and attention-deficit hyperactivity disorder (ADHD) among infants at risk for these disorders.

With Minority Stress Theory and intersectionality as methodological/theoretical frameworks, my thesis seeks to extend the extant literature on TGD and neurodiverse identities, with specific attention to distal (i.e., discrimination, rejection, victimization, harassment) and proximal (i.e., self-stigma, stigma consciousness) stressors and the mental health and academic success for neurodiverse undergraduate students who may experience marginalization along multiple dimensions.

Contact: afarquharleicester@gmail.com

Was there a particular experience that sparked your research interests?

I have always been interested in the intersection of sexual orientation and/or gender identity and online spaces. There has been increased attention to the myriad ways in which technology is changing people's lives, and I was interested in how it may also impact identity exploration and development, specifically for people whose identities are marginalized and less represented in physical spaces that often engender heteronormativity and gender essentialism.

Who has been an influential person in your life?

I cannot narrow down a specific, overall influential person in my life. But, as it relates to academia, Dr. Polen-Petit has been the most influential person in my life. She has and continues to be an ongoing source of support, encouragement, and guidance as I continue my education, clinical work, and research as a doctoral student.

What is your greatest accomplishment?

My greatest accomplishment thus far in my life is developing, planning, and directing a overnight camp in the Midwest for transgender and gender-diverse (TGD) children and their families. I was fortunate to be the Director for the past two years.

Where do you see yourself in 10 years?

Given the nature of graduate school, I am not sure where exactly I will be in 10 years—nor can I accurately envision myself 10 years from now. There is simply too much ebb and flow in my life--and, similarly, the world. I am currently trying my best to keep my options open with private practice, research, and teaching as options for my future.

Subjective Sexual Well-Being Among LGBTQIA+ Students: An Exploration of the Role of Social Networking Sites and Applications

Alexander Farquhar-Leicestser, BA[1] and Nicole Polen-Petit, PhD[2]

The Internet has been shown to serve a myriad of functions for individuals with diverse sexual and gender identities, including managing their identity, exploring sexuality in a safe, mediated space, and engaging in experiential learning (Craig & McInroy, 2013; Fox & Ralston, 2016; Hiller, Mitchell, & Ybarra, 2012). However, little research has examined the role that more focused, specific SNSs and applications, geared towards sexual encounters, dating, and relationships, play in the lives of individuals who self-identify as lesbian, gay, bisexual, transgender, queer, questioning, intersex, asexual, and/or pansexual (LGBTQIA+). By employing thematic analysis, this study examined the role that more focused, specific SNSs and applications play in the lives of LGBTQIA+ college students (N = 15). Additionally, the study explored the possible ways in which such SNSs and applications may contribute to or affect the sexual well-being of LGBTQIA+ college students. Three themes emerged with regard to the use of broad SNSs: (1) the exploration and reaffirmation of identity, (2) connectivity, (3) learning. Three themes also emerged for more specific and focused SNSs and applications: (1) validation, (2) visibility and finding likeness, (3) learning. Participants reported experiences of sexual objectification on more specific, focused SNSs and applications. Participants' responses revealed a delineation between the way they conducted themselves on broad SNSs and specific SNSs and applications: safety and honesty. Future research should explore sexual well-being quantitatively and examine experiences of sexual objectification on SNSs and applications.

Most contemporary lesbian, gay, bisexual, transgender, queer, questioning, intersex, asexual, and pansexual (LGBTQIA+) youth and young adults have access to an immense array of information, media, and connectivity that most theorists and researchers have only recently begun to consider. In the last decade, there have been unprecedented, technological advances with regard to both the availability and complexity of online spaces, especially social networking sites (SNSs) and applications (Boyd & Ellison, 2007; Manago, 2014). Considering such advances, young LGBTQIA+ adults are growing up in a sociocultural shift that is pertinent to their lives and worthy of researchers' attention (Patterson & D'Augelli, 2013; Polen-Petit, 2016). However, at this stage, few researchers have examined the role that more focused, specific SNSs and applications geared towards sexual encounters, dating, and relationships play in the lives of college-aged individuals who identify as LGBTQIA+. Additionally, little is known about how SNSs and applications may contribute to or affect an individual's subjective sexual well-being beyond associated and potential sexual health risks.

Compared to their heterosexual contemporaries, lesbian, gay, and bisexual (LGB) individuals often face added challenges when approaching and exploring their sexual identity, including heteronormativity, cultural marginalization, self-stigma, and fear of/negative experiences with sexual prejudice and discrimination

1 University of Nebraska-Lincoln

2 National University

(D'Augelli & Patterson, 1995; Evans & D'Augelli, 1996; Herek, 2004; Herek, 2009; Herek, 2009; Savin-Williams, 1996). However, as the presence of and accessibility to the Internet grew in the mid-to-late 1990s, individuals with diverse sexual and gender identities were able to utilize the anonymity of online spaces to develop relationships and self-disclose in ways that were often not feasible or safe offline (Burke, 2000; Campbell, 2004; Wakeford, 2002). In fact, early research revealed that individuals who self-identified as lesbian, gay, bisexual, transgender, and queer (LGBTQ) were able to find safe and supportive environments on the Internet and considered the online experiences they had with similar others online were beneficial to their psychological well-being (Campbell, 2004; Wakeford, 2002).

Recently, researchers have argued that the Internet—including new media, social media, and SNSs—has become crucial to the identity development process of LGBTQ individuals (Craig & McInroy, 2014; Fox & Ralston, 2016; Hiller, Mitchell, & Ybarrra, 2012). Specifically, the Internet and SNSs have been shown to provide a myriad of functions for LGBTQ individuals, including exploring and developing a non-heterosexual identity, managing sexuality in a safe, mediated space, and engaging in experiential learning (Craig & McInroy, 2013; Fox & Ralston, 2016; Hiller et al., 2012). Social media and SNSs have also been increasingly integral to the facilitation of the coming out process (Albert & Bettez, 2012; Alexander & Losh, 2010). Dating and the process of seeking romantic partners online is very common among LGBTQ populations (Gudelunas, 2012; McFarlane, Bull, & Reitmmeijer, 2000; Rosser et al., 2011), and gay men have reported using gay-specific SNSs to explore and identify potential romantic and/or sexual partners as well as to fulfill various personal sexual gratifications (Gudelunas, 2012; Miller, 2015).

As outlined, the inception and development of the Internet has provoked curiosity about how such virtual landscapes affect people's lives. While some research has explored the opportunities that the Internet, new media, social media, and SNSs have provided individuals who self-identify as LGBTQ+, less is known about the role of more focused, specific SNSs and applications. Notably, the availability and presence of SNSs and applications have proliferated during the last decade, particularly the last five years (Pew Research Center, 2019). Boyd and Ellison (2007) define SNSs as internet-based services that allow people to "(1) construct a public or semi-public profile within a bounded system, (2) articulate a list of other users with whom they share a connection, and (3) view and traverse their list of connections and those by others within the system" (p. 211). Applications (e.g. apps) refer to computer-run software programs that allow specific SNSs to be run on mobile devices, tablets, and/or wrist watches. Additionally, some SNSs and applications are more broad and general, with a common theme of social networking, while other SNSs and applications have been designed and limited to certain activities or interests.

With increasing accessibility and connectivity via virtual spaces, sexual well-being may be impacted by SNSs and applications. Sexual well-being encompasses an objective, physical state and a subjective, mental state that is characterized by positive and joyful feelings about one's sexual life (Laumann et al., 2006). Sexual well-being also encompasses a state of physical, emotional, and mental prosperity in relation to one's sexuality. In this sense, sexual well-being is not merely the reduced risk or absence of dysfunction, disease, or illness; rather, it is the well-being of an individual across numerous domains which are specifically tied to one's sexuality (Herdt & Polen-Petit, 2014). As noted previously, research suggests that the Internet—specifically new media, social media, and broad SNSs—have given young, LGBTQ people various affordances (Craig & McInroy, 2014; Fox & Ralston, 2016; Hiller, Mitchell, & Ybarrra, 2012), which seems to contribute to their sexual well-being by way of positive emotions, confidence, specific sexual health knowledge, and a sense of self. In spite of the positive and advantageous utilities that online spaces provide, some research indicates that SNS use is associated with risky sexual health and behavior among LGBTQ+ populations. For instance, one study found that individuals who self-identify as LGBTQ and used SNSs for more than a year were more likely to have unprotected sex (Holloway et al., 2015). Furthermore, other research suggests that LGBTQ individuals who use SNSs are more likely to have more than one sexual partner (Bien et al, 2015; Lee et al., 2012; Lehmiller & Ioerger, 2014; Phillips Ii et al., 2014). This is an important consideration, as physical health and safety

are major foundations and determinants of overall sexual well-being (Herdt & Polen-Petit, 2014; Laumann et al., 2006).

While some research has explored the opportunities that the Internet, new media, social media, and SNSs have provided individuals who self-identify as LGBTQ, less is known about the role of more focused and specific SNSs and applications geared toward sexual encounters, dating, and seeking relationships. Additionally, some sexual health and behavior risks have been found to be associated with SNS use, but research has not explored, broadly speaking, the ways SNSs and applications may contribute to or affect one's subjective sexual well-being. Most research has not (1) focused on a college-age population or (2) included other sexual orientations in their inclusion criteria, such as intersex, asexual, and pansexual, or individuals who do not subscribe to identity labels, but still associate themselves within the LGBTQIA+ community.

Given the current limitations of previous research, the present study was designed to investigate the following research questions: (1) what role do more focused and specific social networks sites and applications play in the lives of LGBTQIA+ college students? and (2) do social networking sites and applications contribute to or affect these individual's subjective sexual well-being? This study also sought to gain additional information and insight about broad SNSs and applications. Overall, this study focuses on exploring how LGBTQIA+ college students use SNSs and applications, including how these virtual landscapes are catalysts for developing and furthering sexual well-being.

Most qualitative studies use inductive and deductive processes rather than hypothetical or hypo-deductive processes. As such, most qualitative research does not aim to test or prove a specific research hypothesis. Rather, such research aims to understand cultural phenomena and/or events, meanings, and experiences within a particular social context (Liamputtong, 2009). Under these considerations, there is no hypothesis for this study.

Method

Participants

Participants (N = 15) were recruited from a large public university located in the Central Valley of Northern California. Inclusion criteria included undergraduate student status, being 18 years of age or older, and self-identifying as LGBTQIA+, or not subscribing to identity labels, but associating oneself with the LGBTQIA+ community. Flyers seeking undergraduate students who met the inclusion criteria were posted in lecture halls and the on-campus LGBTQIA+ Resource Center during the two-month data collection period. Snowball sampling techniques were also employed; participants were encouraged to tell other eligible individuals about the study. A waiver of informed consent was granted for this study. As required by the Institutional Review Board (IRB), an informed consent form was reviewed with and given to all participants and verbal assent was obtained. Participants were compensated with a 10-dollar gift certificate to the on-campus café.

Participants ranged in age from 18 to 25 (M = 20.26, SD = 1.79). The sample consisted of individuals who self-identified as gay and lesbian (n = 8), bisexual (n = 3), and queer (n = 4). Participants that self-identified as pansexual or used multiple identity labels were aggregated under queer. Participants identified as cisgender-male (n = 5), cisgender-female (n = 8), and male-to-female transgender (n = 2). The ethnic identities of the participants included Asian/Asian-American (n = 6), Latinx/Chicanx/Hispanic (n = 4), Caucasian (n = 3), and multi-ethnic (n = 2). Most participants (n = 13) had disclosed their sexual/gender identity to their friends and family and had integrated their identity into both their private and public spheres.

Materials

An in-person, semi-structured questionnaire was used to collect information regarding age, ethnicity, sexual orientation, gender identity, coming out experience, dating, and thoughts/usage of SNSs and applications (Appendix A). The questionnaire was developed by the researcher and consisted of 16 items. Example questions included: "Do you believe social networking sites contribute to the formation or maintenance of identity? If so, in what ways?", "What role, if any, have social networking sites and applications that are geared towards sexual encounters, dating, or seeking relationships played with regard to your sexual orientation and/or gender

identity?", and "Why did you use that/those particular social media network(s) and application(s)?" (Table 1). The interview was estimated to take 30 to 60 minutes to complete. A waiver of signed consent was granted for the study. Participants were provided with a written consent form outlining and describing the research during the consenting process as well as a handout on mental health resources. Participants' responses were collected using an audio-recording device, and all interview recordings were transcribed on a secure computer by the researcher. NVivo, a qualitative data analysis software, was used to code the interview data, organize themes, and allow for meaningful interpretation of the data. All study protocols and procedures were approved by the university's IRB.

Procedure

Recruitment flyers informed willing participants to contact the researcher via email. Eligibility screening was conducted through email, and if inclusion criteria was met, participants were asked to choose a time and location for the interview. The time and location of the interview was dependent upon the participant's preference and comfort. If a participant did not have a preference, on-campus locations were suggested. All interviews for this study were conducted on campus.

A written consent form was given to all participants before the interview started and verbal consent was obtained. Participants were told that the study was designed to explore the possible role that SNSs—including those geared toward sexual encounters, dating, and seeking relationships—play in the lives of LGBTQIA+ college students. Participants were also assured that their participation was entirely voluntary and that their responses were confidential. The interviews lasted between 17 to 45 minutes in duration ($M = 23.26$, $SD = 8.62$). After the interview, participants were debriefed verbally and given time to offer constructive feedback to the researcher regarding their comfort level during the interview and the content of the questionnaire items. Each audiotaped interview was transcribed on a secure computer, labelled with a numerical identifier, and then input into the qualitative analysis software. Transcripts were reviewed by a faculty member in the Department of Human Development.

Thematic analysis, an inductive and deductive process of identifying patterns (i.e. themes) within a set of qualitative data, was employed as the analytic framework for the study. This particular method is often used for qualitative studies to explore topics that have been minimally researched (Guest, MacQueen, & Namey, 2012). Each transcription passed through a six-phase framework, as per Braun & Clarke's (2006) guidelines: familiarization of data, initial codes, search for themes, review themes, define themes, and write-up.

First, the researcher cross-referenced and checked the recordings and transcriptions for accuracy. The researcher then re-read the transcripts in order to become familiar with the data. The second phase featured an open coding process, which involved the creation of initial codes through a process of line-by-line and paragraph-by-paragraph coding in NVivo. During this phase, comparative analysis was utilized in order to label codes based on type of SNS and application: broad versus specific. Third, the researcher organized and compiled significant, initial codes into preliminary themes that seemed to fit the data and were relevant to the research questions: (1) what role do social networks sites and applications that are geared towards sexual encounters, dating, and relationships play in the lives of LGBTQIA+? and (2) do social networking sites and applications contribute to or affect these individual's subjective sexual well-being? The preliminary themes reflected overarching patterns in the data. Each theme was described separately from one another. The fourth phase detailed a review of the themes where each was labeled and color-coded in NVivo. The researcher examined core themes, including relating them to other themes and codes, in order to find meaningful interpretations and to see how the themes accurately depicted the data. Themes were then refined, defined, and labeled with regard to the underlying meaning and concepts of the participants' responses and narratives. During the final phase, final themes were compiled on separate documents within NVivo.

Results

Participants' responses (Appendix B) revealed the many ways in which SNSs and applications played a role in their lives. Three themes emerged among broad SNSs: (1) explore and reaffirm identity, (2) connectivity, (3) learning.

Three themes also emerged for more focused and specific SNSs and applications: (1) validation, (2) visibility and finding likeness, (3) learning. Additionally, participants' responses differed in relation to the way they conducted themselves between broad and more specific SNSs and applications. Two themes emerged between board and more specific SNSs and applications: safety and honesty. Some participants also disclosed narratives of sexual objectification in their use and interactions with focused, specific SNSs and applications (i.e., SNSs and applications geared toward sexual encounters, dating, and seeking relationships).

Broad Social Networking Sites

Explore and reaffirm identity

Through the use of broad SNSs—such as Facebook, YouTube, Tumblr, Twitter, and Instagram—participants reported exploring their emerging identities before coming to self-identify as LGBTQIA+ and reaffirming their identities in the presence of similar others (n = 7). In their narratives of identity exploration and reaffirmation, many participants described first discovering or acknowledging their LGBTQIA+ identity by engaging with non-heterosexual information and people on SNSs. Other participants described their process of validating thoughts and feelings about themselves and their specific LGBTQIA+ identity. Some participants specifically noted that this affordance of exploration and reaffirmation through increased accessibility was crucial because they may not experience representation in their immediate, physical environment. Importantly, one participant even reported having overcome negative internalization of their identity as a result of being able to explore and affirm their thoughts and feelings.

Connectivity

Participants reported utilizing SNSs to connect with other individuals who self-identify as LGBTQIA+ and join online communities that share common interests (n = 5). For example, one participant made reference to a SNS called Discord, which allows people to create communities and chat with people over text, voice, and video. This participant reported being able to interact with others in a safe space, which helped solidify identity and foster camaraderie among similar others. Generally speaking, participants noted that broad SNSs afforded them the opportunity to purposely seek out and establish connections with members of various LGBTQIA+ communities that were pertinent to their specific identity and bypass physical and geographical barriers to connectivity.

Learning

Through the use of various SNSs, participants reported the ability to learn about their own identities, communities, LGBTQIA+ topics, and the meaning of a non-heterosexual identity (n = 5). Participant's narratives highlighted that they used various SNSs to engage in different types of learning. First, participants noted using SNSs to directly obtain information about topics like identity labels (i.e., traditional learning). Second, in their connectivity and social interactions online, participants disclosed being able to consider their own identity in relation to others (i.e., social learning). Many participants reported that they were able to achieve some level of self-determination in their process of seeking out information and interacting with similar others. Participants specifically disclosed positive feelings about their sexuality after engaging in the learning process through SNSs.

Social Networking Sites and Applications: Sexual Encounters, Dating, and Seeking Relationships

Validation

In more focused, specific SNSs sites and applications, many participants described receiving validation through their interactions with similar others (n = 4). Specifically, communicating with similar others helped reaffirm their sexual orientation and/or gender identity as well as past and present sexual thoughts, feelings, and attractions. One participant noted that it was difficult to receive such validation elsewhere, due to the sexual stigma that is associated with non-heterosexual behavior. Participants mentioned that receiving support and validation through the use of these SNSs and applications was much easier than face-to-face encounters and provided a low-risk outlet to share personal experiences and narratives, thoughts, and desires about their sexuality and identity.

Visibility and Finding Likeness

Participants reported that the use of such SNSs and applications increased the visibility of similar others in their relative location. This visibility helped reveal the presence of individuals who self-identify similarly and allowed participants to gain a sense of connectedness (n = 2). One participant noted feeling a particular sense of comfort and feeling less isolated as a result of being visible and having access to other members of the LGBTQIA+ community who have gone through similar experiences as a LGBTQIA+ individual. In discussing visibility and likeness, one participant emphasized that it is easier to find and connect with people who have particular, intersectional identities—namely, bisexual people of color.

Learning

By using such SNSs and applications, participants were able to learn about their own and others' identities by connecting and communicating with similar others, which was described as a helpful opportunity (n = 2). One participant noted that more focused, specific SNSs and applications allowed them to learn—through traditional and social learning—about others' identities and experiences on a more intimate, personal level. Another participant described being able to ask about what it's like, personally, to be gay and to discuss and learn about sex.

Safety and Honesty

Participants' responses revealed that they conducted themselves more safely on broader, more expansive SNSs and more honestly on more focused, specific SNSs and applications.

Safety

Broad SNSs and applications allowed participants to manage their identities safely. Specifically, Facebook provided a safe space for participants, which gave them the opportunity to disclose their identity with ease, depending on their individual level of comfort (n = 6).

For instance, broad SNSs gave some participants the ability to avoid potentially uncomfortable in-person responses or reactions as well as be selective in who they communicated with. Additionally, for participants who had not yet disclosed their identity to their broader social group or who were less comfortable with their identity, SNSs such as Facebook provided them with the opportunity to participate in private groups and/or disclose their identity, indirectly, over time.

Honesty

More focused, specific SNSs and applications allowed participants to be honest about their sexual identity, thoughts, and feelings (n = 7). Many participants noted feeling particularly comfortable on SNSs and applications such as Grindr and Tinder, allowing them to freely discuss various aspects of sex and sexuality without censorship. Additionally, unlike broad SNSs, Grindr allowed one participant to be honest and open with their identity, which they could not do on other SNSs due to the risk of having their identity being disclosed.

Sexual Objectification

Participants (n = 2) also reported experiences of sexual objectification in their use of more focused, specific SNSs. Two participants recounted past experiences of being fetishized by straight, cis-gender men—referred to as "chasers" by one participant. One participant described being seen merely as a sexual object among some people on SNSs and applications such as Grindr and Tinder. A second participant received negative comments from people, specifically related to body image, gender expression and identity. Both participants described these experiences of sexual objectification and the interpersonal interactions they had with the perpetrators as distressing.

Discussion

This study found that broader, more expansive SNSs provided important opportunities for LGBTQIA+ college students to explore and develop their identities. Specifically, participants used broad SNSs to explore their emerging identities online, connect with similar others, reaffirm various aspects of their identity, and learn about their own identities, others' identities, and the larger LGBTQIA+ community. These findings parallel previous research on the Internet and social media, which found that LGBTQ individuals use online spaces to connect and engage with accepting communities (Craig & McInroy,

2013) and explore, construct, and practice their identities in the process (Hiller & Harrison, 2007). Research has also shown that LGBTQ individuals are able to learn about identity labels and their meaning (Fox & Ralston, 2016), as well as the gay community, through various online spaces (Hiller & Harrison, 2007).

Unlike most prior research, the present study explored the role of more specific, focused SNSs and applications geared toward sexual encounters, dating, and seeking relationships. The findings of the present study indicate that more focused, specific SNSs and applications provided critical opportunities for LGBTQIA+ college students. Participants seemed to explore their identity in more rich and extensive ways, especially with regard to their sexual orientation and/or gender identity. For instance, although previous research has identified the role that the Internet plays in the exploration and confirmation of same-sex attraction (Hiller et al., 2012), participant's responses demonstrate that such validation seems to happen more explicitly—intimately and interpersonally—on more focused, specific SNSs and applications. The findings of this study also support past research, which found that LGBTQ individuals are able to find and receive a sense of comfort from the presence of similar others (Craig & Mclnroy, 2013; Hiller et al., 2012), learn about various aspects of non-heterosexual sexuality, the specifics of same-sex encounters, and gay culture online (Hiller & Harrison, 2007).

With regard to sexual well-being, participant's narratives suggest that SNSs and applications—both broad and the more specific—provide opportunities for LGBTQIA+ college students to further their identity and personal development, spur connection, promote the acquisition of knowledge, and form relationships. But for more specific SNSs and applications it seems that young, LGBTQIA+ college students are afforded the opportunity to more readily center and leverage their sexuality and sexual lives. This fueling of expression of information, identity, sexual practices, and discourses of sexuality may be crucial for young, LGBTQIA+ college students who are often times imbricated in heteronormative and gender-essentialist environments. The opportunity to navigate and converse—critically and with relative ease—about identity, sexuality, and sex is crucial for one's sexual well-being, especially for communities of abjected social groups. As defined by Laumann (2006), sexual well-being is defined as encompassing cognitive and emotional evaluations of one's sexuality, including feelings of happiness, equanimity, life satisfaction, and fulfillment—especially as it relates to sexuality. Participants described their engagement using SNSs and applications with engendered feelings of validation, fulfillment, and equanimity. These feelings are generally contributed to comfort and a positive outlook about their identities and sexuality as well as the thoughts, feelings, and desires they had. Moreover, the affordance of self-determination, safety, autonomy, self-confidence and the potential for both communicating and traversing sexuality and sexual relations—as reflected in participant's responses—may be advantageous to pleasure, which is a crux of sexual well-being.

Nevertheless, transgender participants in the study sample reported experiences of sexual objectification on more focused, specific SNSs and applications like Grindr and Tinder. These participants' responses seem to highlight both the precarity and potentially-distressing nature of navigating SNSs and applications geared towards sexual encounters, dating, and relationships with an identity that is objectified and/or fetishized by others. Sexual objectification occurs when a person—their body, body parts, and functions—is seen as constituting the entirety of the person and as an object of sexual desire (Bartky, 1990; Moradi & Huang, 2008). According to the Objectification Theory (OT), being sexually objectified can lead to a deleterious internalization process. This internalization process, marked by accepting the beliefs and actions of others in relation to their body, often gives rise to increased body monitoring (e.g., body surveillance) and harmful mental and affective conditions apposite to one's body (e.g., body shame, appearance anxiety) (Fredrickson & Roberts, 1997; Tiggemann & Kuring, 2004).

Specifically, experiences of sexual objectification have been shown to be correlated with body surveillance, body shame, maladaptive eating patterns, substance abuse, and depressive symptomatology (Carr & Szymanski, 2011; Miles-McLean et al., 2015; Moradi, 2010; Moradi & Huang, 2008). Little is known about the specific nature of sexual objectification among transgender individuals

and its ensuing results on well-being. However, a recent qualitative study found that transgender people of color reported numerous experiences of sexual objectification: fetishization based on identities, racialized objectification, negative comments regarding genitalia or gender transition, and body policing (Flores et al., 2018). Echoing the results of Flores and colleague's (2018) study, two participants in the present study reported fetishization based on identity. Experiences of sexual objectification and fetishization may have negative consequences on someone's sexual well-being which may contribute to less self-confidence, fulfillment, happiness, and positive regard for one's sexuality. Interpersonally, experiences of sexual objectification and fetishization may decrease one's self-determination as well as desire to engage with other people with comfort and equanimity.

Safety and Honesty: Context

A particularly interesting finding was the way participants distinguished their use of SNSs and applications as providing either safety or honesty. Although it is clear that the Internet and SNSs allow LGBTQIA+ individuals with the opportunity to conduct themselves both safely and honestly in myriad ways (Craig & McInroy, 2013; Gudelunas, 2012; Hiller & Harrison, 2007; Hiller et al., 2012), participants' responses revealed a possible delineation between how they conducted themselves on broad SNSs (i.e., Facebook) versus more focused SNSs and applications (i.e., Grindr and Tinder).

Participants reported using broad SNSs, such as Facebook, to manage various aspects of their identity in a safe manner, especially with regard to their individual comfort level. Echoing previous research, participants used Facebook to disclose their identity online prior to doing so offline or to disclose their identity indirectly, through posts, indicators of interests or preferences (Craig & McInroy, 2013). Previous research has also highlighted the many ways in which youth and adults utilize the Internet and online spaces to explore and manage aspects of their sexual identity in a safe, anonymous, and/or mediated environment (Albert & Bettez, 2012; Craig & McInroy, 2013; Hiller et al., 2012). Conversely, participants who used more focused, specific SNSs and applications disclosed that they were most honest with various aspects of their identity—specifically with regard to their sexual thoughts and feelings.

However, contrary to the results of this study, Miller (2015) found that men who have sex with men (MSM) felt a sense of safety on SNSs and applications that are geared towards sexual encounters, dating, and relationships. Participants in Miller's (2015) study reported that they perceived such SNSs and applications as constituting a safe space, which afforded them physical and emotional security. Participants also referenced the specific, design and nature of such SNSs and applications, indicating that they knew the other users would be individuals who similarly self-identified. As a result, participants felt they were able to focus on various aspects of attraction without the possible danger and/or distress that may arise from approaching individuals within real-world, offline spaces (Miller, 2015).

Regardless, the results of the present study in conjunction with past research seem to highlight the complex nature in which contextual circumstances, both individual and social, may account for the ways in which LGBTQIA+ individuals conduct themselves on and between differing SNSs and applications. First, it may be that the online environments of more specific and focused SNSs and applications—such as the fact that the primary user base of such applications are individuals who are LGBTQIA+—allowed participants to explore and engage their sexual and/or gender identity more honestly. Along these lines, LGBTQIA+ individuals may feel less confined or limited in what they choose to discuss or reveal about themselves. On the other hand, perhaps it is the more focused, specific design and nature of SNSs and applications that drives such honest self-expression and disclosure. Personal and/or contextual factors, such as cultural identity or 'outness', may also contribute to the different ways LGBTQIA+ individuals navigate and conduct themselves on SNSs and applications. Regardless, it is clear that the question of whether, and more importantly, why, greater safety and/or honesty is provided by targeted SNSs is in need of both further and more specific investigation.

Strengths and Limitations

The results of this study contribute much needed information to a body of research that is lacking due to the rapidly transmuting landscape of the technological

world across both space and time. Understanding how both online spaces and technology impacts sexual and/or gender identity, sexual well-being, and sexual literacy is imperative in a world that has become increasingly virtual. This study provides further understanding of how young, LGBTQIA+ individuals utilize SNSs and applications as part of their lives to advance identity, knowledge, connections and relationships.

Drawing on the experiences of participants, this research gives preliminary support to both positive and negative effects of SNSs and application use among LGBTQIA+ individuals as it relates to sexual well-being. Furthermore,this study highlights that the Internet—and, specifically, SNSs and applications—will continue to provide spaces wherein people with sexual and gender-diverse identities can promote sexual well-being, empowerment, community, and resistance in a heteronormative, gender-essentialist world.

Nevertheless, this study encompasses many limitations. One limitation is the study's sample size. Due to the small sample size, it is not possible to determine if the results are representative. Furthermore, although the researcher attempted to recruit broadly and inclusively, the final sample did not include individuals who self-identify as intersex or asexual. Another limitation may stem from researcher and participant bias. Although the researcher maintained an effort to eliminate all preconceptions during the entire research process, it is possible that some of the researcher's biases affected the interviews and/or data analyses. Research constitutes a shared space that is shaped by both the researcher and the participants; therefore, it is crucial to understand that the identities, and thus position, of both the researcher and participants have the ability to affect the research process. As such, it is important to acknowledge that the researcher's own identity could have altered their interaction with, and perceptions regarding, the interview data. For instance, the researcher's own identity may have resulted in unintentional omissions or biased reporting. Given the nature of self-reported data, it is also possible that participants' responses may have not been entirely accurate. Despite such limitations, the results of this study furthers our understanding of the role that both broad and specific SNSs and applications play in the lives of LGBTQIA+ college students.

Practice Implications

Several clinical and practice-based implications result from this study. First, practitioners can now better understand the context, utility, and intersection of technological change and identity development. The themes of the data further emphasize the ubiquity of SNSs and applications in the lives of LGBTQIA+ college students. Second, the results of this study highlight the need of practitioners to attend to and understand the myriad and salient ways in which LGBTQIA+ college students utilize SNSs to navigate and further construct their identity. Specifically, the narratives of the participants bespeak the advantageous aspects that engaging in narratives of sexual identity, gender identity, possibility, connection, and different types of learning have on sexual well-being. At the same time, however, results of this study also shed light on potentially harmful and disadvantageous aspects of SNSs and applications, such as sexual objectification and fetishization. It may be particularly important for mental health professionals and clinicians to attend to the possibility of sexual objectification, fetishization and various internalization processes that may result for LGBTQIA+ college students.

Future Research

Future research should explore the different ways that LGBTQIA+ individuals conduct themselves on SNSs and applications—especially with regard to safety and honesty. Future research should also employ quantitative methods to better explore and explicate, specifically, how LGBTQIA+ individual's use of and experiences on SNSs and applications affect sexual well-being. Research about transgender identity development, both broadly and more specifically, as it relates to virtual spaces, is limited (Craig & McInroy, 2014) and, as such, should be given specific attention. It may also be advantageous to explore the ways in which sexual and gender-diverse populations experience sexual objectification on focused, specific SNSs and applications, such as those geared toward sexual encounters, dating, and seeking relationship, with particular attention to its potential deleterious effects on subjective sexual and psychological well-being.

Conclusion

The proliferation of the Internet—and more

recently—SNSs and applications has provided individuals with diverse sexual orientations and gender identities with many affordances, providing new ways of communicating, expressing themselves, and learning from others that exceed the boundaries of time and geography. This study is part of a small body of research that has explored the ways in which LGBTQIA+ college students utilize SNSs and applications to self-narrate their own sexuality and other identities—and, importantly, how their use of them affects their lives. Though exploratory, this study provides a basis for understanding how SNSs and applications can impact the sexual well-being of LGBTQIA+ college students. Importantly, this study provides a foundation for and an avenue through which future research may further examine how SNSs and applications contribute to sexual well-being among LGBTQIA+ college students.

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Appendix A

Table 1
Questionnaire Items

Demographics
D1: How old are you? D2: What is your ethnicity?
Sexual Identity
S1: What does your sexual orientation and/or gender identity mean to you as an individual? S2: If you have one, can you tell me a little bit about your 'coming out' experience/story (i.e., the time when you first disclosed your identity/identities)? S3: What challenges, if any, have you faced with regard to dating or seeking relationships?
Targeted Content Questions
SNS1: Broadly speaking, do you believe social networking sites and applications contribute to the formation or maintenance of identity? If so, in what ways? SNS1a: Has this been true for you in your own sexual identity? SNS2: What role, if any, have social networking sites and applications that are geared specifically towards sexual encounters, dating, or seeking relationships played in your personal life? SNS2a, if pertinent: What role, if any, have social networking sites and applications that are geared towards sexual encounters, dating, or seeking relationships played with regard to your sexual orientation and/or gender identity? SNS2b, if pertinent: In particular, what social media sites and applications have you used? SNS2b2, why did you use that/those particular social media network(s) and application(s)? SNS2c, if not pertinent: Why haven't social media sites and applications that are geared towards sexual encounters, dating, and seeking relationships played a role in your life? SNS2d, if pertinent: How are other social networking sites and applications different from those that are specifically geared towards sexual encounters, dating, or relationships?
Sub Question/Probing Questions
SB1: What did that/those experience(s) provide for you? SB2: How did that affect you as a sexual person? P1: Can you tell me more about that? P2: What was so meaningful about that experience?

Appendix B

Explore and Reaffirm Identity

I think it's even true for myself and to a lot of other folks is that we didn't know about ourselves until we were introduced to social media and networking. The Internet is a very cool place to be for figuring yourself out because oftentimes [we're] only limited to anyone who is accessible to us. Social networking eliminates these physical barriers. We are allowed to engage freely, and I, for one, really discovered who I am today as a result. (transgender-female, queer)

The first time that I really started identifying myself as bisexual was when I started becoming a part of these communities and started meeting a lot of people who had those same feelings that I did. I felt I didn't know a lot of people in my everyday life that were LGBT, but I suddenly had access to this community where a lot of people were very comfortable talking about their experiences and being very accepting of everyone else being LGBT. That's when my feelings for people started being put in a context and making more sense for me. I could identify [with] and talk to people about these feelings and feel like it wasn't a bad thing to be a member of this community. (cisgender-female, bisexual)

Connectivity

I am a big member of some gaming communities. There is a site called Discord, which is a social networking site and [it] is a place where people can create different communities. A lot of different gamers who identify as LGBT have started these discords and kinds of spaces for people who specifically [identify] as LGBT or who don't like labels to interact and feel safe, and I think it really helps solidify the kind of identity that people have…a really good space to interact with other people. (cisgender-female, bisexual)

Social networking allows me to go on a computer. Let's say I don't know any trans people in the area. Before I came to [city name] I really didn't. And so, with social networking sites, we are able to link people who would otherwise not be linked. I became very immersed as a result. And we see that with a lot of social movements and identities. And the relationships I've built from those connections are really important to me and my identity (transgender-female, bisexual)

Learning

I call myself a lesbian and it's not really necessarily the dictionary definition of what a lesbian is, and I wouldn't have even known that was a thing. I can use a lesbian label differently than what it is coined to be. I consider myself to be homo-romantic, but I don't necessarily always have attractions to women. But, I know I'll end up with another woman. Mainstream media doesn't really consider that a lesbian. And I wouldn't know that was possible unless I went [to] social media and networking stuff. (cisgender-female, lesbian/queer)

It's just like an influx of information gave people an option to be like I kind of think that I'm more like this than that. So, I found learning more about what it means to be queer or learning more [about] what it meant to be bi really helpful and really a positive force in my sexuality. (cisgender-female, queer)

Validation

I pretty much used Tinder and Grindr to validate the feelings I had…to explore my curiosity and chat with people who were like me. Like, for example, I met a few guys who also didn't have much experience with talking with other gay guys, and we were able to connect and talk [about] our identities and intimate sexual stuff. (cisgender-male, gay)

So, they basically validated the stuff that I think about or feeling sexually. And that was good for me sexually, like, for my identity as a sexual person. It's hard to sometimes get that validation elsewhere…because non-heterosexual sex stuff is super stigmatized and frowned upon, I think, especially in my culture (cisgender-male, gay)

Visibility and Finding Likeness

You just feel out of place when you don't have anyone around who isn't the same or feels the same as you. Once you have that, though, it feels nice because you know all of these people. They have similar stories to you about coming out as well. So, in a sense, you feel connected to them. It's comforting to know that someone like you is near. (cisgender-male, gay)

It lets me know that my community is out there…it's been easier to connect with people and find people…women, specifically, who identify as queer. (cisgender-female, bisexual)

Learning

The most useful part was being able to put myself out there…talk with other people who are gay. Talking to other people who are has been a helpful experience…learning about other people's identities and stories…getting to know them on a more personal level. (cisgender-male, gay)

When I first started talking to people I would ask them questions, like being gay and what it is, and they would explain it and how it works and stuff like that. So that was really helpful. I was also able to like talk about sex a lot. (cisgender-male, gay)

Safety

It's a lot easier to disclose your sexuality and gender identity online than it is with real people…cause when you meet someone online and they're kind of shitty about it, you can just leave most of the time. You don't have to run into them the next day. (cisgender-female, lesbian/queer)

It was helpful, especially when I was figuring it out. I wasn't too confident with myself…being gay and all that. I didn't feel comfortable telling everyone in-person. So, it was helpful to have a way to [convey] my true identity across to people I felt [like] telling with a Facebook post…cause, you know, you can choose who sees [your] posts. And [that] was helpful to have someone else…other people to talk to, who I chose to talk to, when I was ready because you can't always be so straightforward and open with everyone. (cisgender-female, gay)

Well, I'm on Facebook and secret Facebook groups for trans people…cause I'm not out to the world yet, but I want to be…really badly. People post about transitioning and progresses, which is awesome. (transgender-female, bisexual)

I was on Facebook and I made a comment about my name and my gender identifier and my Aunt was like, "oh what do you mean," and I was like, "why do y'all act like y'all don't know." Like I post things on Facebook...[from] the things that you see it's pretty evident. (transgender-female, queer)

Honesty

You don't have to be afraid that someone will take it the wrong way or that somebody will feel different and might want to see you [differently] than who you are as a gay person…and feel comfortable. And Grindr and Tinder allow you to straightforwardly talk with people who are just like you. (cisgender-male, gay)

It really let me play with my sexual side. So, being able to talk in way you wouldn't be able to talk with who you're comfortable with. You can really dig into your sexual side and really get more experience with your own sexual orientation and being gay. (cisgender-male, gay)

Me, personally, I'm out to my parents, but I'm not out to all my other relatives. So, I have all my other family members on Facebook or Instagram, so I never talk [about] or say anything with regard to me being gay on my Facebook or Instagram because I know they follow me. But, like for example, Grindr of course they don't know about. So, it doesn't matter to me. I don't have to worry about being gay on those sites because they don't know about them. (cisgender-male, gay)

Sexual Objectification

But then there are other guys who like seek [transgender people] out and want that, right. Those are guys that I call chasers. And while I don't want to like having...being amorist towards trans people, I also highly causation fetishizing trans people. I've experienced that a lot. I'm just a checkbox...a body and a kink...a dream…having other deeper personal [connections] is a little harder to come by just because a lot of these guys are not really willing to take the relationship outside of the bedroom…the chaser fantasy of this seductive trans girl who's like insatiable in bed, but also want nothing outside of the bedroom, but will keep it a secret. A lot of the men that are attracted to me that I have a lot of interactions with mostly sexually with a semi-serious level tend to be more conservative, republican, Trump-voter type folks and white conservatives. (transgender female, queer)

I've gotten horrid comments about my body or how I'm messed up because I don't fit exactly with what my gender identity is because of my slow progress with transition and hormones…those experiences have definitely thrown me through some dark periods...some dark times. And then the worst is when I get comments like "I've always wanted to have sex with a trans person." Like, who are you? Obviously my identities are important to me but I'm still a person, you know. Like jesus christ people. It's a problem. (transgender female, bisexual)

Emily Fuster, BS
University of California, Los Angeles

Emily Fuster is a recent graduate from the University of California, Los Angeles. In June 2019, she graduated with a Bachelor of Science Degree in Psychobiology and a minor in Scandinavian Studies. During much of her undergraduate career, she immersed herself in the study of autism spectrum disorders through working at the UCLA Child and Adult Neurodevelopmental Clinic, conducting research at the UCLA Brain Mapping Center under the direction of Dr. Mirella Dapretto, and volunteering with SPARK for Autism in the Greater Los Angeles Area. Currently, she is working in her hometown of San Diego as a medical assistant specialized in internal medicine, in addition to moonlighting as a medical scribe for the Palomar Health Emergency Department. These positions have proven to be incredible learning experiences as she applies to medical school this year. Outside of academia, she enjoys creating art and spending time with friends and family.

Contact: emily.fuster21@gmail.com

Was there a particular experience that sparked your research interests?

I attribute my early interests in research and medicine to my dad. Flipping cautiously through his old medical school textbooks (often featuring images which were honestly quite intense for even the most hardcore of 7-year-olds) and peeking into the cages housing rats in his research lab, academic medicine became the final frontier I badly wanted to pursue. From middle school science projects to departmental honors thesis writing at UCLA, he has been by my side the entire way. Early introductions to research in my childhood taught me to approach knowledge as a two-sided coin of application and discovery.

Who has been the most influential person in your life?

I would not be where I am today without the unwavering love and support I have received from my parents. Although I have learned countless valuable lessons from so many of the wonderful people in my life, my parents are responsible for making me into the person I am today. I am forever grateful to them for the opportunities they have given me to succeed.

What is your greatest accomplishment?

It is difficult for me to pinpoint the single greatest accomplishment in my life. I have begun to view each new day as an ever-evolving culmination of my accomplishments. Going to work as a medical assistant or emergency department medical scribe, in addition to advancing through stages of the medical school application process, have only been made possible by my four years of hard work at UCLA. Furthermore, attending college was accomplished through the perseverance I exhibited in high school. Personal, academic, and professional accomplishments (both large and small) have positioned me at the point I am at today.

Where do you see yourself in 10 years?

Wow, 33 feels like a lifetime away! Given that I am currently pursing a career in medicine, I see myself at the end of my medical residency — though I do not yet have my heart set on a particular specialty. I would love to find myself involved in both clinical and academic medicine. More broadly, I do hope that I am making a positive impact, finding time to travel, and surrounded by loving family and friends.

Atypical Relationship of Functional Connectivity Among Youth with Autism Spectrum Disorder to Genetic Risk

Emily Fuster[1]
Faculty Mentor: Dr. Mirella Dapretto[1]

Autism spectrum disorder (ASD) is a neurodevelopmental disorder characterized by altered brain connectivity. Although preliminary studies have shown individual differences in ASD regarding symptoms, genetic load, and patterns of brain connectivity (Bourgeron, 2016; Sandin et al., 2017), further studies are needed to investigate and relate these individual differences. This is one of the first studies to date that relates individual variability in neural connectivity to genetic risk for ASD. Specifically, we examined how functional connectivity within the default mode network (DMN), salience network (SN), and central executive network (CEN) varies as a function of polygenic risk for ASD in a sample of youth with (n = 131) and without ASD (n = 134). Across all three neurocognitive resting-state networks, we observed atypical connectivity in males and females with ASD. This observed genetic-dependency of functional connectivity emphasizes the importance of considering common genetic variation in autistic individuals in future neuroimaging studies and clinical interventions.

Autism spectrum disorder (ASD) is a complex developmental condition that involves persistent challenges in social interaction, speech, nonverbal communication, and restricted and repetitive behaviors (American Psychiatric Association [APA], 2013). According to the Diagnostic and Statistical Manual of Mental Disorder (DSM-5), clinical diagnostic criteria include deficits in social-emotional reciprocity, hyper- or hypo-reactivity to sensory input or unusual interests in sensory aspects of the environment, and highly restricted, fixated interests that are abnormal in intensity or focus. A large body of research has established ASD as a highly heritable disease, often presenting with atypical brain connectivity (Bourgeron, 2016; Sandin et al., 2017). However, despite a remarkably high prevalence in the United States population (1 in 59 children according to the Center for Disease Control [CDC], 2020), gaps remain in understanding its genetic and neurobiological foundation (Berg & Geschwind, 2012) and in developing sufficient treatment interventions (McDonald et al., 2012; Eapen et al., 2013).

Functional magnetic resonance imaging (fMRI) is a prominent tool in neuroscience research for examination of localization and lateralization of brain functions, as well as varied spatial topology in the brain at rest. Resting-state fMRI data is commonly used to map spatially distinct networks of synchronous brain activity that occur in a resting, or a task-negative state, while task-based paradigms have been critical for our understanding of dynamic network activation in response to presented stimuli (See Lee et al., 2012; Buchbinder, 2016; Smitha et al., 2017 for review). When using fMRI to examine the connectivity within and between characteristic networks of synchronous brain activity, the level of co-activation between brain regions is used as a measure of connectivity.

The default mode network (DMN), central executive network (CEN) and salience network (SN) are functional networks of particular interest, as they are interdependent and directly involved in resting-state cognitive functioning. The DMN establishes a baseline state of brain activity and is anti-correlated with task positive networks which comprise the CEN; the SN mediates the activation of either the DMN or CEN as needed (Hull et al., 2017; Raichle et al., 2001; Fox et al., 2005; Menon, 2011). Therefore, the

1University of California, Los Angeles

DMN is deactivated during demanding cognitive tasks, while the CEN is responsible for selecting and successfully monitoring behaviors that facilitate attainment of chosen goals. The SN subsequently coordinates neural responses in response to such stimuli. The DMN is made up of the posterior cingulate cortex, medial prefrontal cortex, and angular gyrus while the dorsolateral prefrontal cortex and posterior parietal cortex form the CEN, and the anterior insula and dorsal anterior cingulate cortex make up the SN. Heritability for DMN connectivity and the genetic factors involved in its functioning have been investigated in past research (Glahn et al., 2010). Atypical engagement of the SN, and consequently the insular cortex, a region within the network, is directly involved in the etiology of numerous neuropsychiatric disorders, including ASD (Uddin, 2013). Studies investigating differences in brain connectivity within the SN report evidence for a significant increase in connectivity in youth with ASD relative to typically developing counterparts. The SN may also be useful in predicting an ASD diagnosis and symptom severity, especially in regards to restricted and repetitive behaviors. Overall connectivity has been shown to predict longitudinal differences in adaptive functioning and behavior in autism (Plitt et al., 2015; Uddin et al., 2015). Recent studies investigating sex differences in ASD suggest significant differences in behavioral and cognitive characteristics (Sedgewick et al., 2016; Frazier et al., 2014), task-based neural activation (Schneider et al., 2013), and patterns of functional connectivity (Alaerts et al., 2016; Lai et al., 2017). However, few studies to date have investigated the connectivity in and between the DMN, SN, and CEN in females with ASD.

Currently, all imaging genetics studies related to ASD have focused on single nucleotide polymorphisms (SNPs) in single genes, which concluded that SNPs significantly impact functioning of neural circuitry (See Fakhoury, 2018 for review). For example, common genetic risk associated with the oxytocin receptor gene (OXTR) has implications in reward circuitry in youth diagnosed with ASD. They displayed dampened connectivity in reward circuitry as a function of increased OXTR risk-allele dosage as well as a positive correlation between risk-allele dosage and symptom severity (Hernandez et al., 2017). Furthermore, a functional ASD risk variant in the Met Receptor Tyrosine Kinase (MET) gene has been identified as a potent modulator of social brain circuitry in youth with and without ASD (Rudie et al., 2012). This study revealed the MET risk genotype as a reliable indicator for atypical fMRI activation and deactivation patterns to social stimuli as well as reduced functional and structural connectivity in brain regions known to have a high concentration of MET. These effects were more pronounced in individuals with ASD. Results from recent studies suggest that the heritability for ASD is likely characterized by the summed influence of many common variants of small effect size, emphasizing the importance of incorporating whole-genome polygenic risk analyses in ASD research (Gaugler et al., 2014). Genome wide association studies (GWAS) have identified have identified single nucleotide polymorphisms (SNPs) and genes associated with increased risk for psychiatric disorders of interest (Dima & Breen, 2015; Buxbaum et al, 2012; Lichtenstein et al., 2010). Such genomic landscapes can be analyzed to calculate a comprehensive polygenic risk score (PRS), an inclusive method for weighing the additive effects of, and interactions between, multiple risk alleles. One study of particular relevance showed that accumulation of multiple risk alleles in a comprehensive genetic score is a useful strategy for assessing the risk of ASD, and may be better than studying single SNPs (Carayol et al., 2010).

Although there have been great advances in genetics-based autism research establishing ASD as a highly heritable disorder (de la Torre-Ubieta et al., 2016; Robinson et al., 2016 for review), the marked complexity of brain-behavior interactions and ASD genetic variability presents a need for further research in genetic predictors for ASD and cognitive functioning. This study aims to further this trajectory of investigation through the study of brain areas affected by polygenic risk and how increased genetic risk differentially influences network connectivity in youth with ASD and typically developing youth. Identifying relationships between sex differences, hallmark neural differences in individuals with ASD, and genetic risk will allow for more personalized treatment and improved clinical screening capabilities. Early identification of risk factors for ASD will further allow for early intervention. To date, this is the only study to evaluate functional connectivity in youth with ASD and investigate how it relates to polygenic risk for the disorder. In this study, we related functional connectivity in the DMN, CEN, and

SN, all of which are networks of interest in resting-state fMRI research, to cumulative SNP-based polygenic risk scores. It was hypothesized that higher polygenic risk for ASD acts as a reliable predictor for atypical functional connectivity in all three resting-state networks in males and females with ASD compared to their typically developing (TD) counterparts. Furthermore, previous research suggests that sex-specific differences likely exist in this hypothesized relationship between polygenic risk for ASD and functional connectivity.

Method

Participants and Demographics

Two separate subject samples were used for this multi-site National Institute of Health (NIH) funded study. Participants from the Autism Centers of Excellence (ACE) Network dataset were previously collected with the intention of examining gender differences in ASD and consisted of individuals recruited from Harvard, Seattle Children's Hospital, UCLA, and Yale. The second sample came from UCLA's ACE Center dataset and only included subjects from UCLA. The final sample consisted of 265 total individuals with fMRI data: 169 males (86 ASD, 83 TD) and 96 females (45 ASD, 51 TD). All participants in the sample were between the ages of 6 and 17 years. Of this sample, 131 had a diagnosis of ASD and 134 were typically-developing (TD) controls. Participants and their legal guardians gave their informed consent, and the experimental protocol was approved by the Institutional Review Board at each participating site.

Phone screeners were initially conducted by the research team to evaluate and enroll potential participants based on predetermined inclusion and exclusion criteria. ASD diagnosis was determined through administration of the Autism Diagnostic Observation Schedule – Generic (Lord et al., 2000) or the Autism Diagnostic Observation Schedule – 2nd Edition (ADOS-2; Lord et al., 2012), in addition to the Autism Diagnostic Interview – Revised (ADI-R; Lord et al., 1994) and best clinical judgement. Exclusionary criteria for the both groups included the presence of implants incompatible with MRI safety standards and a full scale IQ score <70 as measured by the Wechsler Intelligence Scale for Children (WISC) (Wechlser, 2003), the 1st or 2nd edition of the Wechsler Abbreviated Scale of Intelligence (WASI) (Wechlser, 1999, 2011) or the 2nd edition of the Differential Ability Scales (DAS; Elliot, 2007). ASD group exclusionary criteria consisted of any diagnoses of genetic, medical, developmental, or psychiatric conditions in addition to ASD. However, secondary diagnoses of anxiety, depression, and attention- deficit/hyperactivity disorder (ADHD) were not considered grounds for study exclusion due to their common comorbidity with ASD (Lai, Lombardo, & Baron-Cohen, 2014). Exclusionary criteria for TD subjects included any diagnosed psychiatric or neurological disorders, the existence of any first- or second-degree relatives with ASD, and a total t-score >65 on the parent- report version of the Social Responsiveness Scale – 2nd Edition (SRS-2) (Constantino & Gruber, 2012), indicating that the subject was above the mild range of social impairment. During preliminary fMRI data analysis, subjects with excessive head motion were also excluded. A starting sample of 405 individuals was reduced to the final sample of 265 after subjects were excluded due to not meeting the above necessary criteria, failure to provide complete data, or yielding unusable imaging data due to motion after preprocessing was completed.

The groups did not significantly differ in age, mean relative motion, or handedness (all $p>0.05$). However, ASD females and TD females, as well as ASD males and TD males, differed significantly across full scale IQ (FSIQ) scores (both $p<0.0001$). TD females had greater FSIQ scores than ASD females, and TD males had greater IQ scores than ASD males.

Genetic Data Acquisition and Sequencing

Genetic data was obtained through saliva collection and DNA was extracted using the OraGene Collection Kit (DNA GenoTek). Single nucleotide polymorphisms (SNPs) were genotyped by the UCLA Neuroscience Genomics Core using the Illumina Omni-1 or Omni-2.5- exome platforms according to standard manufacturer protocols (Illumina Inc., San Diego, CA). Quality control was performed to meet the following qualifications: <5% per person or per SNP missingness, >1% minor allele frequency, and Hardy–Weinberg equilibrium $P<1*10-7$. Subjects were excluded if genotypic and recorded sex disagreed or if a subject was related to another subject in the study when initially compiling the starting sample of 405 individuals (which, as aforementioned, was further reduced to 265 subjects).

Polygenic Risk Score Calculation

A polygenic risk score was subsequently calculated for each subject using PRSice software (Euesden et al., 2015) to reflect each subjects' overall common genetic load for ASD. This genome-wide score is based on variations in multiple ASD-associated loci and their relative weights. The odds ratio and the p-value of each SNP's association with ASD was informed by a recently published genome-wide association study of ASD (Grove et al., 2019). The polygenic risk score excludes any SNPs in linkage disequilibrium (r2> 0.1) with one another.

fMRI Data Acquisition

Each participant underwent a resting-state functional connectivity magnetic resonance imaging (fMRI) scan. To ensure that subjects were relaxed during the actual scanning session, all participants had the opportunity to participate in a mock scan before the date of their MRI. UCLA ACE Center subjects received a 6-minute fMRI scan on a Siemens 3T Trio whole-body scanner using a 12-channel phased-array head coil. ACE Network sample scans were 5.5 minutes in length and acquired on a Siemens 3T Trio scanner using a 12-channel head coil at each site (Harvard, Seattle, UCLA, Yale) or, after scanner upgrades at two sites (Seattle and UCLA), on a Siemens 3T Prisma scanner using a 20-channel head coil. Subjects were asked to look at a black fixation cross in the center of a white background (TR=3000ms, TE=28ms, field of view (FOV)=192mm, 34 slices, slice thickness=4mm, in-plane voxel size=3x3mm) while the resting-state scan was acquired. Participants viewed stimuli through MR-compatible goggles (Resonance Technology, Inc., Northridge, CA, USA). A T2-weighted high-resolution echo planar scan (Trio: TR = 5000ms, TE = 34ms, FOV = 192 mm, 34 slices, slice thickness = 4 mm, in-plane voxel size of 1.5x1.5mm, acquisition time = 1.5 min; Prisma parameters were identical except TE = 35ms) was also collected for registration purposes.

Resting-State Data Preprocessing and Analysis

Imaging data underwent standard preprocessing using FMRIB's Software Library (FSL) (Smith et al., 2004) and Analysis of Functional NeuroImages (AFNI) (Cox, 1996) including skull stripping, motion correction to the average functional volume using FSL's Motion Correction Linear Registration Tool (MCFLIRT), and smoothing using a 6mm full width at half maximum Gaussian kernel. Functional data were registered to each subject's high-resolution matched bandwidth coplanar image using 6 degrees of freedom, followed by a MNI152 standard brain with 2mm resolution using 12 degrees of freedom. FSL was used to create subject-specific masks of gray matter, white matter and cerebrospinal fluid. We controlled for potential motion confounds by using Independent Component Analysis (ICA)-based Automatic Removal of Motion Artifacts (ICA-AROMA) and including mean white matter and cerebrospinal fluid, as well as their derivatives, as nuisance regressors. The data was bandpass filtered (0.01 Hz < t < 0.1 Hz) to reduce noise. Global signal regression was not used due to concerns about spurious negative connectivity.

We examined functional connectivity within the DMN, the SN, and the CEN using a 5 mm radius seed in the posterior cingulate cortex (PCC) for the DMN (Montreal Neurological Institute [MNI] coordinates -6, -52, 43), a 5 mm seed in the anterior insula for the SN (MNI coordinates 38, 26, -10), and a 5 mm seed in the dorsolateral prefrontal cortex (dlPFC) for the CEN (MNI coordinates 44, 36, 20). The resulting correlation maps were converted to z-statistic maps using Fisher's r-to-z transform. Group-level contrasts were conducted using a mixed effects model in FSL (FLAME1+2) with variance estimated separately for the ASD and TD groups. Our functional connectivity analyses within the DMN, SN, and CEN were thresholded at Z>2.3, with correction for multiple comparisons (P<.05), and demeaned polygenic risk scores served as our covariate of interest.

Results

Effects of PRS on Within-Group Resting-State Connectivity

Within-group contrasts were used to identify group-specific areas in the brain where higher polygenic risk for ASD was significantly correlated with network functional connectivity.

Default Mode Network Connectivity

There was a significant effect of PRS on resting-state functional connectivity in the DMN within typically developing males (Figure 1a). In typically developing

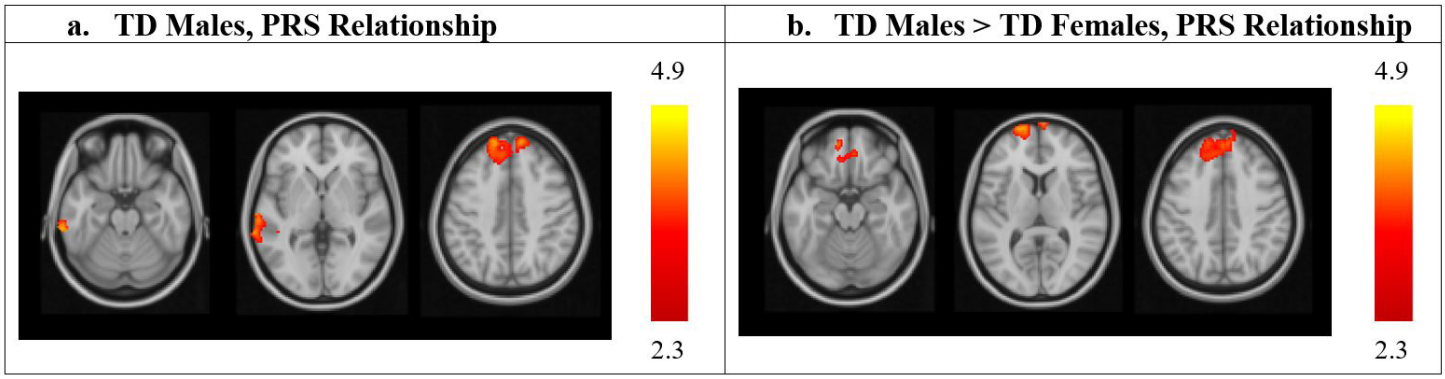

Figure 1: Relationship Between PRS and DMN Connectivity: (a) TD males with increased PRS for ASD showed a positive correlation with functional connectivity with the left superior, middle, and inferior temporal gyrus, bilateral frontal pole, and bilateral superior frontal gyri. (b). When contrasting TD males and females, TD males showed a more positive association between PRS and PCC connectivity with the frontal medial cortex, bilateral frontal pole, and bilateral superior frontal gyrus. Note: Continuum represents connectivity Z-scores, with voxelwise threshold of 2.3<Z<4.9.

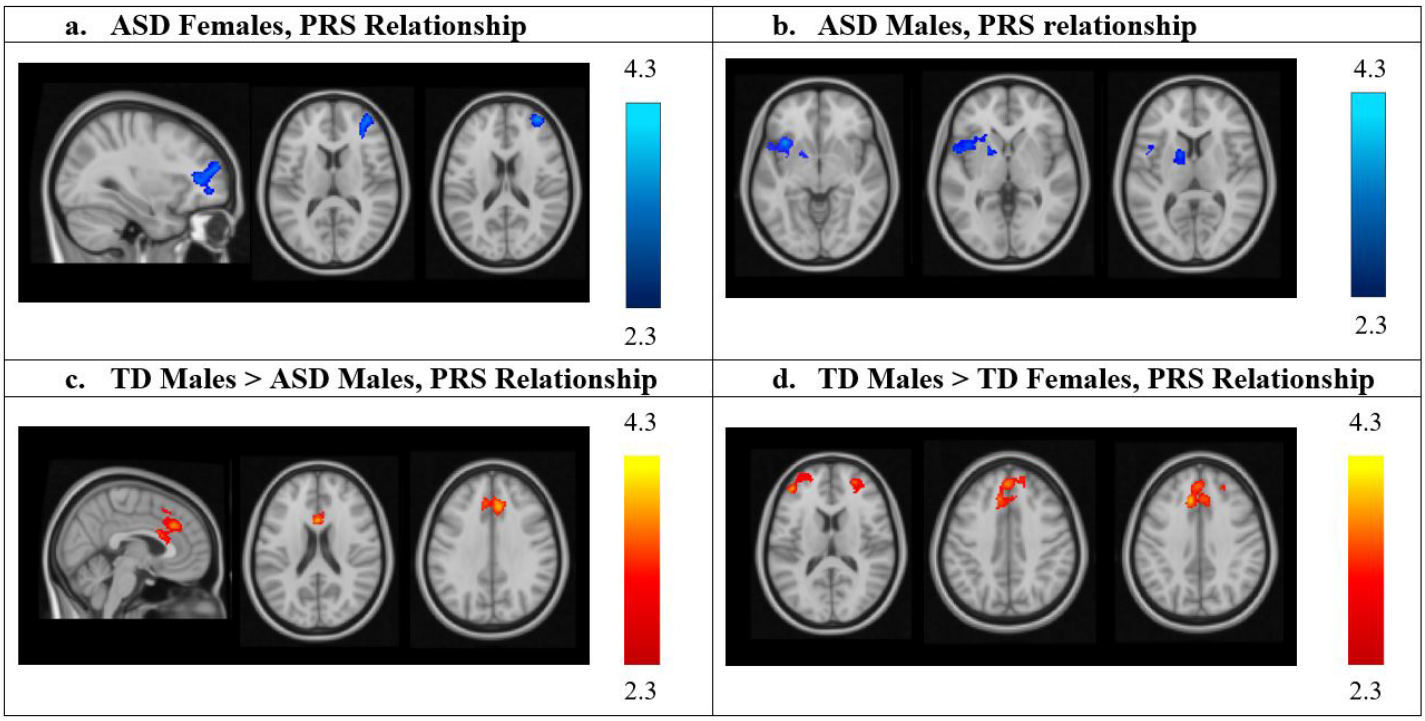

Figure 2: Relationship Between PRS and SN Connectivity: (a) ASD females revealed a negative correlation between PRS and functional connectivity with the frontal pole. (b) ASD males with increased PRS showed decreased connectivity with the insular cortex, left palladium, left putamen, frontal orbital cortex, and frontal operculum cortex. (c) TD males with increased PRS showed greater functional connectivity than their ASD counterparts in the ACC, paracingulate gyrus, and superior frontal gyrus. (d) Compared to their female counterparts, higher PRS in TD males was also associated with more positive functional connectivity with the bilateral frontal pole, paracingulate gyrus, and superior frontal gyrus. Note: Continuum represents connectivity Z-scores, with voxelwise threshold of 2.3<Z<4.3.

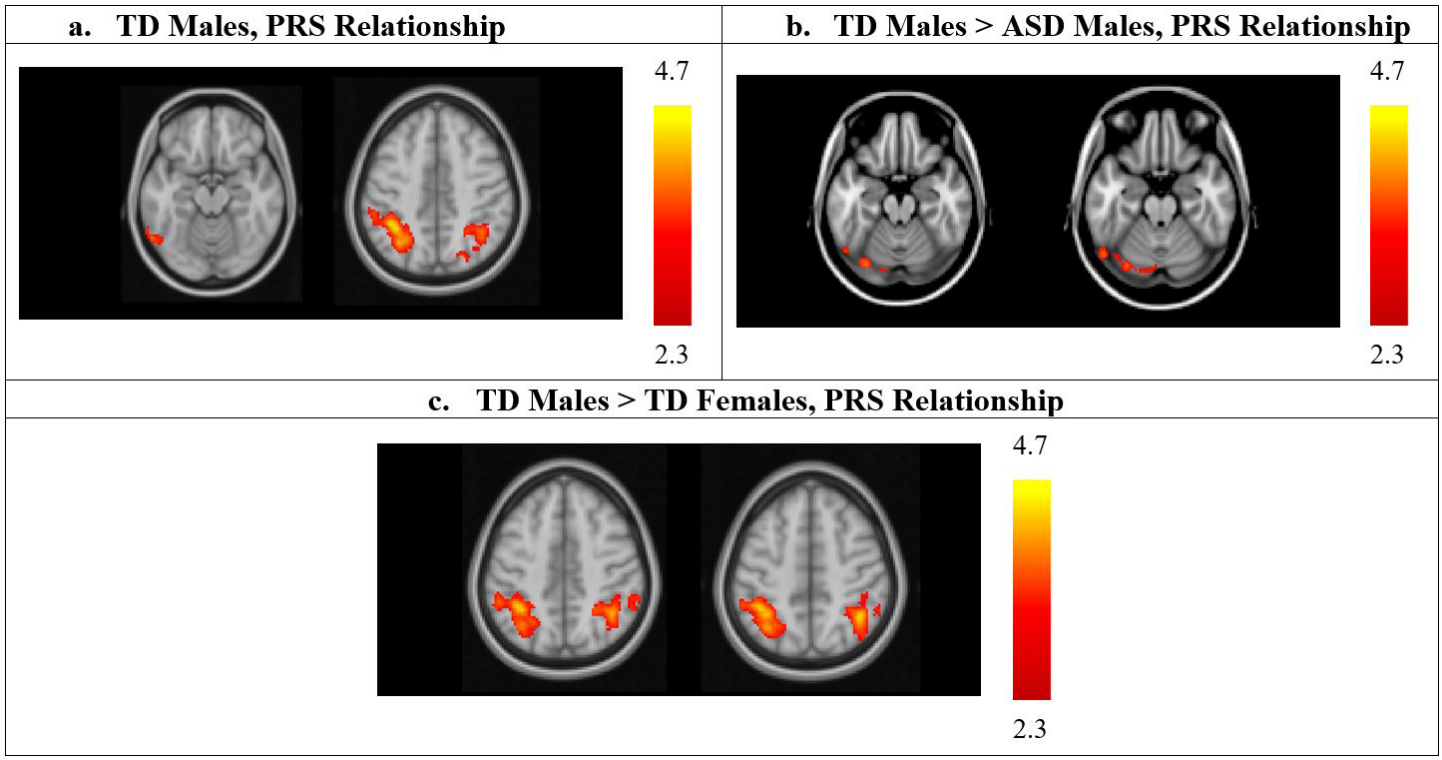

Figure 3: Relationship Between PRS and CEN Connectivity: (a) TD males exhibited a positive relationship between PRS and CEN seed connectivity with the left inferior temporal gyrus, left middle temporal gyrus, bilateral angular gyrus, bilateral superior parietal lobe, superior lateral occipital cortex, and left cerebellum. (b) TD males with higher PRS displayed more positive functional connectivity with the left lateral inferior occipital cortex, occipital fusiform gyrus, and left cerebellum than their ASD counterparts. (c) Compared to their female counterparts, high-PRS TD males showed less negative functional connectivity in the left occipital fusiform gyrus, bilateral superior occipital cortex, bilateral angular gyrus, bilateral superior parietal lobe, and bilateral supramarginal gyrus. Note: Continuum represents group-specific connectivity Z-scores, with voxelwise threshold of 2.3<Z<4.7.

males, greater PRS for ASD was significantly correlated with increased connectivity between the PCC core brain region of the DMN, the left superior, middle, and inferior temporal gyri, the bilateral frontal pole, and the bilateral superior frontal gyri. There were no significant positive or negative correlations between PRS and DMN functional connectivity in TD females, as well as within the ASD male and female groups.

Salience Network Connectivity

ASD females with higher PRS exhibited reduced functional connectivity with the frontal pole. Conversely, greater PRS in ASD males was associated with significantly less connectivity between the anterior insula hub of the SN and the globus pallidus, left putamen, frontal orbital cortex and frontal operculum cortex. ASD males also showed reduced local functional connectivity between the SN and the anterior insula in relation to increased polygenic risk. In comparison, TD females and males showed no significant correlations between polygenic risk and SN functional connectivity (Figure 2a, 2b).

Central Executive Network Connectivity

In TD males, greater genetic load for ASD was associated with increased functional connectivity between the dlPFC seed and the left inferior temporal gyrus, left middle temporal gyrus, bilateral angular gyrus, bilateral superior parietal lobe, superior lateral occipital cortex, and left cerebellum (see Figure 3a). TD females, along with individuals of both genders with an ASD diagnosis, showed no significant relationships between polygenic risk and CEN connectivity.

Between-Group Effects of Connectivity and PRS

Between-group contrasts were used to locate areas of the brain where higher polygenic risk for ASD was more highly correlated with network connectivity in one participant group compared to another. Specifically, we contrasted same-sex groups so that ASD males were compared to TD males and ASD females were contrasted with TD females. Additionally, we analyzed sex differences in youth with and without ASD; we compared ASD males to ASD females and TD males to TD females.

Default Mode Network Connectivity

There were significant differences in the relationship between PRS and resting-state functional connectivity in the DMN between TD males and females. Relative to TD females, TD males with higher PRS had significantly more positive functional connectivity between the PCC seed and the frontal medial cortex, bilateral frontal pole, bilateral superior frontal gyri, and the right cerebellum (Figure 1b). Significant differences in the relationship between DMN functional connectivity and PRS were not found between ASD males and females or between the TD groups and their same-gender counterparts with ASD.

Salience Network Connectivity

There were significant differences in the association between PRS and resting-state functional connectivity in the SN between males with and without an ASD diagnosis, as well as between typically developing males and females (Figures 2c, 2d). TD males with higher PRS exhibited a more positive functional connectivity relationship between the anterior insula seed and the anterior cingulate cortex (ACC), paracingulate gyrus, and superior frontal gyrus than their ASD male counterparts. Compared to TD females, higher polygenic risk in TD males was also associated with more positive functional connectivity with the bilateral frontal pole, paracingulate gyrus, and superior frontal gyrus. ASD males and females did not significantly differ in their relationship with polygenic risk and SN functional connectivity. Furthermore, females across the two diagnostic groups did not show significant between-group interactions between PRS and SN functional connectivity.

Central Executive Network Connectivity

TD males showed a significantly more positive relationship between PRS and CEN connectivity than TD females as well as their same-sex counterparts with ASD. Compared to their ASD male counterparts, TD males with increased PRS showed increased functional connectivity between the dlPFC seed and the left lateral inferior occipital cortex, occipital fusiform gyrus and left cerebellum. In addition, compared to TD females, TD males with higher PRS exhibited more positive functional connectivity in the left occipital fusiform gyrus, bilateral lateral superior occipital cortex, bilateral angular gyrus, bilateral superior parietal lobe, as well as the bilateral supramarginal gyrus (Figures 3b, 3c). No significant differences were found between ASD males and females in their relationships between PRS and CEN connectivity.

Discussion

In this study, we aimed to relate individual differences in resting-state functional connectivity in three major resting-state networks to genetic risk for ASD among TD youth and youth diagnosed with ASD. We assessed a large sample of males and females which contrasts with previous genetic studies performed on much smaller samples focused primarily on ASD in males. We found that youths with ASD, relative to TD youth, exhibited atypical relationships between polygenic risk for ASD and patterns of resting-state functional connectivity within the DMN, SN, and CEN.

Overall Findings Across Three Resting-State Networks

In all three networks, TD males showed a significantly more positive relationship between severity of polygenic risk for ASD and functional connectivity than their TD female counterparts. However, this sex-dependent effect of polygenic risk on functional connectivity was not observed when comparing ASD males to their ASD female counterparts. To date, very few neuroimaging studies comparing males and females with ASD have been conducted. Some prior neuroimaging studies examining sex differences in ASD, although preliminary, have shown significant differences in patterns of functional connectivity between males and females with ASD (Alaerts et al., 2016). However, these studies have yet to relate polygenic risk to sex-differentiated patterns of

Most of the genetic differences observed in individuals with ASD involve synaptic plasticity and connectivity (Bourgeron, 2015). Furthermore, Bourgeron posits that, because risk involves the entire genome (Anney et al., 2012; Gaugler et al., 2014), females might have some X-linked mechanism which buffers them from this whole-genome component to genetic risk. Combining these findings with ours suggests that this compensatory mechanism for increased PRS severity in males through more positive functional connectivity in resting-state networks is altered in males with ASD. For years, there has been a need for additional comprehensive studies to further understand the genetic origins of this sex-specific component to functional connectivity in ASD (Geschwind, 2011). Across all four subject groups, the consistently altered connectivity in relation to increased polygenic risk detected in males was not observed in females. This relates to previous findings in which sex-specific variation exists in genetic load for ASD and reinforces the claim that females may need to inherit more genetic factors related to ASD than males do to show traits of the condition (Tsai et al., 1981; Werling & Geschwind, 2013; Werling & Geschwind, 2015).

Various fMRI studies investigating social reward and motivation corroborate that ASD is characterized by diminished activity in the nucleus accumbens, a structure robustly involved in reward processing (Delmonte et al., 2012; Kohls et al., 2014). The ACC, which is one of the major regions involved in the SN (Menon & Uddin, 2010), plays a crucial role in reward processing and reward-based decision making (Hayden et al., 2009; Kennerley et al., 2006; Bush et al., 2002). Previous studies indicate neurons in the nucleus accumbens are involved in the signaling of reward salience and decision making in terms of reward-based approach behaviors (Saunders and Robinson, 2012), further suggesting a link between these accumbal neurons and the ACC as a core brain region in the SN. Our results suggest that genetic variance in youth with ASD likely plays a role in this diminished functional connectivity with reward circuits. When contrasting males with and without ASD, TD males exhibited a more positive correlation between increased PRS and ACC connectivity in the SN. Given that the ACC also plays a crucial role in evaluating the behaviors of others and in estimating others' motivations (Apps, Rushworth, & Chang et al., 2016), this overall atypical engagement of reward circuitry in ASD males may be mediated by their increased polygenic risk for the disorder.

More broadly, this decrease in social motivation through negative connectivity with the SN likely affects the desire to attend to social stimuli. Because the SN acts as the modulatory network between the DMN and the CEN, its decreased connectivity with the ACC, as observed in high-PRS individuals with ASD, might result in failure to detect a potentially rewarding social stimulus and subsequently responding to it. In one study, ASD individuals exhibited normal feedback error-related negativity (fERN) modulation, an event-related potential that occurs when an expected reward does not occur, during monetary choices and inverted fERN and ACC responses in social options than did controls (Gonzalez-Gadea et al., 2016). Another behavioral study revealed that girls with autism were similar to their TD female counterparts in social motivation and friendship quality, while boys with ASD significantly differed from their TD male counterparts, ASD females, and TD females in aspects of their friendships and motivation for social contact (Sedgewick et al., 2016). Follow-up studies connecting such behavioral phenotypes to polygenic risk for ASD would be valuable to our understanding of possible protective behaviors in females in response to increased genetic risk for the disorder.

Negative Relationship between PRS and a Modulatory Salience Network in ASD

The only instance of within-group difference among individuals with ASD was observed in relation to SN connectivity; notably, we observed significantly less positive connectivity with SN regions in relation to increased polygenic risk across both males and females with ASD. The SN is thought to be directly involved in the assignment of saliency to external stimuli or internal mental events (Seeley et al., 2007; Menon & Uddin 2010). Previous studies suggest that alterations in the SN might cause social stimuli to be less salient and predict a diagnosis of ASD (Uddin, 2015). Individuals with ASD who have increased polygenic risk for the disorder, and thus reduced connectivity with the SN, may have difficulty reaching a threshold of salience required for adequate detection and response of internal or external stimuli.

Lastly, although both boys and girls with ASD displayed significant differences in SN connectivity in relation to increased PRS, the cortical regions involved in this shared negative relationship differed by gender. While females with ASD displayed decreased connectivity in the right frontal pole, males with ASD conversely showed decreased connectivity with the insular cortex and left basal ganglia. The SN, and most notably the anterior insula (AI), is central in mediating dynamic interactions between other large-scale brain networks involved in externally oriented attention and internally oriented self-related mental processes (Menon & Uddin 2010; Medford & Critchley, 2010; Goulden, Khusnulia, & Bracewell et al., 2014). Such research posits that one of the functions of the insula is to recognize salient stimuli for additional processing and initiate appropriate control processes. This involves bottom–up detection of salient events, employing other large-scale cognitive networks in order to access attention and working memory resources when a salient event is detected, and coordinating a reaction to such salient stimuli. The salience network assists target brain regions in the generation of appropriate behavioral responses to salient stimuli. Thus, genetically-mediated differences in connectivity observed in individuals with ASD might provide insights into challenges with social cognition and appropriately responding to social stimuli.

Decreased connectivity between the insula and the SN in ASD males as a result of increased genetic risk provides evidence for altered within-network connectivity and initiation of hallmark behaviors of ASD rooted in difficulties regulating resting-state network initiation and connectivity. An earlier paper from Menon and Uddin (2010) concludes that the SN is well positioned to influence not only attention but also motor responses to salient sensory stimuli because of von Economo neurons, which facilitate rapid signaling between the AI and the ACC. Higher PRS for ASD in our present study revealed decreased SN functional connectivity with the insula in ASD males as well as less positive connectivity with the ACC in comparison with TD males. The heritability of von Economo neuron function (Yang et al., 2018) may explain the reason for this simultaneous atypical connectivity between the SN, AI, and ACC, which was observed solely in males with ASD.

Limitations

Although these findings strongly further our understanding of the neurobiology of ASD, some limitations in this study can be addressed. Studies investigating the effects of polygenic risk should be mindful of the inherent variability that exists in predicting disease risk using a constantly growing GWAS sample as a reference group (Wray & Visscher, 2007; Dudbridge, 2013). As the GWAS sample increases in size over time with the inclusion of new subjects, polygenic risk scores will become slightly more accurate in response to the changing size and distribution of risk effects in the reference group. In reference to our final sample for this study, although relatively large compared to other preliminary genetic studies, a larger size might have ideally allowed us to further match the groups on IQ and scan location. Performing more sophisticated analyses to calculate individual p-values and effect sizes would present significant and non-significant interactions with even greater clarity. Finally, performing additional formal analyses to directly compare data resulting from a pipeline integrating global signal regression to ours, which used no global signal regression, might make these results more generalizable to past and future research regardless of signal regression approach (Murphy & Fox, 2017). With the advent of concern that modern clinical assessments are restrictive and catered toward the male manifestations of ASD, females who present with less readily apparent socio-communicative impairments may not be appropriately captured by currently available clinical diagnostic tools (Ratto & Kenworthy et al., 2019). Although very standard practice in this field of research, our use of stringent cutoff scores on these assessments as requirements for inclusion in the study might have compromised the representation of females in our 'ASD Female' group.

Future Directions

Understanding how neural differences in individuals with ASD are dependent on sex and genetic risk for ASD would allow for more personalized and efficacious treatment. Early identification of risk factors for neurodevelopmental disorders such as ASD will lead to earlier diagnosis and intervention, potentially before observable behavioral symptoms arise. Such implications are particularly

cognitive ability, and sex leads to differential presentations of a shared diagnosis among diverse populations (Constantino & Charman, 2016; Masi et al., 2017). Thus, there is a constant need for improved clinical screening methodologies and more accurate approaches to making sample group comparisons in research. Establishing a genetic baseline as a primary approach to diagnosis and treatment might solve this dilemma. Furthermore, using PRS comparisons as predictors for atypical patterns of functional connectivity and as a common denominator for diverse symptomology could fill this gap in treatment. The study of the impact of causal genetic variants provides a starting point for a new mechanistic understanding of ASD, enabling connection of genes to brain function, cognition, and behavior.

As mentioned in the above sections, follow-up studies investigating the behavioral effects of polygenic risk for ASD would warrant even broader conclusions about symptomology and sex-specific protective effects. Additionally, researching the interaction between polygenic risk for ASD and network functional connectivity during task performance would allow us to compare alterations in network connectivity in the brain at rest to the brain during stimulus processing.

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Celine Lu, BA
University of California, Los Angeles

Celine Lu graduated with a Bachelor of Arts in Psychology and a Specialization in Computing from the University of California, Los Angeles (UCLA) in Spring of 2019. At UCLA, she was a research assistant in Dr. Bruce Chorpita's Child FIRST Lab for two years, where she completed her honors thesis. She is currently a research coordinator in Dr. Jennifer Silk's Families, Emotions, Neuroscience and Development Lab at the University of Pittsburgh. Her main role there is to coordinate the SmartCAT in the Community Project, a study which aims to implement an adjunct mobile app for anxiety treatment in various community settings. Celine is interested in studying innovative treatments for children in community settings and dissemination and implementation science. In her free time, Celine enjoys baking, making pottery, and playing Animal Crossing on the Nintendo Switch.

Contact: celinelu@ucla.edu

Was there a particular experience that sparked your research interests?

I remember sitting in my Research Methods in Psychology class in my second year of college when the graduate student teaching assistants were taking turns telling the class what they were studying. One of the teaching assistants had simply put that her research involved improving mental health treatments for children in the real world – and it clicked for me: "That's what I want to do!" Despite it being the first day of class, I rushed to the teaching assistant's office hours that day to ask more about research opportunities in the lab that she was in. I eventually became a research assistant in the Child FIRST Lab and was introduced to the world of dissemination and implementation science. I had never known that this sector in clinical psychology existed and that there are oftentimes difficulties in translating clinical research in community settings. Being in the Child FIRST Lab has affirmed my dedication towards improving mental health treatments for children in the community.

Who has been the most influential person in your life?

A handful of people have been influential in my life. Firstly, I have great admiration for my parents, who both escaped war-torn countries and sought refuge in the U.S.. They instilled in me their values of perseverance, diligence and kindness that I hold closely in my day to day life. Secondly, my mentors during and post-college have encouraged me to pursue a career in academia, and have given me the necessary tools for it to hopefully come into fruition. I am so thankful that they took the time to help me develop research skills, offer professional development advice, and provide me their moral support.

What is your greatest accomplishment?

Having lived in California my whole life, the thought of moving across the country to Pittsburgh, Pennsylvania and starting anew was nerve wracking to me. Experiencing below freezing temperatures for a quarter of the year seemed miserable but turned out to be bearable and actually quite enjoyable at times. Although being away from family has been difficult, especially during the COVID-19 pandemic, being able to thrive independently so far from home has been a rewarding experience.

Where do you see yourself in 10 years?

I hope to be a professor at a university with my own research lab. Although my research interests may change in the next 10 years, I am positive that I want to conduct research involving mental health in the community in some form or another. I would love to have graduate and undergraduate students in my lab that I could mentor and pass along knowledge that I would hopefully have gained throughout the years. Mentorship is extremely important for me because I wouldn't be where I am today without the great mentors I had during and post-college.

Is poor engagement in treatment associated with lower likelihood to participate in research? A study of families in school-based mental health

Celine Lu,[1] Alayna L. Park,[2] Kimberly D. Becker,[3] and Bruce F. Chorpita[1]

Treatment engagement, or a client's involvement in their own therapy, is of research interest because more than 50% of clients drop out of treatment before their mental health needs are met. Mental health researchers have sought to develop treatments that are both effective and responsive to the diverse needs of the service-seeking population, but it is possible that clients who are less engaged in treatment may also be less likely to participate in these clinical trials. This study examined whether types of engagement problems (e.g., poor therapeutic alliance, low expectations of therapy) influenced youth and caregiver clients' willingness to participate in a clinical trial that aimed to improve youth and families' experience of mental health treatment. A 35-item, self-report questionnaire was used to assess clients' treatment engagement along five domains: Relationship, Expectancy, Attendance, Clarity, and Homework. Clients with low engagement scores were invited to participate in the clinical trial. Results showed no significant associations between types of engagement problems and rates of research participation. However, results showed a significant association between caregiver and youth participation rates. Findings suggest that clinical trials are unlikely to systematically exclude participants with a variety of engagement problems, thus supporting the external validity of such studies.

Recruitment of representative samples is imperative for the generalizability of research findings. Within the field of clinical psychology, research studies yield valuable insights into the etiology and treatment of mental illnesses. To promote human well-being and functioning, it is important for clinical trials testing mental health treatments to include samples that are representative of the service-seeking population. Given the sensitive nature of mental health, it can be difficult to engage individuals in mental health treatments—let alone research studies testing mental health treatments. In this paper, we examined factors that influenced the extent to which individuals with mental health needs participated in a clinical trial that aimed to improve youth and families' experience of mental health treatment.

Youth and family engagement in mental health treatment (i.e., clients' commitment to their own treatment) presents a significant public health concern. A national survey found that only 25% to 50% of children and adolescents with mental health needs receive treatment (Burns et al., 2004; Merikangas et al., 2011). Even when these youth are connected to treatment, an estimated 20% to 50% will drop out of treatment prematurely (Olfson et al., 2009; Pellerin et al., 2010). Compounding these issues, youth who terminate from treatment prematurely have been found to have worse treatment outcomes and higher rates of unmet mental health needs than youth who complete treatment (Boggs et al., 2005; Coatsworth et al., 2001). Promisingly, strong treatment engagement has been shown to predict faster treatment completion and better clinical and functional outcomes (Clarke et al., 2015; Danko, et al., 2016).

1 Department of Psychology, University of California, Los Angeles
2 Department of Psychology, Palo Alto University
3 Department of Psychology, University of South Carolina

An increasing number of initiatives have focused on better understanding the construct of treatment engagement (Becker et al., 2018; Dean et al., 2016; Haine-Schlagel & Walsh, 2015; Huey & Jones, 2013; Kim et al., 2012). A recent review found that the vast majority of studies operationalize treatment engagement as attendance (Chacko et al., 2016). However, researchers have proposed that treatment engagement includes other aspects of the treatment process such as clients' alliance with their therapist and treatment homework completion (e.g., clients may be assigned treatment homework of practicing a relaxation skill that they learned in their previous session) (Clarke et al., 2015; Danko et al., 2016; Meyer et al., 2002). For example, Becker and colleagues (2018) developed a multidimensional framework for measuring treatment engagement along five domains: Relationship (therapeutic alliance), Expectancy (perceived treatment outcome), Attendance (presence at therapy sessions), Clarity (understanding the approach of and roles in treatment), and Homework (in-session participation and homework completion)–hereafter referred to as the REACH domains of engagement.

Although the construct of treatment engagement has received longstanding scientific attention, concerns have been raised about the influence of treatment engagement problems on the generalizability of clinical trials (Huey & Jones, 2013; Interian et al., 2013). For example, ethnic minority groups have been found to be less engaged in treatment (Huey & Jones, 2013), and are also less likely to participate in research (Miranda, 1996; Scharff et al., 2010; Williams et al., 2012). For this reason, clinical trial samples may not be representative of the treatment engagement problems that exist within the service-seeking population. Therefore, it is important for clinical trials to examine whether types of engagement problems (e.g., poor alliance between client and therapist, poor attendance by caregivers in their youth's treatment) and overall levels of engagement affect research participation. To our knowledge, no studies have examined treatment engagement as a predictor of research participation.

Some studies have identified factors potentially relevant to treatment engagement that may influence research participation. For instance, studies have found that trust in an institution, which is most related to the relationship domain of engagement, influences individuals' decisions about whether or not to participate in research. As an example, African-American men have been found to have high levels of institutional mistrust as well as limited research participation (Scharff et al., 2010). Furthermore, when young adults with type 1 diabetes were asked about factors that influenced their participation in mental health research, mistrust that their research data would be misused (e.g., personal information being sold to health insurance companies) was cited as a significant barrier to research participation (Clarke et al., 2015). Additionally, perceived risks and benefits to research participation, which may be related to the expectancy domain of engagement, are major factors that influence individuals' decisions to consent to participate in studies. Potential benefits of research participation were nominated by caregivers as the most important factor influencing their decision to enroll their child in a research study (Miller & Feudtner, 2016). Moreover, in a longitudinal study on postpartum depression, participants listed the benefits of gaining support, having the opportunity to learn, and improving their sense of self-worth as influences on their research participation (Andrighetti et al., 2017).

Given that caregiver consent is required for youth to participate in research studies, it is possible that youths' willingness to participate in research may also be affected by their caregivers' own perceptions about participating in a research study. Social learning theory posits that our attitudes, beliefs, and behaviors are shaped by others, and this is especially true for youth and their caregivers (Bandura & Walters, 1977). Thus, youth may share similar beliefs to their caregivers regarding research participation, and one study found that youth and their caregivers tend to agree on the overall benefit of research participation (Wiener et al., 2015). Similar attitudes surrounding research participation between youth and their caregivers may also be present in their decision to participate in the clinical trial.

Current Study

The present study sought to explore factors that may influence the willingness of youth and caregivers to participate in a clinical trial that aimed to improve youth and families' experience of mental health treatment. The first aim of this study was to examine the association

between the types of engagement problems reported by youth and caregivers and their research participation rates. We elected to use the REACH framework to operationalize types of engagement problems, as this framework offers a holistic and comprehensive evaluation of treatment engagement. Types of engagement problems were determined through the use of a self-report treatment engagement questionnaire called the My Thoughts About Therapy (MTT) questionnaire. Research participation rates were operationalized as youth and caregiver consent, or assent for youth under the age of 18, to participate in the clinical trial, as indicated by signed consent forms. The second aim of this study was to examine the association between youth and caregivers' overall levels of engagement and their research participation rates. Overall levels of engagement were operationalized as youth and caregivers' total scores on the MTT. Lastly, the third aim of this study was to examine the association between caregiver and youth research participation rates.

The first hypothesis was that youth and caregivers with a relatively poor relationship with their therapist would be less likely to participate in the clinical trial since mistrust in an institution (i.e., therapist) has been cited as a barrier to participation in research studies (Clarke et al., 2015; Scharff et al., 2010). The second hypothesis was that youth or caregivers who expect a positive treatment outcome (expectancy domain of engagement) with their usual care would be less likely to participate in the clinical trial. Given that the anticipated benefit of participation has been shown to be a motivator for participating in research (Andrighetti et al., 2017; Miller & Feudtner, 2016), individuals who expect a positive treatment outcome might perceive the relative benefit of research participation as lower compared with those who expect a suboptimal treatment outcome. No a priori hypotheses were made about the influence of the attendance, clarity, and homework domains on research participation since these associations have not been previously researched. Given that some domains of engagement may impact research participation rates, our third hypothesis was that overall levels of treatment engagement would be associated with research participation rates. Lastly, given that youth and caregivers tend to agree on the benefits of research participation, our fourth hypothesis was that caregiver willingness to participate in research would be significantly associated with youth willingness to participate in research.

The present study addresses a gap in current research on the generalizability of clinical trials by enhancing the field's understanding of factors that might influence youth and caregivers' willingness to participate in research related to mental health treatment.

Method

Participants

Youth and Caregivers

Participants included youth (N = 108) and their caregivers (N = 173),[1] who were enrolled in school-based mental health services; 81% of families were from Los Angeles County, California, and the remaining families were from the Pee Dee and Santee Wateree regions of South Carolina. Youth participants ranged in grade from 2nd to 12th grade (M = 7.31, SD = 2.82). There was a relatively even gender distribution in our sample, with 53% of youth identifying as females. Youth were predominantly Latinx/ Hispanic/ Spanish (n = 84), followed by Black/ African American (n = 12), White/ European-American/ Caucasian (n =3), and Asian/ Asian-American/ Pacific Islander (n = 1). With the exception of one youth who had a primary language of Spanish, all youth had a primary language of English. Eight youth did not report any demographic information

Caregivers included 86 biological mothers, 21 grandmothers, 7 biological fathers, 2 grandfathers, and 5 "other" caregivers (e.g., foster mothers). Seventy-four caregivers reported a primary language of English, and 29 caregivers reported a primary language of Spanish. Fifty-two caregivers did not report their relationship to the youth, and 70 did not report their primary language.

1 Most participants included youth and caregiver dyads; however, there were several instances in which data were available for youth only or caregiver only. Data were available for only caregivers if youth was younger than 3rd grade, as it was expected that these youth would not be able to comprehend the self-report questionnaire. Additionally, only youth and caregivers who were actively participating in therapy were asked to complete the self-report questionnaire about their therapy experiences.

Therapists

One hundred forty-one therapists were assigned to provide school-based mental health treatment to these youth and their caregivers. The majority of therapists (n = 129) identified as female. Therapists ranged in age from 23 to 79 years (M = 41.96, SD = 10.20). Therapists identified as Latinx/ Hispanic/ Spanish (n = 54), White/ European-American/ Caucasian (n = 23), Black/ African American (n = 5), Asian/ Asian-American/ Pacific Islander (n = 4), and "other" ethnicity (n = 6). All therapists were fluent in English, and 54 endorsed that they were at least proficient in Spanish; 46 therapists reported that they deliver services in Spanish. The majority of therapists had a master's level education (n = 130), and 59 therapists were licensed by their respective states. On average, therapists had 8.47 years of clinical experience since earning their degree (SD = 7.08) and worked at their respective school districts for 6.58 years (SD = 6.90). One therapist did not report ethnicity, language, or experience information. Therapists characterized their primary theoretical orientation as cognitive behavioral (n = 87), eclectic (n = 25), humanistic/ client-centered (n = 12), family systems (n = 7), psychodynamic (n = 5) and other (n = 4).

Measures

My Thoughts about Therapy

Treatment engagement was evaluated using the My Thoughts about Therapy (MTT) questionnaire, a 35-item self-report questionnaire that assesses youth and caregivers' experiences with therapy. The MTT is comprised of five subscales (Relationship, Expectancy, Attendance, Clarity, and Homework), which correspond with the REACH domains of engagement. Each subscale includes seven items, which are summed to produce the subscale score. Items are rated on a 4-point Likert scale ranging from 0 (Strongly Disagree) to 3 (Strongly Agree), such that higher scores indicate better treatment engagement. There are separate versions of the MTT for youth and caregivers. The youth version of the MTT includes questions about youth's perceptions of their own therapy experiences (e.g., "I like meeting with my counselor"), whereas the caregiver version of the MTT includes questions about caregivers' perceptions of their youth's therapy (e.g., "I like meeting with my child's counselor"). The MTT is available to youth and caregivers in English and Spanish. The MTT has been used in other studies to measure treatment engagement (e.g., Becker et al., 2019).

Consent

The consent forms used in this study contained information about participating in the clinical trial. The consent form described that the purpose of the clinical trial was to learn how to improve families' experiences with therapy. It specified that potential risks or discomforts of participation included growing tired of answering the MTT questionnaires and feeling uncomfortable with being recorded during treatment sessions. However, the consent forms stated that if at any point the youth or caregiver was uncomfortable with being recorded, they could notify the therapist to turn off the recorder. Potential benefits of participation included having a more positive experience in therapy and contributing to research that would inform improved mental health services for youth and families. The terms of consenting included agreeing to be audio-recorded during two of the youth's therapy sessions and to completing the MTT three times. Additionally, consent forms indicated that youth and caregivers would not receive payment for participating in the clinical trial. Furthermore, consent forms outlined that any identifying information would be kept confidential and would only be disclosed with the youth or caregiver's permission. Both English and Spanish consent forms were available for youth and caregivers.

Procedures

The school's mental health clinic staff administered the MTT to youth and caregivers during the clients' fourth treatment session. MTT responses were entered into an online data collection platform and were reviewed by research staff through a data share agreement with the participating school districts. Youth and caregivers who had a score of 13 or less on at least one of the REACH subscales (i.e., reported at least one statement of low engagement) were considered at risk for poor treatment engagement and were deemed eligible to participate in the clinical trial.

Research staff notified the therapist about the family's

eligibility, and the therapist invited the youth and caregiver into the clinical trial at their next therapy session. The therapist reviewed the assent and consent forms with the youth and caregiver. The therapist explained the study to the caregiver over the phone if the caregiver was physically unavailable for the discussion. Youth who agreed to participate in the clinical trial signed a youth assent (if under the age of 18) or consent (if over the age of 18) form. Caregivers provided signed consent for their youth and/or for themselves to participate in the clinical trial.

Data Analysis

To examine the association between types of treatment engagement problems in the REACH domains and the participants' willingness to participate in the clinical trial, we conducted separate logistic regressions for each REACH domain predicting (a) youth's assent/consent to participate (yes or no); (b) caregivers' consent for their youth to participate (yes or no); and (c) caregivers' consent to participate (yes or no). Separate analyses were conducted to maximize the number of cases included in each statistical test since several participants did not complete all subsections of the MTT[2] (Table 1, Table 2, and Table 3). Additionally, to examine youth and caregivers' overall engagement and willingness to participate in the clinical trial, we conducted another three logistic regression tests examining (a) youth's overall MTT score predicting youth's assent to participate (yes or no); (b) caregivers' overall MTT score predicting caregivers' consent for their youth to participate (yes or no); and (c) caregivers' overall MTT score predicting caregivers' consent for themselves to participate (yes or no). Three Pearson's chi-square tests were used to analyze (a) the association between caregivers' willingness for themselves to participate and youth's willingness to participate; (b) the association between caregivers' willingness for youth to participate and youth's willingness to participate; and (c) the association between caregivers' willingness for themselves to participate and caregivers' willingness for youth to participate.

Results

Sixty percent of youth assented to participate in the clinical trial, 62% of caregivers consented for themselves to participate, and 63% of caregivers consented for their youth to participate.

MTT subscale scores ranged from 0 to 21, and average youth MTT subscale scores were: Relationship = 15.04 (SD = 3.54), Expectancy = 14.57 (SD = 3.56), Attendance = 12.57 (SD = 2.49), Clarity = 14.78 (SD = 3.56), Homework = 14.32 (SD = 3.17). Average caregiver MTT subscale scores were: Relationship = 15.88 (SD = 4.26), Expectancy = 15.76 (SD = 4.22), Attendance = 14.10 (SD = 3.40), Clarity = 15.37 (SD = 3.79), Homework = 15.22 (SD = 3.41). MTT overall scores ranged from 0 to 105, and the average MTT overall score for youth was 71.92 (SD = 13.83), and for caregivers was 76.68 (SD = 17.27).

Results illustrated that youth MTT REACH subscale scores and overall youth MTT scores did not significantly predict youth assent/consent to participate in the clinical trial (Table 1). Caregiver MTT REACH subscale scores and overall caregiver MTT scores did not significantly predict caregiver consent for themselves (Table 2). Caregiver MTT REACH subscale scores and overall caregiver MTT scores also did not significantly predict caregiver consent for youth (Table 3).

Results revealed that caregiver consent for self was significantly associated with youth assent to participate in the clinical trial, $\chi 2$ (1, n = 108) = 76.783, p <.001 (Table 4). Additionally, results demonstrated that caregiver consent for youth was significantly associated with youth assent to participate in the clinical trial, $\chi 2$ (1, n = 169) = 102.75, p <.001 (Table 5). Lastly, caregiver consent for self was significantly associated with caregiver consent for youth to participate in the clinical trial, χ 2 (1, n = 169) = 144.84, p <.001 (Table 6).

2 Youth who completed all subsections did not significantly differ from youth who did not complete all subsections of the MTT in grade level (p = .93), gender (p = .80), ethnicity (p = .28), or primary language (p = 1.00). Caregivers who completed all subsections of the MTT did not significantly differ from caregivers that did not complete all subsections of the MTT in primary language (p = .71); no other demographic information was collected for caregivers.

Table 1

Logistic Regression Analyses for Youth MTT Scores and Youth Consent for Self

Youth Engagement Domain	*n*	Assented *M* (*SD*)	Declined *M* (*SD*)	df	B	S.E.	Exp(B)	*p*
Relationship	107	15.49 (3.22)	14.30 (3.96)	1	.10	.06	1.10	.10
Expectancy	108	14.93 (3.29)	14.02 (3.93)	1	.07	.06	1.08	.20
Attendance	104	12.56 (2.64)	12.57 (2.27)	1	.00	.08	1.00	.98
Clarity	108	15.05 (3.42)	14.33 (3.77)	1	.06	.06	1.06	.31
Homework	103	14.65 (3.13)	13.76 (3.22)	1	.09	.07	1.09	.18
Overall	94	73.20 (13.97)	69.68 (13.49)	1	.02	.02	1.02	.25

Table 2

Logistic Regression Analyses for Caregiver MTT Scores and Caregiver Consent for Self

Caregiver Engagement Domain	*n*	Consented *M* (*SD*)	Declined *M* (*SD*)	df	B	S.E.	Exp(B)	*p*
Relationship	173	16.09 (4.21)	15.54 (4.35)	1	.03	.04	1.03	.41
Expectancy	172	16.04 (3.91)	15.31 (4.65)	1	.04	.04	1.04	.27
Attendance	168	14.12 (3.35)	14.08 (3.51)	1	.00	.05	1.00	.94
Clarity	172	15.37 (3.75)	15.35 (3.87)	1	.00	.04	1.00	.97
Homework	168	15.15 (3.50)	15.33 (3.28)	1	-.02	.05	.98	.74
Overall	162	76.77 (17.48)	76.29 (17.07)	1	.00	.01	1.00	.86

Table 3

Logistic Regression Analyses for Caregiver MTT Scores and Caregiver Consent for Youth

Caregiver Engagement Domain	*n*	Consented *M* (*SD*)	Declined *M* (*SD*)	df	B	S.E.	Exp(B)	*p*
Relationship	169	16.09 (3.92)	15.58 (4.40)	1	.03	.04	1.03	.43
Expectancy	168	16.09 (3.79)	15.29 (4.78)	1	.05	.04	1.05	.24
Attendance	164	14.32 (3.12)	14.01 (3.59)	1	.03	.05	1.03	.55
Clarity	168	15.52 (3.67)	15.28 (3.96)	1	.03	.04	1.03	.51
Homework	164	15.19 (3.49)	15.31 (3.33)	1	-.01	.05	.99	.83
Overall	158	77.24 (16.81)	76.18 (17.42)	1	.00	.01	1.00	.70

Table 4

Caregiver Consent for Self and Youth Assent/Consent for Self

		Youth Assent/Consent for Self	
		Yes	No
Caregiver Consent for Self	Yes	63	3
	No	5	37

Table 5

Caregiver Consent for Youth and Youth Consent for Self

		Youth Consent for Self	
		Yes	No
Caregiver Consent for Youth	Yes	68	1
	No	0	38

Table 6

Caregiver Consent for Self and Caregiver Consent for Youth

		Caregiver Consent for Youth	
		Yes	No
Caregiver Consent for Self	Yes	102	1
	No	5	61

Discussion

The present study examined the association between (a) types of treatment engagement problems of youth and caregivers and research participation rates; (b) overall levels of treatment engagement and research participation rates; and (c) caregiver and youth research participation rates in the clinical trial. Through better understanding the impact of treatment engagement problems on research participation rates, we hoped to identify factors that might influence youth and caregivers' assent and consent to participate in the clinical trial and, therefore, speak to the generalizability of mental health treatment research.

In support of the representativeness of the clinical trial sample, results revealed that the types of problems in the REACH domains of engagement did not significantly predict willingness to participate. Specifically, problems in the relationship domain of engagement were not shown to be associated with research participation. This finding was inconsistent with our hypothesis that youth and caregivers with a better relationship with their therapist would be more willing to participate in the clinical trial. A possible explanation for the therapy relationship having relatively little impact on research participation is that the relationship domain of engagement encompasses not only trust in an institution, but also other factors such as bond and working alliance. Previous research has found that trust in an institution influences research participation (Andrighetti et al., 2017; Scharff et al., 2010), yet bond and working alliance have not been researched as predictors of research participation.

Additionally, results demonstrated that problems in the expectancy domain of engagement were not associated with research participation. These findings were inconsistent with our hypothesis that youth and caregivers who expected a positive treatment outcome would be less likely to participate in the clinical trial. It is possible that youth and caregivers' decisions about study participation may have been influenced by other factors, such as personal benefits to participation or the desire to contribute to global improvements in mental health care.

Results demonstrated that problems in the attendance domain of engagement were not associated with research participation. However, it is worth noting that we collected data around the fourth treatment session, and it is possible youth and caregivers with severe engagement problems may have already dropped out of treatment before even being identified as a potential participant in the clinical trial. The applicability of clinical psychology research findings to this subsample of the service-seeking population should thus be further studied.

Additionally, results illustrated that problems in the clarity domain of engagement were not associated with research participation. These results are encouraging for a couple of reasons. First, these findings support the generalizability of research findings from clinical trials. Second, because youth and caregivers were asked about their mental health treatment experience shortly after completing intake interviews, it is likely that their responses to the clarity subsection items from the MTT may reflect a prior understanding of the approach and roles of treatment rather than newly obtained knowledge from their treatment participation. Since individuals are typically invited to participate in clinical trials prior to receiving any treatment, these findings provide further support for the

representativeness of samples for clinical trials.

Results also illustrated that problems in the homework domain of engagement were not associated with research participation. Since the MTT was administered early in the treatment process, youth and caregivers may not have had the opportunity to be assigned or to complete homework. One potential reason for this is that families might have only completed intake interviews and might not have begun learning coping skills at the time the MTT was administered. Alternatively, therapists might not have assigned homework even if families were past the intake interview phase of treatment. Although homework is an integral part of effective mental health treatment, homework is rarely assigned during treatment in application (Trask et al., 2018).

In further support of the external validity of clinical trials, we found that overall levels of engagement did not predict willingness to participate in research. In other words, youth and caregivers with relatively low engagement in treatment consented to research participation at similar rates as youth and caregivers with relatively high treatment engagement. This finding was inconsistent with our hypothesis that overall levels of treatment engagement would be associated with research participation rates. However, motivations behind research participation might be different for families with relatively low versus high overall treatment engagement. For example, youth and caregivers who were highly committed to their own treatment might have been willing to take additional actions, such as participating in the clinical trial, to improve their mental health. On the other hand, youth and caregivers with relatively low treatment engagement might have been motivated to participate in the clinical trial in hopes that it would improve their experience with treatment. It could also be the case that the prospect of a better experience in therapy was similarly appealing to families regardless of their overall treatment engagement levels.

Results also showed that caregiver consent was significantly associated with youth assent/consent. This finding was consistent with our hypothesis that caregivers and their youth tend to share similar perceptions about the benefits of research participation (Wiener et al., 2015). For future researchers recruiting youth-caregiver dyads, it may be useful to consider that youth will likely agree to participate in research studies if their caregiver consents, and vice versa. When considering whether to first invite youth or caregivers to participate in a research study, it is worthwhile to contemplate potential ethical and developmental factors. For instance, younger children may have difficulty understanding the information in an assent form and thereby may be unable to give informed consent. Accordingly, when conducting research with families with younger children, it may be desirable to invite the caregiver before the youth or to invite the youth with the caregiver present. For adolescents, it may be more beneficial to invite the youth before inviting the caregiver, in order to respect the youth client's growing autonomy. Some states such as California allow minors as young as 12 to consent to their own mental health counseling without requiring parent consent (Mental Health Services for At-Risk Youth Act of 2009-2010), suggesting that adolescents are capable of providing informed consent.

In this examination of factors that influence research participation rates, it is worth mentioning some additional considerations. One factor that might influence research participation rates is the amount of information provided to potential participants. A review on informed consent in clinical trials found that more information presented to potential participants about a study was associated with higher understanding of the research procedures but lower participation rates (Edwards et al., 1998). Youth and caregivers' perceptions of the benefits and risks of participating might also be an important factor in their decision to participate in a clinical trial. Our study's clinical trial involved minimal risks (i.e., discomfort with being audio-recorded or with completing self-report questionnaires), with the potential benefit of improving youth and caregiver clients' experiences in treatment. Participation in this study also required little additional effort from the youth and caregivers (i.e., completing a brief questionnaire on three occasions). Given the relatively high ratio of benefits to risks, it is possible that our findings reflect more willingness to participate in research than would be seen in studies with less advantageous benefits or more risks.

Limitations and Future Directions

This study has several strengths including its large sample

size, inclusion of participants from both urban and rural environments, and examination of a research question that is sparsely featured in the extant literature. A limitation of this study is that youth and caregivers were invited to participate in the clinical trial by their therapists. Although therapists completed a standard training on how to obtain informed consent, there may have been individual differences in the way therapists presented the study to youth and caregivers, potentially influencing youth and caregivers' willingness to participate in the clinical trial. Therefore, it could be beneficial for future research to more closely examine how youth and caregivers are invited to participate in clinical trials and to identify effective strategies for obtaining informed consent. Additionally, this study examined predictors of research participation but did not explore whether these factors may have influenced study completion. To comprehensively assess external validity, future research should investigate whether treatment engagement predicts study completion.

Conclusion

Results from this study indicate that samples from clinical trials may represent individuals with varying engagement problems and levels of overall engagement. These findings should give confidence to researchers developing and testing mental health treatments about the external validity of their studies. Results also suggest that youth and caregivers may agree in their decisions about whether or not to participate in research, posing considerations for mental health services researchers contemplating their informed consent process. These findings contribute to the extant literature on research participation, and provide encouraging support for the generalizability of clinical trials involving mental health treatments.

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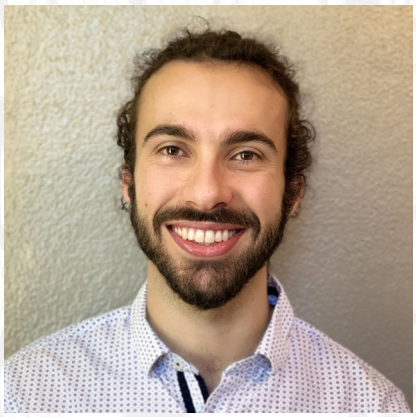
Isaac A. Mirzadegan, BA
University of California, Los Angeles



Isaac Mirzadegan graduated from UCLA magna cum laude in 2016 with a bachelor's degree in Psychology and a minor in Society and Genetics. While at UCLA, he worked in Dr. Janet Tomiyama's Dieting, Stress, and Health (DiSH) Lab as well as Dr. Michelle Craske's Anxiety and Depression Research Center, where he completed his honors thesis. Isaac also received the Chancellor's Service Award, having served as Program Coordinator for UCLA's Mentorship Program; Training Director for UCLA's chapter of Active Minds; a counselor for the charitable organization, UniCamp; and President of his collegiate a cappella group, the ScatterTones. After graduating, he worked as a research coordinator in Dr. Allison Harvey's Golden Bear Sleep and Mood Research Clinic at UC Berkeley, managing a large, community-based sleep treatment study. He is now a rising third-year graduate student in the clinical psychology doctoral program at Florida State University, working under the mentorship of Dr. Alexandria Meyer. His current research focuses on parenting interventions for anxiety, parental engagement and parent education, dissemination and implementation science, and increasing equity in clinical psychology. His non-research interests include capoeira, comedy, dancing, backpacking, and tending to his exceptionally needy cat, Luna.

Contact: mirzadegan@ucla.edu, Twitter @IsaacMirzadegan

Was there a particular experience that sparked your research interests?

I first discovered how satisfying research could be while working in Dr. Tomiyama's DiSH lab. I learned that I love the process of collaborating with other scientists to refine research questions and design novel studies. In Dr. Harvey's lab, I discovered the field of implementation science, and I've become convinced that implementation science is the future of clinical psychology; evidence-based treatments are only as effective as their reach. Throughout my learning, the importance of early psychological intervention has also become clear to me, given that many poor mental health outcomes are linked with early adverse events. Relatedly, I think most parents are not given adequate support when it comes to child-rearing, especially when a child shows early signs of mental health problems. I am passionate about changing our culture so that parents can be more empowered and supported to raise healthy, well-adjusted children.

Who has been the most influential person in your life?

While I can't choose just one name, I am deeply grateful to my past and present research mentors who evoked my passion for research and clinical psychology. I am also grateful to my friends and family, who have shown me the power of hard work and service, in addition to the importance of making time to have fun. On a lighter note, my current academic crushes are Dr. Matthew Sanders (a prolific parenting researcher and implementation scientist) and Dr. Jessica Schleider (implementation scientist and brilliant mental health advocate), and my current comedy crush is Hannah Gadsby (known for her comedy specials, "Nanette" and "Douglas"). My current hybrid academic-comic crush is Dr. Rachel Brenner (a counseling psychologist and researcher who studies help-seeking, stigma, and psychometrics – and an avid TikTok influencer).

What is your greatest accomplishment?

My greatest accomplishment is a work-in-progress; over the last few years, I've made strides toward embracing failure and imperfection. I've been learning to view rejections and "failures" as an inevitable, ubiquitous, and helpful part of the scientific process. My current academic advisor, Dr. Meyer, does research on the neural impact of teaching kids that it's OK to make mistakes; I think this is a great message for children and adults, alike! I've also developed a useful way to deal with imposter syndrome. I fully accept that I am indeed an imposter, but probably so is everyone else… and while I have everyone fooled, I might as well keep on working toward my goals!

Where do you see yourself in 10 years?

I have greatly appreciated the training in clinical science I've received thus far at Florida State University, and I look forward to pursuing licensure in clinical psychology after earning my PhD. I enjoy many aspects of teaching, research, and clinical work, and at this point I'd like to pursue a career that allows me to work in all three of these areas. In addition, I plan to continue doing advocacy work to increase inclusion and equity in the field, and I'd like to engage in more science communication with lay audiences.

Associations between Early Life Adversity and Anxiety Sensitivity

Isaac A. Mirzadegan[1]

Anxiety sensitivity (AS) predicts the onset of anxiety and mood disorders, including major depression, post-traumatic stress disorder, and panic disorder. Previous research has shown that there are gender differences in AS, with females scoring higher on global measures of AS, as well as gender differences in the lower-order subfactors of social concerns, mental incapacitation concerns, and physical concerns (Stewart et al., 1997). Childhood trauma is known to contribute to the development of AS, but it is not known whether different types of childhood trauma differentially affect AS. To examine these relationships, we performed secondary analyses on a subset of data collected for longitudinal examination of common and specific risk factors for psychopathology (n = 439; Mage = 16.9). Results confirmed gender differences in both the higher- and lower-order factors of AS, with women scoring higher on measures of global and physical AS. Individuals who experienced high amounts of sexual abuse during adolescence had significantly elevated physical AS concerns compared to individuals who did not. Findings have implications for possible gender differences in anxiety pathology and anxiety-related correlates of early sexual adversity.

Anxiety disorders are the most common form of mental illness; moreover, many have an early age of onset and are associated with substantial impairment (Beesdo, Knappe, & Pine, 2009; Copeland, Angold, Shanahan, & Costello, 2014; Kessler et al., 2005; Merikangas et al., 2010). Thus, it is critical to identify factors that predict early anxiety. Anxiety sensitivity (AS) is defined as the tendency to believe that symptoms of anxiety, such as rapid heart rate, sweating and nervousness, have detrimental consequences (Reiss, Peterson, Gursky, & McNally, 1986). Elevated AS in youth has been found to predictpredicts higher levels of anxiety symptoms, , over and above baseline anxiety symptoms, and it has been found to moderate the negative effects of stressful life events (McLaughlin & Hatzenbuehler, 2009; McLaughlin, Stewart, & Taylor, 2007).

The three proposed lower-order subfactors of AS are cognitive concerns, physical concerns, and social concerns (Taylor et al., 2007; Zinbarg, Barlow, & Brown, 1997). Cognitive AS represents the fear that one's thoughts associated with the experience of anxiety are harmful, or a sign of severe mental illness..mental illness. For example, a person with high cognitive AS who has difficulty focusing on a task may report that they are "going crazy" simply because they cannot focus. In contrast, physical AS is fear that interoceptive sensations associated with anxiety (e.g., rapid heart rate, sweating, hyperventilating) are dangerous or signs of a serious health problem (e.g., heart attack). Finally, social AS is the fear of public embarrassment as a result of experiencing symptoms of anxiety. Additionally, the subfactors have been shown to differentially predict other mental health symptoms, such as social concerns predicting social phobia symptoms (McLaughlin et al., 2007), and cognitive

1 Florida State University and University of California, Los Angeles

Corresponding Author: Isaac A. Mirzadegan, Florida State University, Department of Psychology, 1107 W Call St, Tallahassee, FL 32306-4301. Email: mirzadegan@ucla.edu

concerns predicting suicide risk (Oglesby, Capron, Raines, & Schmidt, 2015). These subfactors tap into important constructs, as gender differences have been found among the subtypes of AS (Stewart, Taylor, & Baker, 1997).

Although women score higher on the higher-order (i.e., global) factor of global AS , multiple studies support gender differences in the lower-order subfactors of AS in both adults (Stewart et al., 1997) and children (Walsh, Stewart, McLaughlin, & Comeau, 2004). In adults, men score higher on the cognitive concerns factor, and women score higher on the physical concerns scale, while men and women exhibit comparable social AS (Stewart et al., 1997). There are several potential explanations for these documented gender differences in both the higher and lower order factors of AS, but one possibility is that it stems from gender role socialization over an individual's lifetime. For example, women may be more socially rewarded than men for outwardly expressing their symptoms of anxiety; women may be more likely to learn over the course of their lifetime to focus on the social rewards of expressing anxiety, whereas men learn the opposite (Stewart et al., 1997). Further understanding sex differences in AS may help contextualize findings on differences in anxiety etiology between men and women (Olatunji & Wollitsky-Taylor, 2009).

The developmental perspective of psychopathology also emphasizes the importance of adversity experienced during youth (Cicchetti & Rogosh, 2002). Multiple investigations have found that childhood trauma predicts a variety of internalized problems later in life, including an increased risk for major depressive disorder (MDD) and panic disorder (PD) (Gibb, Chelminski, & Zimmerman, 2007; Kessler & Magee, 1993). Furthermore, data from the National Comorbidity Survey-Replication (NCS-R) have shown that distinct dimensions of childhood adversity are differentially related to the development of specific disorders. Notably, childhood sexual abuse was found to uniquely predict onset of PD and generalized anxiety disorder, while physical abuse significantly predicted onset of post-traumatic stress disorder (PTSD) (Cougle, Timpano, Sachs-Ericsson, Keough, & Riccardi, 2010).

AS has been shown to be elevated in those with PD more so than those with other anxiety diagnoses (Taylor, Koch & McNally, 1992). One prospective study examined individuals during a stressful time period (i.e., basic military training) and found that highly elevated AS predicted the development of spontaneous panic attacks after being exposed to the period of prolonged stress, even after controlling for panic symptomatology and trait anxiety history (Schmidt, Lerew, & Jackson, 1997). According to Reiss' expectancy theory, panic and AS are dependent on one another; an increase in AS may lead to symptoms of panic, and symptoms of panic may additionally lead to heightened AS, creating a positive feedback loop (Reiss, 1991). The misinterpretation of one's own bodily sensations as a detrimental and catastrophic event is a central feature of PD (McNally, 2002). Given that AS concerns are integral to the symptomatic presentation of PD, and that early sexual abuse uniquely predicts the onset of PD (Cougle et al., 2010), the relationship between early sexual abuse and global AS concerns should be examined more closely.

Limited research has been conducted on the relation between childhood adversity and AS. A cross-sectional examination of AS, gender, and childhood adversity found that experiencing traumatic events uniquely predicted AS in adults (Martin, Viljoen, Kidd, & Seedat, 2014). Using the Childhood Anxiety Sensitivity Index (CASI; Silverman, Fleisig, Rabian, & Peterson, 1991) and the Childhood Trauma Questionnaire (CTQ; Bernstein & Fink, 1998), they found that although childhood trauma was comparable between boys and girls, girls later showed increased AS as a result. However, this study was limited in that it was cross-sectional, so causality should not be inferred from these findings.

A large body of work has demonstrated the psychiatric sequelae of early life adversity. In addition, ample research has shown that AS is elevated in anxiety disorders and, in particular, PD. However, the mechanism by which early life adversity, specifically sexual abuse, is associated with elevated AS remains unclear. Multiple studies have found gender differences in AS, but findings on this topic to date have been somewhat mixed (McLean & Anderson, 2009). In the present study, we examine the differential effects of early life adversity on AS. We expect that those who have experienced more childhood and adolescent trauma will score higher on global measures of AS. We also predict that adults who have experienced early sexual abuse will

experience greater symptoms of physical AS. Finally, we expect to see higher global and physical AS symptoms in women.

Method

Participants

Participants consisted of high school juniors (n = 439; 69% female) recruited from two ethnically and socioeconomically diverse high schools: one in suburban Los Angeles, and one in suburban Chicago. This subset was drawn from a larger prospective study (Youth Emotions Project; total N = 627; M age at first interview = 16.9, SD = 0.4) examining predictors of psychopathology in young adulthood. In our analyses, we used only those who completed the following two measures: a self-report AS survey collected at baseline and a retrospective early life adversity interview completed by phone six years after the baseline assessment. During recruitment, students were oversampled for neuroticism (i.e., those who were in the top third of the total sampled for neuroticism were invited to participate) in order to recruit a high-risk sample, given associations between neuroticism and risk for anxiety and depressive disorders (Zinbarg et al., 2010). Potential participants were screened with the Neuroticism subscale of the revised 23-item Eysenck Personality Questionnaire (EPQ–R–N; Eysenck & Eysenck, 1975). A detailed description of the selection criteria can be found in Zinbarg et al. (2010).

Measures

Early Life Adversity. Participants completed the semi-structured Childhood Trauma Interview (CTI; Fink, Bernstein, Handelsman, Foote, & Lovejoy, 1995), a measure in which an individual shares traumatic experiences that occurred from birth to the age of 16 (participants completed the interview retrospectively at age 20-23). The CTI delineates six domains of adversity: 1) separation from or loss of a caregiver; 2) neglect by a caregiver; 3) emotional abuse; 4) physical abuse; 5) witnessing violence; and 6) sexual abuse or assault. For each adversity, interviewers rated the perceived severity of the event on a Likert scale from 1 (minimal or mild) to 6 (very severe, sadistic). This method of scoring that accounts for severity is explained in detail in Vrshek-Schallhorn et al. (2014). Interviewers received extensive training on administration and scoring protocol. Adversities that occurred during childhood (ages 0-8) were analyzed separately from adolescent adversities (ages 9-16). If a single adversity spanned from childhood to adolescence, it was scored in both categories. The sums of adversities between childhood and adolescence, weighted for severity, were calculated within each of the six domains of adversity. Additionally, overall sum scores were computed separately for both childhood and adolescence. This method of scoring has been shown to predict onset of mood and anxiety disorders (Vrshek-Schallhorn et al., 2014).

Anxiety Sensitivity. Participants also completed the Anxiety Sensitivity Index (ASI; Reiss, et al., 1986), a 16-item questionnaire assessing participants' sensitivity to somatic and psychological symptoms of anxiety. Questionnaire items address fear of bodily sensations associated with anxiety (physical), mental incapacitation associated with anxiety (cognitive), and negative social evaluation associated with anxiety (social). For each item, participants rated how much they agree with statements expressing sensitivity to anxiety (e.g., "It scares me when I feel shaky") on a Likert scale from 0 (very little) to 4 (very much). Zinbarg et al. (1997) fitted a hierarchical model to the ASI; the resulting factor structure yielded 15 items contributing to the global AS score (one item was omitted due to poor factor loadings), 8 items contributing to the physical AS score, and 3 separate items each contributing to cognitive and social AS. This validated method of scoring was used in the present study. Mean scores rather than total scores were reported to make comparison across subfactors more intuitive, given that the three subfactors were composed of different numbers of items.

Neuroticism. Neuroticism was the only covariate in our analyses. The composite of four self-report questionnaires was used to determine neuroticism: the Big-Five Mini-Markers Neuroticism scale (Saucier, 1994), the Neuroticism scale of the International Personality Item Pool-NEO-PI-R (IPIP-N; Goldberg, 1999), the Behavioral Inhibition System scale (BIS; Carver & White, 1994), and the Neuroticism scale of the Eysenck Personality Questionnaire (EPQ-R-N; Eysenck & Eysenck, 1975; note that we omitted item 12 as well as a suicide item for the purposes of this study; see Zinbarg et al., 2010 for details

on the psychometric properties of the Neuroticism composite). All questionnaires were administered at baseline with the exception of the EPQ-R-N, which was completed during an initial screening (a median of four months [range 1-14 months] earlier).

Procedure

Participants were recruited for screening procedures in their junior year of high school. Once enrolled, participants received a battery of questionnaires and underwent a semi-structured diagnostic interview, and follow-up diagnostic interviews were conducted annually. Diagnostic information was not used in the present study. Our analyses examined ASI scores obtained at baseline. The CTI was administered during year 6-7 of the 10-year study. Individuals were contacted annually whether or not they had completed the previous interviews (see Vrshek-Schallhorn et al., 2014, & Zinbarg et al., 2010 for further recruitment and assessment details). All analyses conducted in the present study were secondary analyses from this larger project.

Statistical Analysis

Multiple regression analyses were conducted using the standard statistical modeling software, SPSS 26.0. Neuroticism was entered as a covariate in each of our analyses. First, we assessed the relationship between overall childhood and adolescent adversity (IVs) and global AS (DV). In order to investigate unique effects of the six different domains of adversity, individual categories were entered into a regression predicting global AS. Specific associations between early sexual abuse and physical AS were also examined with regression, and this association was subsequently tested at high-severity levels of early sexual abuse (1SD above the mean). We also investigated whether gender differences existed in AS using t-test comparisons.

Results

Descriptive Statistics

Participants had lower average scores on measures of childhood sexual abuse ($M = 0.21$, $SD = 0.85$) than adolescent sexual abuse ($M = 0.41$, $SD = 1.72$), $t(438) = -2.38$, $p = .02$. Overall scores of childhood adversity, ($M = 9.37$, $SD = 9.88$) were lower than scores of adolescent adversity ($M = 18.93$, $SD = 14.42$), $t(438) = -18.68$, $p < .001$, as measured by the sum of the six adversity dimensions.

Participants had a low average score on total AS ($M = 1.08$, $SD = 0.56$). Overall scores between the lower-order factors differed: physical AS ($M = 1.24$, $SD = 0.72$) was greater than cognitive AS ($M = 0.57$, $SD = 0.74$), $t(438) = 19.98$; social AS ($M = 1.92$, $SD = 0.78$) was greater than both cognitive AS, $t(438) = -30.19$, and physical AS, ($t(438) = 17.12$; all $ps < .001$).

Gender Differences

As predicted, female scores of total AS ($M = 1.13$, $SD = 0.57$) were significantly higher than male scores ($M = 0.97$, $SD = 0.52$), $t(437) = -2.81$, $p < .01$. Confirming prior findings, females also had significantly higher physical AS ($M = 1.34$, $SD = 0.74$) than males ($M = 1.02$, $SD = 0.63$), $t(437) = -4.35$, $p < .001$. Moreover, there were no gender differences within cognitive AS (females: $M = 0.59$, $SD = 0.75$; males: $M = 0.53$, $SD = 0.71$), $t(437) = -0.68$, $p = .50$, or social AS (females: $M = 1.91$, $SD = 0.77$; males: $M = 1.95$, $SD = 0.80$), $t(437) = 0.55$, $p = .58$.

Contrary to prior findings, social concerns within males were greater than both physical concerns, $t(135) = 14.02$, and cognitive concerns, $t(135) = -18.56$; additionally, male physical concerns were significantly greater than cognitive concerns, ($t(135) = 8.73$; all $ps < .001$). The same pattern was found within females, with social concerns surpassing both physical concerns, $t(302) = 11.85$, and cognitive concerns, $t(302) = -24.01$; moreover, physical concerns in females were also significantly greater than cognitive concerns, ($t(302) = 18.43$; all $ps < .001$).

Early Adversity

Using a linear regression model and covarying for neuroticism, severity of childhood adversity did not significantly predict scores of global AS, ($\beta = .01$, $t(438) = 0.26$, $p = .80$). We found similar null results for adolescent adversity, ($\beta = .01$, $t(438) = 0.19$, $p = .85$). Our second and third linear models examined the effects of each domain of early adversity on total AS, and no significant effects were found for any domain of childhood or adolescent adversity (see Tables 1 & 2).

Table 1

Regressions with Six Domains of Childhood Adversity (CASI) Predicting Global Anxiety Sensitivity (ASI)

Predictors	*B*	*SE B*	β	*t*	*p*
Neuroticism	.30	.03	.43	9.68	< .001
Childhood Adversity Domain					
Separation/Loss	.00	.01	.02	0.34	.73
Neglect	.01	.01	.04	0.87	.39
Emotional Abuse	-.02	.01	-.08	-1.52	.13
Physical Abuse	-.01	.01	-.06	-1.17	.24
Witness to Violence	.02	.01	.09	1.73	.08
Sexual Abuse	.03	.03	.05	1.00	.32

Note. CASI = Child Anxiety Sensitivity Index; ASI = Anxiety Sensitivity Index

Table 2

Regressions with Six Domains of Adolescent Adversity (CASI) Predicting Global Anxiety Sensitivity (ASI)

Predictors	*B*	*SE B*	*β*	*t*	*p*
Neuroticism	.29	.03	.41	9.32	< .001
Adolescent Adversity Domain					
Separation/Loss	-.00	.01	-.02	-0.34	.73
Neglect	-.00	.00	-.04	-0.83	.41
Emotional Abuse	.01	.01	.05	0.87	.39
Physical Abuse	-.00	.01	-.03	-0.47	.64
Witness to Violence	.01	.01	.05	1.02	.31
Sexual Abuse	-.01	.02	-.02	-0.33	.74

Note. CASI = Child Anxiety Sensitivity Index; ASI = Anxiety Sensitivity Index

Sexual Abuse & Anxiety Sensitivity

Contrary to our hypotheses, severity of sexual abuse experienced during childhood did not significantly predict physical AS, ($\beta = .02$, $t(438) = 0.54$, $p = .59$), nor did severity of sexual abuse experienced during adolescence, ($\beta < .01$, $t(438) = 0.01$, $p = .99$). A separate t test compared those who were greater than 1SD above the mean for child sexual abuse (n = 37) with those below this cutoff (n = 402). Results revealed that this group with the highest severity of child sexual abuse displayed greater physical AS (M = 1.48, SD = 0.85) than the rest of the sample (M = 1.22, SD = 0.71), $t(437) = -2.06$, $p = .04$. However, the same pattern was not found for those with the highest severity of adolescent sexual abuse (n = 34; M = 1.26, SD = 0.66) compared to the rest of the sample (M = 1.24, SD = 0.73), $t(437) = -0.12$, $p = .91$.

Discussion

We examined the relationship between retrospectively reported indices of childhood trauma and self-reported symptoms of anxiety sensitivity (AS). In addition, we explored gender differences on the global factor and within the lower-order factors of AS. Our hypotheses regarding gender differences in AS were largely supported by the results. We obtained the same results as prior research showing that females exhibit greater AS overall. Additionally, our hypothesis that females would score higher than males on measures of physical AS, but not on the other AS subfactors, was confirmed. As mentioned previously, this gender difference may be due to a number of factors. One possible explanation incites different societal standards for men and women: women may be allowed, even encouraged, to express bodily concerns and symptoms of anxiety, whereas men are more often discouraged from doing so (Ehlers, 1993; Watt, Stewart, & Cox, 1998). This may result in a dissimilar presentation of anxiety symptoms between men and women.

Perhaps our most surprising finding was that both males and females scored significantly higher on social AS than on either of the other two factors. As far as we know, these findings oppose previous research comparing lower-order factors of AS. Consistent with part of our findings, Stewart et al. (1997) found that cognitive AS and social AS scores did not significantly differ among men and women. However, in women, physical AS scores were significantly greater than both cognitive and social AS, whereas in men, the opposite pattern was found: physical AS scores were significantly lower than the other two subfactors. A slightly different scoring mechanism was used by Stewart and colleagues (1997), and some work has demonstrated the importance of scoring methods in predicting gender

differences via the ASI (Van Dam, Earleywine, & Forsyth, 2009). However, Stewart et al. (1997) employed the same hierarchical structure of AS that was used in the present study, with three lower-order factors.

Another study in outpatients with PD found that women had higher physical AS than men, whereas men had higher social AS than women (Foot & Koszycki, 2004). Unfortunately, this study did not directly compare subscale scores to each other. In our study, we expected social AS scores to be lower than the other lower-order factors of AS. Our sample consisted of a similar demographic to previous research (e.g., Stewart et al., 1997). One key difference, however, is that subjects in our study consisted of those highest in neuroticism (see sampling method described in Zinbarg et al., 2010). It is possible that the association between early life adversity and AS differs in highly neurotic samples. Additionally, our sample consisted of high school juniors, while Stewart et al. (1997) sampled college students. It may be the case that the ratio of physical AS to social AS increases with age, with social AS being a more common presentation in younger samples. This interpretation is partially supported by Walsh et al. (2004), who showed that in children and adolescents, males had greater social AS than the two other forms of AS. It is also possible that high school students who are high in neuroticism are more prone to experiencing social AS because of the intense social pressures of high school (Crosnoe, 2011). It could be that societal pressures on men and women regarding the expression of anxiety symptoms differ across the lifespan. However, none of these hypotheses have been confirmed, and more research should be done to compare social AS of high-neuroticism individuals with that of the general population.

As for our findings regarding early adversity and AS, we did not find any significant results (other than the robust positive association between neuroticism and AS, for which we covaried). In addition to the possible explanations stated above for gender differences (i.e., our recruitment method oversampled for neuroticism; effects of gender may vary by age), we postulate that our null results might be explained by these effects being largely washed out when covarying for neuroticism. There is a notably small body of research that predicts AS from early life adversity. This may indicate that the relationship is not a very strong one, or that AS is better predicted by other variables. Early adversity does affect trait anxiety, and AS is often an important factor in trait anxiety; however, AS might not be the specific mechanism by which adversity leads to anxiety disorders.

We hypothesized that because sexual abuse uniquely predicts panic disorder, and AS is highest in those with panic disorder as compared to other anxiety disorders, sexual abuse would predict greater AS. We specifically predicted higher physical AS because of the central role that physical symptoms of anxiety play in panic attacks and PD. Our examination of the specific effects of sexual abuse on AS partially supported our hypotheses. We found significantly increased physical AS in the subset of our sample that was 1SD above the mean for child sexual abuse. Interestingly, we did not find the same pattern for those 1SD above the mean for adolescent sexual abuse. We acknowledge the possibility of a memory recall bias, in which subjects have greater memory acuity for adolescence than for childhood. One study revealed that documented instances of sexual abuse that had occurred early in childhood were less likely to be recalled by adults than abuses that had occurred later in childhood (Williams, 1995). It is unclear whether subjects can retroactively distinguish between traumas that occurred during childhood and those that occurred during adolescence. However, it is possible that sexual abuse occurring during childhood, or at least memories of abuse occurring during childhood, may be indicative of more severe or psychologically harmful forms of trauma than memories associated with adolescence. More work should be done in this area to clarify the role of physical AS in the development of PD after high exposure to sexual abuse.

This study had several limitations. Retrospective evaluation of childhood adversities is known to be significantly less reliable than prospective evaluation of adverse events (Hardt & Rutter, 2004). The CTI distinguishes between childhood and adolescent adversities; however, adversities in the first few years of life (i.e., approximately ages 0-2) are likely to only be known from secondhand report (e.g., from a parent or social worker), which introduces an additional source of error. Thus, it is likely that adolescent adverse events were more reliably reported. In addition, some researchers have highlighted the importance of

different broad domains of early life adversity, such as outcomes associated with deprivation and threat (McLaughlin, Sheridan, & Lambert, 2014), or harshness and unpredictability (Ellis, José Figuerido, Brumbach, & Schlomer, 2009; Marshall, van Dulman, & Stigall, 2017). It is possible that examining early life adversity using these frameworks, as opposed to classifying adversity along the six dimensions used in the present study, would yield novel findings. Finally, while this study covaried for neuroticism, it did not include a measure of trait anxiety. Trait anxiety tends to share substantial variance with neuroticism. Including a specific measure of trait anxiety in future research could yield unique insights on the overlap between AS and other anxiety symptoms, beyond its overlap with neuroticism. Examining the relationship between adversity and other anxiety symptoms, in addition to AS, might provide a stronger test of the expectancy model of panic (Reiss, 1991).

Conclusion

There are many potential future directions for this research. To ascertain whether the gender differences found are a byproduct of extra high neuroticism, replication research should be carried out in populations with normative levels of neuroticism. Additionally, more work should be done to understand why AS is especially elevated in PD patients, as well as in individuals who have experienced sexual abuse. Finally, research into genetic factors that affect AS with respect to early maltreatment has shown great promise. Previous work indicates that there may be genetic underpinnings for AS, but this relationship is highly moderated by factors such as childhood trauma (Stein et al., 2008). These findings parallel genetic models that predict MDD, and researchers may be able to gain incredible insight into this field by understanding the role of gene-by-environment interactions.

Results of this study have potential implications for gender differences across the subfactors of AS, which may vary by age. In addition, these results provide preliminary evidence for the unique role early sexual abuse may play in the development of anxiety sensitivity symptoms, relevant to panic disorder. Future work should aim to further elucidate gender differences in AS, across the age span, and examine whether interventions to prevent early adverse experiences can protect youth against developing impairing anxiety symptoms or disorders in adulthood.

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Lara Hoffmann Nassar
University of San Francisco

My name is Lara Hoffmann Nassar and I am a junior Psychology major and Neuroscience minor at the University of San Francisco (USF). I am a research assistant at Dr. Knight's Emotional and Cognition and Dr. Wagner's Aging and Diversity laboratories at my university. Mental health and the individual human experience are some of the topics that interest me the most. I am currently developing a research project of my own on strategies to enhance our Metamemories, in other words, mechanisms that could help us become more aware of our personal memories.

Born and raised in Brazil, I co-founded the Brazilian Student Association at USF of which I am currently the president. I am an event coordinator for Psi Chi, the international honors society in psychology. I love languages and speak Portuguese, German, English and am currently learning French.

Contact: lhnassar@dons.usfca.edu, www.linkedin.com/in/larahnassar

Was there a particular experience that sparked your research interests?

As a freshman, I was (and still am) heavily impacted by the support and kindness of my professors. In particular, by Dr. Marisa Knight, who helped me tremendously in writing this article. I vividly remember reading her research on the interplay between emotions and memory as those were one of the first research articles I read. Fascinated by them, I emailed Dr. Knight introducing myself and asking a few questions about her work. To my surprise, she made a point that we met in person and I was soon a member of her research team at the Emotion and Cognition Laboratory. I think I was always driven towards learning more about psychology and neuroscience but having mentors as encouraging as Dr. Knight was certainly crucial to make me realize that research was something I would love to pursue.

Who has been the most influential person in your life?

Both my parents left their countries in their 20s and moved to the United States in search of personal growth and better opportunities. At nineteen years of age, I followed their example. They have both become great professionals, parents, and people, and by 'great' I really mean the best that they could possibly be. I learn a lot from their determination and the hard work they put into being 'great' at whatever it is they chose to do. They have taught me to always give the best of me and learn from my results, be they accomplishments or failures.

What is your greatest accomplishment?

I do not have a single great accomplishment yet. However, I recognize how passionate and eager I am to learn everything I can about mental health and how it is tied to the human brain. My own insecurities constantly remind me that it takes courage to reach out to people you admire professionally and ask for guidance and opportunities. It can be very intimidating to do research when you are still learning how to, especially because everyone in the field seems to know so much. As someone who is often afraid of not doing a perfect job, I consider my greatest accomplishment to be trying anyway, and feeling foolish and insecure, in order to grow professionally and personally. It is a constant challenge with several ups and downs but I am proud of the many tiny victories it has given me.

Where do you see yourself in 10 years?

I plan on continuing studying mental health for a long time, and will probably start by enrolling in a graduate program upon completion of my bachelor's degree. I would love to have a balance between academic research and clinical practice. Someday, I hope to enter a doctorate program with clinical focus and am really excited to conduct clinical studies. My family, friends, and colleagues constantly ask me where I would like to live; Brazil? The United States? Maybe even somewhere in Europe? The truth is, I do not know. No matter where I will be in ten years, I want to feel that I will be the best professional I can possibly be.

Transcranial Direct Current Stimulation and Major Depressive Disorder

Lara H. Nassar[1]

Major Depressive Disorder (MDD) is the leading psychiatric disease and the most prevalent cause of disability worldwide. Yet, there are no proven physiological explanations to the causes of this disorder (Strakowski et al., 2013). Moreover, treatment techniques currently available remain unable to effectively treat a significant percentage of depression cases. Given these circumstances, further advancements in the understanding and treatment of depressive disorders are necessary. Transcranial Direct Current Stimulation (tDCS), a neuromodulatory technique that consists of applying low-frequency electrical currents to an individual's head, is gaining recognition as a potential way of addressing these aspects. Empirical findings point to the potential of tDCS to provide physiological explanations of depression while simultaneously exerting antidepressant effects. The aim of this literature review is to provide: 1) a brief historical background of tDCS and its development; 2) a basic explanation of the mechanisms of action of tDCS; 3) a brief overview of the neurological origins of depressive disorder and of the major techniques currently applied in MDD treatments; and 4) an analysis of cutting edge studies on tDCS to illustrate how promising yet enigmatic this technique is as an antidepressant. Major conclusions and future directions for tDCS in the diagnosis and treatment of MDD will be discussed. In

Major depressive disorder (MDD) is the preeminent cause of disability worldwide. The World Health Organization describes it as the most common of all psychiatric disorders and states that it currently affects more than 300 million people of all ages worldwide (WHO, 2018). One in every six people will suffer from depression during their lifespan (American Psychiatric Association, 2017). Moreover, of the 800,000 globally documented suicide cases, up to half have been found to occur in association with depression (Otte et al., 2016). Thus, finding treatments that are successful in alleviating the symptoms of depression could potentially improve well being, reduce economic burden, and increase global happiness and productivity.

While advances in treatment efficacy over the last decades have been observed in the most common psychopharmacological and psychotherapeutic interventions (Kupfer et al., 2014), findings show that more than 30% of patients do not recuperate from MDD after persistent treatment attempts with these techniques (Otte et al., 2016). As a result, interest in alternative ways of treating depression is ever-growing, with recent developments in electrical brain stimulation showing promise as a potential effective treatment intervention. Transcranial Direct Current Stimulation is a neuromodulatory technique that consists of applying low-frequency electrical currents to an individual's head. tDCS specifically stands out as a non-invasive and typically safe method that can lead to long-lasting results. Moreover, tDCS has the potential of answering questions regarding the physiological root causes of depression. With the capability to target predetermined regions of the brain and explore relationships between structure and function, tDCS can be a vital tool in understanding

1University of San Francisco

Correspondence concerning this article should be addressed to Lara H. Nassar. Email: lhnassar@dons.usfca.edu

the neurobiology of depressive disorders.

The aim of this literature review is to provide: 1) a brief historical background of tDCS and its development; 2) a basic explanation of the mechanisms of action of tDCS; 3) a brief overview of the neurological origins of depressive disorder and of the major techniques currently applied in MDD treatments; and 4) an analysis of cutting edge studies on tDCS to illustrate how promising yet enigmatic this technique is as an antidepressant. Major conclusions and future directions for the role of tDCS in the treatment of MDD will be discussed. The etiology and treatment of major depression will be examined through a biological perspective.

Historical Background and Development of tDCS

When research on neural stimulation began, experiments were largely implemented on non-human brains. In the 1950s and 1960s, some of the first tDCS studies were carried out on animals (Nitsche et al., 2009). Through the placement of anodes—positively charged extremity of a battery—on or above the cerebral cortex, neural activity increased, while with cathodes—negatively charged terminal on a battery—fixed to the same location activity decreased (Bindman et al., 1964; Purpura & McMurtry, 1965). Pioneer animal studies found that tDCS had the potential of provoking long-lasting effects on neural excitability (Nitsche et al., 2009), and further non-human research investigated the long-lasting effects of tDCS. Since enhancements in excitability last for hours after stimulation resumes, researchers speculated that tDCS is most likely linked to protein-synthesis-dependent mechanisms (Nitsche et al., 2009). Proteins are essential for cellular functioning, such as substance transportation, chemical reactions, and communication between cells, rely heavily on proteins. Therefore, the presence of functioning proteins are crucial for both physical and mental health. Consequently, problems with protein production could be associated with mood disorders such as MDD (Neves-Pereira et al., 2002). Observed antidepressant results of tDCS could be due the exertion of correcting forces for such synthesis malfunctionings (Martinowich et al., 2007), as will be further discussed in this article.

The first human experiments directed tDCS at the motor cortex, as this is the region where excitability shifts can be measured without major obstacles. In more recent investigations, researchers began targeting the prefrontal areas, which has led to a growing body of findings regarding the use of tDCS in treating depression, especially with stimulation to the dorsolateral prefrontal cortex (DLPFC; Nitsche et al., 2009). This area, located at the end point of the dorsal pathway, is responsible for executive functioning such as integrating and interpreting multimodal stimuli and responding to changes in the environment. The DLPFC is also important for emotion regulation and an unevenness between the left (hypoactive) and right (hyperactive) side has been measured in those with depression (Grimm et al., 2008). As extensive research began to yield greater insight into the neural correlates of depression, neurologists and neuroscientists started to more seriously consider tDCS as a means of correcting hemispherical imbalances and, by doing so, addressing depressive disorders. This is the case because such asymmetries in functioning between regions of the left and right sides of the brain, where one is abnormally more/less active than it should be—often observed in DLPFC hemispheres—could have a negative impact on mental health (Grimm et al., 2008). Other applications of tDCS, especially to the left DLPFC, have shown significant enhancements in working memory (Andrews et al., 2012), decision making, and other cognitive and emotional tasks such as impulse control (Boggio et al., 2010; Fecteau et al., 2014).

Mechanisms of Action and Application

Applying tDCS consists of attaching an anode and a cathode to specific areas of the head or other key regions of the nervous system (Reinhart et al., 2017). As explained by Woods et al. (2015), tDCS does not provoke neural activity in resting neurons, as is the case for pharmacological agents, but synthetically modulates spontaneous (i.e., naturally occurring) activity instead. The anode acts by decreasing the membrane potential's negative charge of the area above which it is attached, causing neurons to fire. tDCS can enhance neural activity via anodal stimulation by more intensely depolarizing the membrane and facilitating excitatory postsynaptic potentials. As a result, the likelihood that the threshold of excitation will be met increases significantly, leading to

more action potentials and localized neural activity (i.e., more communication between cells). The cathode, on the other hand, has the opposite effect of hyperpolarizing the membrane by inducing inhibitory postsynaptic potentials. Consequently, neural activity is reduced in the targeted region via stimulation of cathodes.

Decisions regarding the optimal type of stimulation (cathodal, anodal, or both), along with the optimal battery end placements, is crucial for the achievement of desired effects. As the use and impacts of tDCS have yet to be fully explored and understood, more research is needed to establish protocols, guidelines and best practices for human applications. Due to the complex functioning of brain regions and extensive overlap in intra-regional communication, it has not yet been possible to effectively map out the stimulation sites for each desired effect. A technique commonly applied in tDCS research is bipolar stimulation, which involves simultaneously attaching the anode to one hemisphere of the brain and the cathode to the other. However, tracking which one of the two interventions—the anodal increase in activity or the cathodal decrease—is responsible for the desired effects is a common obstacle of this type of application (Reinhart et al. 2017). There is still much to be understood about how brain functioning responds to tDCS stimulation, which poses challenges for the measurement of its effects. Due to its neuromodulatory mechanism of action, tDCS relies heavily on the baseline status of brain function and neural activation levels at the time of stimulation. The great variability of those factors across individuals is one major challenge to generalizing application strategies, such as location, intensity, and duration of stimulation, to a larger population. Nevertheless, in spite of the uncertainties, there is evidence to suggest that tDCS can potentially serve as a revealing tool for cognitive and emotional processing (e.g., Reinhart et al., 2017).

Contributions of tDCS Findings as Applied to Theories of MDD and its Treatment

As mentioned above, the potential of tDCS lies not only in ameliorating the treatment of MDD, but also in answering vital questions regarding the physiological mechanisms driving the disorder. There have been significant findings regarding possible neurobiological factors correlated to MDD; however, no theory is yet able to fully account for the root causes of this extremely prevalent disorder. Presented here are some of the most significant contributions of tDCS' findings as applied to theories of MDD and its treatment.

It is now widely believed that depression is not a result of irregularities in a single brain region or neurotransmitter complex, but a systems-level disorder that connects different pathways, limbic regions and cortical sites (Mayberg et al., 2005). One hypothesis is that depressive episodes are correlated with hippocampal volume, with a smaller size of this brain region linked to an increased risk of developing MDD (Etkin et al., 2015). Evidence suggests that this limbic system irregularity could be targeted by tDCS with the hopes of possibly increasing hippocampal volume; in a recent study, repeated anodal tDCS was found to induce neural plasticity-associated gene expression in the hippocampus (Zhang al., 2017).

Findings also point towards abnormalities in the amygdala—a structure highly involved with emotions, emotionally charged memories, and depression. Recent work has shown an especially active amygdala, with higher-than-usual connectivity, observed in patients with depression (Kupfer, et al., 2016). tDCS offers a potential solution to this irregularity with the discovery that stimulation of the amygdala can consistently change the physiological basis of emotion (Inman, et al.,2018); this stimulation has yet to be practiced using the tDCS technique. tDCS acts by inducing shifts in the autonomic functioning of the brain, altering areas associated with emotional processing—especially the limbic system—and, consequently, changing the individual's emotional experience. Data also confirmed that no significant concurrent subjective emotional responses or health consequences followed these physiological changes (Inman et al., 2018). This safety advantage further supports tDCS as not only well fit to target depression, but also for the investigation of the neurobiological drives of emotion and of how emotional disorders come into being. If tDCS reaches antidepressant efficacy by changing activity rates in a brain structure associated with emotions (e.g. the amygdala), this would be compelling evidence that this structure—or other structures it connects to and influences—plays a role in depressive symptoms.

One of the widely accepted physiological explanations

for depression links it with a pathological alteration of neural activity and mechanisms of action in the prefrontal cortex (Nitsche et al., 2009). More specifically, findings point towards an asymmetry of functioning between the left and right dorsolateral regions of the prefrontal cortex (DLPFC). This could be due to hyper-or-hypo activation of the DLPFC (Nitsche et al., 2009). Shifts in connectivity (i.e., 'neurological mis-wirings') and/or activation of neural networks, such as cognitive control and affective systems, are another possible root cause of MDD (Kupfer et al., 2016). The potential link between these hemispheric abnormalities to depression was empirically evidenced by tDCS: Improvement in depression scores of tDCS-induced increases and decreases of opposing hemispherical activities—carried out by anodal and cathodal electrodes respectively—confirm that cortical imbalances are indeed strongly related to MDD (Brennan et al., 2017; Brunoni et al., 2016). These findings have guided tDCS applications to target frontal cortical regions, especially the DLPFC, when addressing depressive disorders.

To evaluate plausible explanations for depression, it is important to examine its possible genetic and molecular roots. A key molecule that has been linked with depression is Brain Derived Neurotrophic Factor (BDNF), a gene-manufactured secretory protein. BDNF is essential for the survival of nerve cells in the brain and spinal cord (CNS); it directs their growth, maturation and differentiation from other types of cells, and maintenance (U.S. National Library of Medicine, 2019). Research points towards a possible relationship between deficiencies in the BDNF gene and the expression of emotion-related diseases, such as depressive disorders (Neves-Pereira et al., 2002). Based on empirical findings, researchers have proposed that a reduction in the BDNF-protein in the hippocampal area could be a neurological-molecular cause of stress-induced depression (Martinowich et al., 2007). This seems to be a bidirectional process, as additional empirical findings show that stress and stress-induced depression might lead to hippocampal volume reduction and diminishment of BDNF genetic expression (Yang et al. 2015). This continuous dynamic in which neuro-molecular consequences of depression are themselves the causes of the disease becomes especially informative when seeking treatment alternatives. If the symptoms of stress and depression are contributing to physiological abnormalities, it seems logical to direct treatment at those symptoms, through psychotherapy or environmental changes. Correspondingly, if physiological irregularities are the source for the disorder, treatment targeting the hippocampus, such as tDCS, becomes the logical route to take. Now, if the symptoms of stress-induced depression both cause and result from physiological changes, a multilateral approach—psychotherapy together with brain stimulation— becomes extremely promising in treating the root causes of depression via both behavioral and biological approaches.

Brunoni et al. (2018) adopted a pathophysiological theory that puts an abnormality in the immune system in a causal relationship with MDD to address the possibility of treating the disorder with tDCS. Researchers have proposed that a depression-leading phenotype stands in relation to the activation of the immune system both centrally and peripherally (i.e., of both the neuroimmune system and the immune structures located outside of the brain barriers; Dantzer et al., 2008; Leonard & Maes, 2012; Raison et al., 2006). A significant presence of pro-inflammatory cytokines—a group of different substances secreted by immune system cells—may drive depressive episodes (DellaGioia & Hannestad, 2010). Brunoni and colleagues (2018) recorded the effects of tDCS on participants with unipolar depression by analyzing how plasma levels of several cytokines changed with treatment. They found that cytokine plasma levels indeed predicted early depression improvement for tDCS when compared to Escitalopram, an antidepressant drug (Brunoni et al., 2018). These findings demonstrate that biomarkers, such as cytokine plasma levels, have the potential of becoming a reliable measuring tool to evaluate tDCS as a depression treatment.

Current Treatment Strategies and its Limitations

The primary method to treat severe depression is pharmacotherapy (i.e., with prescription drugs). As soon as the antidepressant effects of monoamines, serotonin, noradrenaline, and melatonin were discovered, the search for and mass production of drugs that manipulate their concentration and action increased markedly (Otte et al., 2016). The common mechanism of action of pharmacological antidepressant agents is preventing the presynaptic neuron from reabsorbing its released

neurotransmitter (i.e., blocking reuptake). By doing so, the substance has its action prolonged, which presumably leads to an increase in its antidepressant effects. Selective serotonin reuptake inhibitors (SSRIs) and noradrenaline reuptake inhibitors (NRIs) are two common agents that act in such a way (El-Hage et al., 2013). The goal of treatment is to achieve a 'remission' state in which symptoms are only trivial or secondary; however, research has shown the efficacy of these treatment options to be somewhat limited, with remission states observed for roughly 50-60% of cases treated with pharmacotherapy (El-Hagel et al., 2013). Another limitation of these findings is that the results rely on self-reports and could thus have their reliability and validity threatened by subjectivity. Among studies that have searched for possible biomarkers for depression, they have yet to find biomarkers capable of reliably measuring the biological effects of antidepressant drugs.

Psychotherapy is also commonly applied as a method to treat depression, yet remission rates remain similar to the ones of pharmacological treatments (Otte et al., 2016). Vagal nerve stimulation (VNS), electroconvulsive therapy (ETC), and repetitive transcranial magnetic stimulation (rTMS) are treatment options in cases where pharmacological or psychotherapy interventions are ineffective. Even though there is empirical evidence to support antidepressant results of those strategies, they all carry core limitations. VNS requires surgery and often only leads to minor antidepressant effects (Nitsche et al., 2009). In turn, ETC is a somewhat invasive procedure that involves anesthesia and the induction of a convulsive seizure. Moreover, ETC has been strongly associated with the induction of cognitive side effects (Nitsche et al., 2009). Lastly, rTMS does not yet have a proven mechanism of action, and its therapeutic effects have a short-lasting nature (Nitsche et al., 2009). tDCS could address these concerns by virtue of its potentially high efficacy, non-invasive nature, and minimal side effects.

Research on tDCS as a Treatment Alternative

The tDCS intervention has shown strong antidepressant efficacy for otherwise treatment-resistant patients. Resistance to treatment takes place when the body develops immunity to a drug or a certain dosage of it or in cases where the organism was never affected by it. Martin et al. (2018) observed how medication-resistant patients (i.e., not showing any improvement to at least two drugs) diagnosed with major depressive disorder (MDD) responded to tDCS and Cognitive Emotional Training (CET). Using a bilateral approach to treatment—psychotherapeutic and physiological—tDCS and CET were received simultaneously. Stimulation was applied at 2mA strength with the anode placed over the DLPFC and cathode over the right arm. CET sessions were structured using the Emotional Faces Memory Task in which participants were asked to recognize different emotions they had previously seen portrayed on different faces.

Participants' mood enhanced significantly when compared to baseline; forty-one percent met criteria for treatment effectiveness (i.e., antidepressant effects) and ameliorations in depression scores, self-rated psychological symptoms, rumination levels, as well as in quality of life reports were observed. The beneficial effects of tDCS seen in this study are notable because of their impact on individuals who previously showed resistance to standard treatments. These findings suggest a particular promise for tDCS in cases of depression that present the greatest challenge to treat. Regarding treatment safety, several studies have reported minimal side effects related to tDCS. Those usually include mild to moderate tingling or burning heat sensation during the session. Additionally, some study participants experience minor redness of the skin where electrodes were positioned (Alonzo et al., 2019; Nitsche et al., 2009).

Although several studies, such as the one conducted by Martin et al. (2018), demonstrate successful antidepressant effectiveness of tDCS, the literature is mixed. This was illustrated by Loo et al. (2018) among others through an investigation of the effects of tDCS on unipolar and bipolar depression. From the randomly selected participants diagnosed with either unipolar or bipolar depression, an equal number of individuals with each diagnosis was randomly assigned to one of two conditions. The first group received sham (inactive) stimulation and served as a control group, and the second was subjected to tDCS; participants did not know whether they were receiving actual treatment or a placebo. tDCS was applied at 2.5 mA with the cathode positioned over the right frontal area and the anode over the left DLPFC.

The study did not provide empirical evidence supporting the hypothesis that tDCS has therapeutic effects against depression. It was instead found that participant mood significantly improved during treatment for both unipolar and bipolar depression, regardless of treatment condition. In fact, among participants with unipolar depression, mood enhancements were higher for those in the sham group than for those who received the active tDCS intervention. It remains unclear whether all participants could have experienced mood enhancements unrelated to treatment and if, in such case, tDCS could have exerted anti-therapeutic effects. This question remains unanswered, but one possible explanation was that there was a placebo effect through which participants believed they were being treated could be the cause for mood improvements, entirely unrelated to stimulation. This could be the case if pre-treatment expectations—possible for both the placebo and the treatment group—provoked the release of endorphins. Research points towards a major relationship between this polypeptide and mood disorders; however, this has yet to receive strong empirical support (Ghadirian et al., 1988). An alternative explanation for the study's unexpected results is that the supposedly inactive sham was actually minimally active, with a 0.0034 mA current discharge at certain periods of the sham stimulation positively influencing mood. It could even be the case that tDCS was counter-therapeutic for the individuals with unipolar depression, possibly because the 2.5mA stimulation was too strong. However, more evidence is needed to draw any clear conclusions.

Bulubas et al. (2019) investigated how tDCS' antidepressant effects were associated with prefrontal gray matter volumes. In this study, the therapeutic properties of tDCS were examined in comparison to those of the selective serotonin reuptake inhibitor (SSRI) Escitalopram. In addition to showing empirical evidence for the effectiveness of tDCS, Bulubas et al. (2019) were pioneers in establishing that MRI scans could be used to determine which patient groups would benefit from a tDCS antidepressant intervention by revealing the cortical-anatomical characteristics capable of predicting the success of stimulation. Participants were randomly divided into Escitalopram, tDCS, or placebo groups, and required to abstain from any other antidepressant therapy. The anode was placed over the left dorsolateral prefrontal cortex (DLPFC) and the cathode over the right DLPFC, and stimulation was applied at 2mA. For the sham group, the current was turned off without the participant's awareness. Results showed no significant differences in antidepressant effects between Escitalopram and placebo. tDCS, on the other hand, was found to produce significant antidepressant effects for individuals with MDD, in comparison to placebo and the SSRI. Researchers investigated MRI parameters linked to antidepressant improvements of tDCS at the prefrontal level and found no significant gray matter differences between the left and the right regions of the anterior cingulate cortex (ACC), observed through MRI scans upon tDCS application. For the prefrontal cortex, larger gray matter volumes in the left dorsal side were associated with tDCS depression improvements compared to sham, while stimulation to the right PFC did not lead to anti-depressing results (Bulubas et al., 2019). In conclusion, these findings suggest that the left portion of the PFC is most likely to benefit from the antidepressant effects of tDCS.

As previously mentioned, tDCS stands out compared to other existing electrical stimulation techniques for its less invasive, safer, and user-friendly nature. Alonzo et al. (2019) conducted a study that illustrates these features of tDCS. Researchers chose a unique approach in evaluating the potential of tDCS to treat depression by carrying out the study in participants' homes, instead of a laboratory, with treatment self-administered by participants, rather than by staff. The goal here was to investigate the feasibility, effectiveness, and tolerability of home-based tDCS as an antidepressant. Results provide initial evidence that tDCS can indeed be applied at home with remote supervision only. Stimulation was applied using a pre-programmed device specifically designed for home-based application, and accompanied by remote professional supervision. The anode was positioned over the left DLPFC and the cathode over the right temporo-orbital area. Participants reported their mood status after every session, and the results showed a clinically significant mood enhancement of 45%. Depressive response and remission rates, defined as no recurrence for one month upon therapy conclusion, also confirmed a significant positive effect of tDCS in reducing depressive symptoms. The demonstration of the feasibility and success of home-based remotely guided tDCS as a depression treatment. Alonzo et al. (2019)

highlighted the flexibility and convenience of home-administered therapy directly contributed to high rates of session completion and dedication to the therapeutic process. Significant results are consistent with those of several other tDCS studies, such as in Brunoni et al. (2016), and serve to verify the quality of patient-administered tDCS application instructed and guided by experts.

Concerning potential side effects of tDCS, Ironside et al. (2016) found that frontal cortex tDCS can reduce vigilance to threat. Two groups of healthy participants received 2mA tDCS targeting different brain regions. the first had both the anode and cathode placed on the left and right DLPFC, respectively (bipolar balanced montage); the second had the anode attached to the left DLPFC and the cathode to the supraorbital ridge (bipolar unbalanced montage); a third group received sham treatment. Vigilance to threat was assessed based on a task in which participants were shown paired images (faces) and occasionally presented with a probe (two dots in two different orientations) on a computer screen. They were asked to identify, as quickly as possible, when a probe appeared behind either of the paired images. Ironside et al. (2016) found that participants in the bipolar balanced montage group showed a significant reduction in vigilance to threatening stimuli when compared to sham, while those receiving bipolar unbalanced stimulation did not. This could possibly be indicative that vigilance decline is a side effect exclusive to one type of electrode positioning but not others, which can be a key aspect to consider when deciding where exactly to apply tDCS in order to avoid this side effect. On the other hand, a reduction in vigilance to threat can be considered anti-depressant and, thus, regarded as a beneficial effect of tDCS. Empirical findings support hypersensitivity to threatening stimuli to be strongly correlated with depression (Sylvester et al., 2016; Mathews et al., 1996), which explains the therapeutic outcomes following vigilance diminishment. All participants recruited by Ironside et al. (2016) were healthy and thus did not suffer from the bias in vigilance to threat experienced by those with depression. In conclusion, a reduction in vigilance is likely to have normalizing and, consequently, antidepressant effects on those with depression, while posing more negative and hindering outcomes to healthy individuals who are not hypervigilant at baseline.

Altogether, these studies highlight some important aspects of tDCS as an intervention to treat major depression. This technique can lead to mood improvements that are both statistically and clinically significant, and possibly long-lasting. Moreover, research has demonstrated that tDCS can be user-friendly, effective in treatment-resistant cases, and linked to minor side-effects.

Discussion of Research Findings and the tDCS-MDD Future

The tDCS technique has shown potential in improving mood and decreasing symptoms of depression. However, based on the growing body of findings exploring the benefits and costs of tDCS, it is important to also acknowledge the need for a cautious approach and more research. The more than 50 experimental and 20 clinical studies supporting the antidepressant effects of tDCS are still challenged by contrary research findings. This being the case, several researchers have begun to explore and develop more valid and reliable methods to track the results of this stimulation technique.

Brunoni et al. (2018) found that cytokine plasma levels predicted early depression amelioration after tDCS. This study revealed that biomarkers, here cytokine plasma levels, have the potential of becoming a reliable tool to assess tDCS' antidepressant strength and its therapeutic results. This knowledge is a promising first step in efforts of evidencing the consistency of tDCS as an antidepressant agent as it objectively measures MDD improvements. MRI scans have also shown promise as a successful measurement technique for tDCS experiments and could help in the search for depression biomarkers (e.g., Bulubas et. al, 2019).

The tDCS has been incredibly promising in the search for the neurological basis of depression. It has, for example, demonstrated anew that abnormalities in cortical volumes and rates of activity are associated with the development and persistence of depression (Yang et al. 2015; Bulubas et al., 2019). This transcranial stimulation technique also generated empirical findings on the tight relationship between hemispherical activation imbalances and MDD (Brennan et al., 2017; Brunoni et al., 2016). The tDCS is unique in its capability of investigating possible causes of depressive disorders while exerting

antidepressant functions: Brunoni et al. (2018) speculated that abnormalities in the immune system could be a cause for depression. By applying tDCS and measuring how the immune system responded as depression improved clinically, they were able to generate empirical evidence to confirm that the immune system is indeed associated with depression. This example illustrates how tDCS acts simultaneously as an antidepressant and a causality-detecting agent.

There are many questions still to be answered regarding therapeutic neural stimulation. Unlike a majority of studies, Bulubas et al. (2019) found that neither the right PFC nor any area of the ACC were linked to antidepressant effects of stimulation, while the left PFC region was. Research should further explore the PFC domain as a potential neurobiological predictor for the benefits of tDCS as a tool to treat depression. In the study by Loo et al. (2018), the sham group—subjected to a very low current—benefited more from tDCS as an antidepressant agent than those in the treatment group. The possibility that tDCS was anti-therapeutic, or had no effect at all, remains. However, considering the otherwise positive empirical evidence generated in several studies, it seems probable that differences in methodology and, in particular, the magnitude of the stimulation, may have contributed to the outcomes observed by Loo et al. (2018). Other similar empirical studies have reported successful results in mood enhancement with lower stimulation intensities (e.g., Chew et al., 2015; Nitsche et al., 2009). Taken together, these findings suggest more empirical findings are needed to better understand the optimal dosage and stimulus intensity for the therapeutic effects of tDCS. Even then, it is possible that there will never be one intensity adequate for all and, if this is the case, methods on how to assess and tailor the appropriate frequency, intensity and duration of stimulation on individual levels will have to be developed.

Even though several questions remain in the application of tDCS as a therapeutic technique, its remarkable antidepressant power highlights the need for continual persistence in its exploration. This is evidenced in Martin et al 's. (2018) demonstration of how tDCS can be applied in combination with another therapeutic approach, CET. This study generated empirical evidence for tDCS as a successful antidepressant in otherwise treatment-resistant patients. The study by Alonzo et al. (2019) shows the potential for applying tDCS in a convenient home-based setting with fading remote professional intervention only. The tDCS has the potential of reducing burdens of strong drug side effects, hours dedicated to therapy, and even periodic visits to the hospital for stimulation sessions. Altogether, tDCS is very promising in the treatment of depression with the potential to improve the way we care for the most prevalent psychiatric disease in the world. Medical advances in this domain have the potential to significantly improve the lives of over 300 million people worldwide.

Besides being an effective antidepressant, the capability for tDCS to solve biological questions around depression could diversify and improve the clinical diagnosis of MDD. Currently, the DSM-5 criteria that classify a major depressive disorder are purely based on its symptoms; those include, but are not limited to, the expression of an irritable or depressed mood, difficulties concentrating, reduction in pleasure or interests, and feelings of fatigue. The subjective and imprecise nature of those criteria make it difficult to establish an objective diagnosis, often resulting in cases of depression that go undetected and undiagnosed. According to Kupfer et al. (2014), one possible cause of diagnostic issues is the close relationship between depression and anxiety; symptoms for both disorders can be very similar and often take place simultaneously, making it hard to determine confidently when MDD is exclusively present. Given the extremely high prevalence of depression worldwide and the severity of the disorder and its consequences, further research is needed to improve diagnosis. As tDCS aids in the discovery of neurobiological origins of MDD, a change in diagnosis criteria towards a more objective 'brain-based' approach becomes conceivable. Effectively updating the DSM-5 criteria for depression to encompass neurobiological findings relies on more empirical findings regarding the concrete physiological basis of MDD. This would make diagnosis easier, more specific and potentially more accurate. A more palpable and testable definition could also induce destigmatization of this disease by increasing awareness. As a result, such an effort could increase the number of patients who seek a diagnosis and professional care while also offering a viable new treatment for those who do.

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Andrea C. Ng, BA
University of California, Los Angeles

Andrea Chi Ern Ng is an international student from Malaysia, and her interest in clinical psychology began when she attended Pasadena City College before transferring to UCLA. In Spring 2019, Andrea graduated UCLA (Psychology major/Asian American Studies minor) and will be pursuing a Clinical Psychology PhD program at the University of Hawaii, at Manoa this Fall. Her research interests lie in examining how evidence-based treatments are implemented across different public mental health contexts (community clinics, schools, university clinics, state-level, etc.), specifically, how they can be adapted to better treat communities of unique backgrounds in different cultures. Personal interests include cooking and exploring LA (soon Hawaii) for new foods!

Was there a particular experience that sparked your research interests?

Growing up in Malaysia, mental health is often ridiculed or joked about. For example, newspaper headlines covering suicide would always refer to the mentally ill as "weak" or "cowardly." Moving to the US, I was excited to be in an environment where mental health is more accepted. When I was at community college, I pursued an opportunity to work as a counselor at New York University's Child Study Center, a high-intensity therapeutic camp for children with ADHD and other behavioral disorders. Actively applying cognitive-behavioral skills every day, I saw how complex therapy could become when factors such as comorbidity and lack of engagement were introduced. Furthermore, I found myself wondering how the kids at camp would cope when they returned to school systems that lacked appropriate accommodations for those with severe ADHD. Although I think my research interest slowly developed over time, I believe this experience was what first sparked my strong desire to see how research efforts could assist in the dissemination and implementation of evidence-based practices in community settings.

Who has been the most influential person in your life?

My parents have always been my earliest role models, and even though we each have very different careers (aspirations, in my case), they both taught me skills that I take with me every day. My mother was always working and showed me that even though you have to fight tooth and nail, women can succeed in a corporate workplace run mainly by men, and that women do not need to sacrifice their family in order to advance their career. While I derive my strong work ethic from my mom, my dad has taught me to always have a big heart and be compassionate to others. Every time I think I've learned all there is to know, they show me that that will never happen.

What is your greatest accomplishment?

Although it is not quantifiable, I believe my greatest accomplishment lies in the friendships and connections that I've made during my time in Los Angeles. When I first moved here at 17 years old, I was terrified because I knew no one and I did not know any other Malaysian that went to community college. But I pushed myself to always step out of my comfort zone, adapt and always be willing to learn. Because I pushed myself, I've been able to form genuine friendships with people from all walks of life, and they always teach me something new.

Where do you see yourself in 10 years?

Honestly, I don't really know! 10 years ago I didn't know I would have laughed at and dreaded the idea of moving oceans away from my family to a land I only saw on TV, and even a year ago, I did not imagine that I would be going to graduate school in Hawaii! Ideally, I would still be a foodie, happy and satisfied with where I am in life.

Life Happens: Relationship Between Provider Response to Emergent Life Events and Client Attendance

Andrea C. Ng[1], Karen Guan[1] & Bruce F. Chorpita[1]

Despite significant progress made in developing evidence-based treatments (EBTs) to treat youth mental health problems, more than 50% of youth and families still drop out of treatment prematurely. Another contributing factor that is not addressed by treatment are emergent life events (ELEs) which are sudden unexpected stressors in a client's life, like expulsion from school or parent separation. When faced with an ELE during treatment sessions, therapy providers are often not specifically trained on how to respond and may therefore improvise. Previous research identified three possible provider responses to ELEs, in order of frequency: 1) Respond with non-EBT content either related or unrelated to the ELE (e.g., supportive statements, information gathering); 2) Incorporate EBT content unrelated to ELE; 3) Incorporate EBT content related to ELE (i.e., use the ELE as a "teaching moment" for EBT skills) (Guan et al., 2018). Using data from the Child STEPs California trial (Chorpita et al., 2017), this study seeks to expand on previous findings by examining how provider responses to ELEs may influence client engagement, using short and long-term attendance in therapy as a measure. Two-level regression models (clients nested within providers) reveal that provider response was not a significant predictor of short or long-term attendance. This study had limited power due to a small sample size, so an effect may be found with a larger sample. Future papers should further examine provider responses to ELEs in relation to other forms of engagement such as therapeutic alliance and homework.

Mental health continues to be an issue affecting youth, with one in five children suffering from mental health problems (O'Connell, Boat, & Warner, 2009). Despite this, only half of youth in need of mental health services actually receive treatment (Merikangas et al., 2010). In response to the demand for services, there was an increase in the development of evidence-based treatments (EBTs), which are treatments, typically in the form of therapy, that incorporate therapeutic techniques approved by randomized-controlled trials. Despite these developments, studies have shown that more than 50% of clients and their families drop out of therapy prematurely (Nock & Ferriter, 2005; Pellerin, Costa, Weems, & Dalton, 2010). Thus, it is important to further examine factors that influence client engagement.

A potential contributing factor may be because many EBTs often fail to account for life stressors that may make it different for clients to continue treatment. These stressors are known as emergent life events (ELEs) and have been reported by providers as a major obstacle when delivering EBTs (Reding et al., 2016). Currently, studies have not, however, specifically examined how therapy provider responses to these events may affect client engagement in therapy.

To elaborate, even though EBTs have been shown to be successful in randomized control research trials, community mental health providers have reported that it can be difficult to implement them in community settings, as their clients' cases are often so complex that carefully-designed treatments may not fully

1University of California, Los Angeles

Correspondence concerning this article should be addressed to Andrea Ng. Email: andreance@ucla.edu

address them (Addis and Krasnow, 2000). In response to this issue, researchers have created modular treatments that are more flexible than standard EBTs, in that they include decision-making guidelines meant to address client complexity. For instance, the Modular Approach to Treatment for Children with Anxiety, Depression, Trauma, or Conduct Problems [MATCH] (Chorpita & Weisz, 2009) can be used to treat multiple problem areas and includes five decision flowcharts that can be used to flexibly address issues such as comorbidity, the client's developmental level, or experiences of trauma (Chorpita & Weisz, 2009). Randomized controlled trials testing MATCH showed that youth treated with MATCH improved significantly faster when compared with youth treated with standard EBTs (Weisz et al., 2012; Chorpita et al., 2017).

Engagement

Despite advancement in addressing client complexity, modular protocols for therapy rarely explicitly address other threats to treatment effectiveness like client engagement. The definition of engagement varies throughout the literature. Very broadly, it is a process that starts with parents or other adults recognizing that a child is in need of mental health services and ends with the child receiving those services (McKay & Bannon, 2004). Research on the wide range of engagement issues such as clients frequently arriving late to therapy, lack of motivation during session, or failing to complete assigned homework, has shown that poor engagement interrupts effective treatment and is associated with worse outcomes (Haine-Schlagel & Walsh, 2015).

A common measure of engagement outcomes is client attendance (Becker et al., 2018). Attendance is often measured using the number of times clients are present at scheduled appointment times with providers, which can range from meeting in-person at a clinic or school, to having appointments through the phone. Attendance has also been shown to predict treatment outcomes. Specifically, higher attendance was correlated with positive treatment outcomes (Smith, Glass & Miller, 1980; Weisz & Weiss, 1993).

Emergent Life Events

ELEs are an issue that could influence client engagement. Elaborating on the definition above, ELEs are sudden, unexpected stressors that occur in a client's life, such as suspension or expulsion from school, eviction from home or death in the family (Chorpita, Korathu-Larson, Knowles, & Guan, 2014). One of the biggest concerns surrounding ELEs is its effect on the implementation of EBTs as well as client outcomes. Because providers are often not trained on how to use skills taught in EBTs to help clients cope with ELEs, they often report being thrown "off-track" from their planned treatment when presented with an ELE in session (Guan et al., 2017). Researchers found that ELEs are predictors of lower provider adherence to EBT modules like MATCH (Guan et al., 2017). Furthermore, a study using observational coding to explore community provider responses found that, when faced with an ELE, providers responded in a variety of ways: 1) Using non-EBT responses (e.g., provide empathy, gather information about the ELE, etc.) [100%]; 2) Incorporating EBT content unrelated to the ELE [55%]; 3) Incorporating EBT content related to the ELE [40%] (Guan et al., 2018b).

When providers relate EBT content to the ELE, they are using the ELE as a "teaching moment" for clients to learn skills from MATCH. For example, a provider might teach the client relaxation after s/he was suspended due to a fight at school (Guan et al., 2018b). Although providing emotional support and empathy may actually help build provider-client rapport, it may be more beneficial if providers were also able to provide clients certain skills to cope with the event. According to MATCH experts, this is a feasible option. Experts identified roughly 64% of ELEs as fully addressable through a "teaching moment" for a MATCH skill and 96% of ELEs as partially addressable (Guan, Boustani, & Chorpita, 2018). Yet, the actual rate of provider "teaching moment" responses was much lower at 40%.

Studies examining how provider responses to ELEs can impact treatment outcomes found a correlation with a 14% to 20% declining rate of clinical progress when providers continued sessions with an ELE without any elements of EBT (Guan, Park, & Chorpita, 2019). Furthermore, ELEs are also associated with negative effects beyond the session in which they were reported. Compared to when an ELE did not occur, the likelihood that providers would continue with the original treatment plan in either the same or next session following the occurrence of an

ELE lowered by 2.94-fold (Guan, Park & Chorpita, 2019). This may be because ELEs, such as getting expelled from school, or parents going through a divorce, usually do not leave the youth's life after one or two days. Thus, ELEs may continue to delay planned treatment, potentially threatening clinical progress.

The Present Study

ELEs are still an understudied problem in literature. Yet, it has been demonstrated that they can affect clinical outcomes if not addressed effectively (Guan, Park, & Chorpita, 2019). Thus far, there have not been studies that examined how ELEs and client engagement in therapy relate to one another. Therefore, this study will examine how provider responses to ELEs may affect engagement, using attendance as a measure. Provider response was broken down into three types: 1) EBT content that is related to the ELE ("teaching moment"); 2) EBT content that is not related to the ELE; 3) no EBT content (e.g., gathering information about the ELE, empathetic listening). Short-term attendance was defined as the youth's attendance to the session immediately following when the ELE was reported, while long-term attendance was defined by whether treatment was completed as planned or terminated early.

We hypothesized that: 1) Provider responses that relate the ELE to MATCH elements ("teaching moments") would positively correlate with short-term and long-term attendance because clients may feel that they benefited more from therapy when they were taught concrete skills that would help them cope with the ELE; 2) Responses using MATCH elements but do not relate to the ELE would negatively correlate with both short- and long-term attendance, as the client would feel that the skills they were taught were not applicable to their life; 3) Lastly, responses that do not incorporate any MATCH content into the session would positively correlate with short-term attendance as empathetic listening would build client-provider rapport, encouraging attendance. However, we also believed that excluding any MATCH content would negatively correlate with long-term attendance because although clients received a space to discuss their feelings short-term, they were not provided with helpful skills that they could use to deal with the ELE.

Method

Participants

This study selected participants from the modular EBT condition (MATCH) of the Child STEPs California study, a randomized clinical trial conducted at three large community mental health agencies in urban California (Chorpita et al., 2017). Providers in this study did not receive any a priori training on how to respond to ELEs if they were reported in a session. If an ELE was reported, study consultants made recommendations during the subsequent consultation session on how to proceed with future treatment sessions. Details on the inclusion and exclusion criteria for the randomized control trial as well as the flow of youth into the study according to CONSORT guidelines are reported in the original paper (Chorpita et al., 2017). All study procedures were approved by the [Institution] Institutional Review Board and Institutional Review Boards of participating service agencies that requested independent reviews.

Youth participants. There were 35 clients (51% male; 49% female) in this study between the ages of 5 and 16 years (M = 10.20), out of which only one was born outside the United States. Among the sample of clients, their reported race/ethnicity was 86% Latino/Hispanic, 9% Black/African American, and 6% Mixed Race. Youth's primary problem areas were 37% disruptive behavior, 37% depression, 23% anxiety and 3% trauma.

Caregiver participants. The 35 caregivers included in this study were 97% female and ranged from 26 to 63 years (M = 35.56). Their reported race/ethnicity was 91% Latino/Hispanic and 9% Black/African American. Of the 35 caregivers, 63% were born outside of the United States and 80% had an annual household income of $0 - $19,000. Thirty-four percent reported that the highest degree of education they completed was below a high school degree, 17% achieved a high school diploma or GED, 31% reported at least 1 year of college, 9% received a college degree and 3% held a professional or graduate degree. Six percent did not report the highest degree received.

Provider participants. Eighteen providers were included in this study, of which 94% were female, with a mean age

of 32.39 years (range 25-42 years). Regarding education, 94% of providers listed their highest degree completed as either a master's degree in Arts, Science, or Social Work. Data from the remaining 6% were missing. Their reported race/ethnicity was 39% Spanish/Hispanic/Latino, 39% White, 17% Mixed Race/Ethnicity, and 6% Asian.

Procedures

A subset of sessions from the Child STEPs California trial was analyzed. In order to be included in the current study, sessions were required to meet the following criteria: 1) client was from the MATCH condition; and 2) client identified at least one ELE during the session, according to observational coding of a large sample of 274 sessions from a previous study (Guan et al., 2019). Of the 274 sessions coded, 71 sessions were coded as having at least one ELE. Throughout these 71 sessions, a total of 79 ELEs were reported; therefore, 16 out of 79 ELEs were one of multiple ELEs reported in a single session.

Measures

Provider Responses to ELE

Emergent Life Events Coding System – Revised. ELEs were identified using a revised version of the Emergent Life Events Coding System (ELECS) (Guan et al., 2017). Provider responses were originally coded into four broad categories (See Table A1). In the present study, provider responses were consolidated into three categories: 1) any unstructured activity, regardless if it was related or unrelated to the ELE, 2) structured activity related to the ELE, and 3) structured activity unrelated to the ELE. The two types of unstructured responses were combined in order to increase power and because previous research demonstrated that a provider response of only unstructured activity, related or unrelated to the ELE, was associated with slower clinical progress (Guan, Park & Chorpita, 2019).

Short-term Attendance

Short-term attendance was defined as the client's attendance of the session immediately following a session in which an ELE was reported. Short-term attendance with regard to the next session was categorized as: 1) Session held as planned; 2) No show or session cancelled by family; 3) Missed attempt, provider-initiated or other (e.g., client was participating in after-school activity or had exams, session cancelled by provider, etc.). See Appendix B for a description of measures used.

Long-term Attendance

To assess long-term attendance, we used the CONSORT Status Instrument to report on clients' treatment completion outcome. Codes assigned at the final treatment session included: 1) Routine termination (i.e., termination of treatment as mutually agreed upon by the family and the provider); 2) Withdraw/lost (i.e., family decided to withdraw from treatment without agreement of the provider or the provider no longer being able to contact the family); 3) Provider reason/other (i.e., termination for reasons outside of the family's control either pertaining to the provider, such as provider leaving the clinic, or other reasons such as the family moving to another city) (Chorpita et al., 2017). See Appendix B for a description of this measure.

Analyses

Descriptive statistics. All descriptive statistics were performed with SPSS. It was used to calculate frequencies and percentages of each of the three variables of provider responses to ELEs, next-session attendance, and treatment completion (Table 1).

Short-term attendance analyses. Analyses were conducted in a software called Hierarchical Linear Model (HLM) 7 (Raudenbush, Bryk, Cheong, & Congdon, 2011). The data were structured in three levels, where the ELEs (n = 79) were nested within clients (n = 35) nested within providers (n = 18). To examine the relationship between provider response to ELE and short-term attendance, we first ran an unconditional model to see if all three levels were necessary to maintain in the analysis. Provider-level ICC was significant and above .01. Thus, the final model was two-level (ELEs within providers), with provider response (ELE-level) as a predictor of next-session attendance (ELE-level). The initial model included random intercepts and Level 1 (ELE-level) predictor slopes at the provider level; variance components with $p > .500$ were subsequently removed to achieve a more parsimoniou-

structure.

Table 1

Frequencies of Provider Response, Next Session Attendance and Treatment Completion

Variable	Frequency [95% CI]
Provider Response to ELE	
Unstructured activity related to ELE	100% [95%, 100%]
Unstructured activity unrelated to ELE	66% [54%, 76%]
Structured activity unrelated to ELE	54% [43%, 66%]
Structured activity related to ELE	38% [28%, 50%]
*Mutually Exclusive Provider Response to ELE (n = 79 ELEs)	
Structured activity related to ELE	38% [27%, 49%]
Structured activity unrelated to ELE	35% [25%, 46%]
Unstructured activity only	27% [18%, 38%]
Next Session Attendance (n = 79 sessions)	
Session held	73% [62%, 82%]
No-show/Cancelled by family	14% [8%, 23%]
Missed attempt/Cancelled by provider/Other	9% [4%, 17%]
Missing data	4% [1%, 11%]
Treatment Completion (n = 35 clients)	
Routine termination	43% [27%, 59%]
Lost to provider/Family withdrew	23% [11%, 39%]
Provider issue/Other	34% [20%, 51%]

* Used for analysis

Long-term attendance analyses. Analyses were conducted in HLM 7. Because treatment completion was a client-level outcome, provider responses were aggregated to the client level and calculated as the proportion of ELEs per client with a specific provider response. An unconditional model was run to see if both client and provider levels were necessary. Provider-level ICC was significant and above .01; thus, the final model was two-level, with clients (n = 35) nested within providers (n = 18). To examine the relationship between provider response and treatment completion, we ran two different analyses. First, we investigated the percentage of ELEs per client with provider response of unstructured activity only (client-level) as a predictor of treatment completion (client-level). Second, we investigated the percentage of ELEs per client with provider response of a non-teaching moment (unstructured activity, structured activity unrelated to ELE) as a predictor of treatment completion (client-level). The initial models included random intercepts and Level 1 predictor slopes at both the client and provider levels; variance components with p > .500 were subsequently removed to achieve a more parsimonious structure.

Results

Short-term Attendance

The final model for provider responses to ELE as a predictor of clients' short-term attendance included random intercepts and ELE-level predictor slopes at the provider level. Results of the final two-level hierarchical linear model revealed that provider response to ELE (unstructured activity only, structured activity related to the ELE, structured activity unrelated to the ELE) was not a significant predictor of clients' next-session attendance (session held; no-show or cancellation by family; missed attempt, cancellation by provider, or other). Specifically, the odds of a missed attempt, cancellation by the provider, or other cancellation in the next session as compared with the session being held were not significantly different when providers responded to an ELE with structured activity unrelated to the ELE as compared with structured activity related to the ELE (OR = 2.92, p = .403); the odds of a missed attempt, cancellation by the provider, or other cancellation in the next session compared to the session being held were not significantly different when providers responded to an ELE with unstructured activity only as compared with structured activity related to the ELE (OR = 0.61, p = .771); the odds of a no-show or cancellation by the family in the next session compared to the session being held were not significantly different when providers responded to an ELE with structured activity unrelated to the ELE as compared with structured activity related to the ELE (OR = 2.46, p = .447); and the odds of a no-show or cancellation by the family in the next session compared to the session being held were not significantly different when providers responded to an ELE with unstructured activity only as compared with structured activity related to the ELE (OR = 1.04, p = .974). To maximize power, analyses were also run using a binary provider response to ELE variable (unstructured activity only; structured activity related or unrelated to ELE) as well as a binary short-term attendance variable

(no-showed or cancelled by family; session held, missed attempt, cancelled by provider, or other). The pattern of results was the same; thus, the most thorough results were reported. Results are presented in Table 2.

Long-term Attendance

Provider response: unstructured activity only. The final model for percentage of ELEs per client with provider response of unstructured activity only as a predictor of long-term attendance included random intercepts only at the provider-level. Results of the final two-level hierarchical linear model revealed that the proportion of ELEs per client with a provider response of unstructured activity only was not a significant predictor of client's treatment completion status (routine termination; lost to provider or family withdrawal; provider issue or other reason). Specifically, the odds of a termination due to provider or other issue as compared with routine termination were not significantly different when providers responded with unstructured activity only as compared with structured activity related or unrelated to the ELE (OR = .997, p ~ .743); and the odds of a termination due to lost to provider or withdrew as compared with routine termination were not significantly different when providers responded with unstructured activity only as compared with structured activity related or unrelated to the ELE (OR = .998, p ~ .881). To maximize power, analyses were also run using a binary long-term attendance variable (i.e., routine termination; lost or withdrawn, provider issue, or other reason). The pattern of results was the same; thus, the most thorough results were reported. To maximize power, analyses were also run using a binary long-term attendance variable. The pattern of results was the same; thus, the most thorough results were reported. Results are presented in Table 3.

Provider response: non-teaching moment. The final model for percentage of ELEs per client with provider response of non-teaching moment (unstructured activity only and structured activity unrelated to ELE) as a predictor of long-term attendance included random intercepts only at the provider-level. Results of the final two-level hierarchical linear model revealed that proportion of ELEs per client with a provider response of non-teaching moment was not a significant predictor of treatment completion status (routine termination; lost to provider or family withdrawal; provider reason or other reason). Specifically, the odds of

Table 2

Provider Response to ELE as a Predictor of Next Session Attendance

Predictor	*b*	*SE*	*OR*	95% CI
For outcome of missed attempt, cancellation by provider, or other				
Intercept	-2.81	1.03	0.06	[0.00, 0.53]
Response: Structured activity unrelated to ELE [b]	1.07	1.25	2.92	[0.21, 40.92]
Response: Unstructured activity only [b]	-0.49	1.67	0.61	[0.02, 20.71]
For outcome of no show or cancelled by family [a]				
Intercept	-2.41	0.98	0.09	[0.01, 0.71]
Response: Structured activity unrelated to ELE [b]	0.90	1.16	2.46	[0.21, 28.27]
Response: Unstructured activity only [b]	0.04	1.17	1.04	[0.09, 12.40]

[a] Outcome as compared with reference group of session held

[b] Dummy codes with provider response of Structured activity related to ELE as a reference group

* p < .05

Table 3

Provider Response to ELE (Unstructured Activity Only) as a Predictor of Treatment Completic

Predictor	*b*	*SE*	*OR*	95% CI
For outcome of provider issue or other [a]				
Intercept	-0.124	0.496	0.883	[0.310, 2.517]
Response: Unstructured activity only [b]	-0.003	0.010	0.997	[0.976, 1.018]
For outcome of family withdrew or lost to provider [a]				
Intercept	-0.604	0.584	0.547	[0.159, 1.876]
Response: Unstructured activity only [b]	-0.002	0.012	0.998	[0.975, 1.022]

[a] Outcome as compared with reference group of routine termination

[b] Percentage of ELEs per client with this provider response

* p < .05

Table 4

Provider Response to ELE (Non-Teaching Moment Response) as a Predictor of Treatment Completion

Predictor	*b*	*SE*	*OR*	95% CI
For outcome of provider issue or other [a]				
Intercept	-1.170	0.927	0.311	[0.044, 2.194]
Response: Unstructured activity or structured activity unrelated to ELE [b]	0.014	0.012	1.014	[0.990, 1.038]
For outcome of family withdrew or lost to provider [a]				
Intercept	-0.322	0.773	0.725	[0.142, 3.699]
Response: Unstructured activity or structured activity unrelated to ELE [b]	-0.006	0.011	0.994	[0.972, 1.017]

[a] Outcome as compared with reference group of routine termination

[b] Percentage of ELEs per client with this provider response

* p < .05

a termination due to provider issue or other reason, as compared with routine termination were not significantly different when providers responded with a non-teaching moment as compared with structured activity related or unrelated to the ELE (OR = 1.013, p ~ .248); and the odds of a termination due to lost to provider or family withdrew as compared with routine termination were not significantly different when providers responded with a non-teaching moment as compared with structured activity related or unrelated to the ELE (OR = .994, p ~ .607). To maximize power, analyses were also run using a binary long-term attendance variable (routine termination; lost or withdrawn, provider issue, or other reason). The pattern of results was the same; thus, the most thorough results were reported. Results are presented in Table 4.

Discussion

Previous studies have shown that ELEs are negatively associated with provider adherence to MATCH, which may in turn reduce client progress in treatment (Guan, Park, & Chorpita, 2019; Guan et al., 2018). Because it is also possible that the way a provider responds to an ELE may change a client's willingness to attend therapy, this study therefore sought to examine the relationship between provider responses to ELEs and client short- and long-term attendance using a diverse sample of youth seeking services in community health settings. For short-term attendance, results indicated that provider responses to ELEs were not a significant predictor of clients' next-session attendance. For long-term attendance, provider responses to ELEs were also not a significant predictor of client treatment completion. These results ran counter to our hypotheses, which predicted an improvement in client attendance when providers responded to ELEs with a "teaching moment" as compared to other responses.

Due to the lack of statistical power, it is unclear if the results are truly nonsignificant. However, if they are truly nonsignificant, there is still a valuable lesson that can be taken away. Therapeutic relationship problems largely accounted for clients' decision to drop out of therapy, and positively predicted premature treatment termination (Garcia & Weisz, 2002). Thus, some community mental health providers may feel that using EBTs overemphasize on techniques rather than the individual, leading to poor therapeutic relationship and ultimately, premature termination (Addis, Wade & Hatgis, 1999; Garcia & Weisz, 2002). In the event of an ELE, it is possible that providers may be less inclined to use EBTs for fear of making the child feel unheard and thus damaging rapport. If true, the results of this study suggest that there is no difference and effect on client attendance regardless if their response includes EBT elements or if it is purely supportive. For providers who are worried about compromising their relationship, this may further encourage them to be more open to incorporating EBTs.

Relatedly, the therapeutic relationship between provider and client may itself be a potential explanation for the nonsignificant results as it may have had a stronger influence on client attendance than the provider's response to the ELE. Prior studies have shown that a better therapeutic relationship is associated with a more consistent increase in attendance compared to more effective therapeutic techniques (Duncan, Miller, Wampold, & Hubble, 2010). For the purposes of analyses, provider responses to ELE were divided into three mutually exclusive categories. However, it is important to note that providers almost universally utilized non-EBT responses - supportive statements and information gathering about the ELE - for all ELEs, regardless of how their overall response was categorized; 38% of providers also incorporated EBT responses related to the ELE (See Table 1). Thus, it is possible that these empathic and supportive responses to ELEs in and of themselves were enough for clients to "feel heard" and maintain rapport, which may have contributed to the nonsignificant findings of overall response (e.g., responding through teaching skills or not) as a predictor of client attendance. In other words, the quality of the therapeutic relationship may be more important than learning skills in encouraging clients to stay in treatment.

In addition, the construct of attendance in this study was complicated by several factors. First, this study relied on the assumption that client attendance would be informative about the client's attitude towards the session in which the ELE was reported. However, attendance may not be a direct measure of client satisfaction with a session as youth are often in treatment because they are required to by their school or caregivers. For example, some of the data in this study were collected in school-based mental

health clinics, where providers have the ability to pull students out of class, even if the youth does not wish to attend a session that day. On the other hand, youth may also be dependent on caregivers for transportation to treatment. Thus, a provider's response to a youth's ELE may not affect the youth's later therapy attendance.

When investigating engagement, attendance may be a more distal engagement outcome compared to other indicators such as homework completion and client comprehension of therapy processes. These latter engagement indicators may be better able to demonstrate decreased client engagement prior to the more extreme outcome of not attending a session or dropping out of treatment prematurely. Thus, it is equally important to take into account how well clients are engaging in session and absorbing the knowledge provided. Increased client comprehension of content covered in session has been found to be positively associated with client attendance and homework completion, which is also a significant predictor of positive clinical outcome (Park, et al., 2018; Kazantzis, Whittington, & Dattilio, 2010; Danko, Brown, Schoick, & Budd, 2015). Overall, these factors indicate that using attendance alone may not be the most appropriate indicator of clients' decreasing engagement (Park, et al., 2018).

Limitations

During the analyses for treatment completion, predictors were aggregated at the client level rather than ELE-level, resulting in a small sample size of 35 clients, giving the study limited power. Thus, it is unclear if results represent truly non-significant associations or if the findings were due to the limitations in the methodology used for this study. Furthermore, we were unable to look at differences in attendance if providers had been randomized to respond to ELEs in different ways, which would increase the level of confidence in results to claim a causal relationship.

Future studies

Future studies should consider using multiple measures to more comprehensively assess client engagement. For example, researchers could assess for clarity, specifically how well the client understands what was covered in session, as well as homework completion. Researchers could also take into account the severity (i.e., duration and intensity) of these ELEs in relation to provider responses and client engagement. Severity of ELEs may be a determining factor of how clients feel about a provider's response to their ELE. For example, if an ELE is less severe (i.e., failing an exam), clients may not feel a need to be taught a skill and may be content with just "being heard". If an ELE is more severe (i.e., client's parents are going through a divorce, resulting in client moving away from best friends), clients may seek more guidance in the form of skills. It is also possible that having a more moderate ELE may mean that the client is less distressed and thus may be able to better apply an EBT skill in their life. These relationships have yet to be explored.

In conclusion, the results of the present study show that provider response to ELEs are not significant predictors of client next-session attendance or treatment completion. However, this conclusion is not definitive and may have resulted from the study's methodology and its limitations. It is also important to note that, if the results are truly nonsignificant, the results could contain beneficial information that may encourage community mental health providers to incorporate EBTs into sessions. Further study investigating provider response to ELE would better inform training of mental health providers to address these events in a way that maximizes client outcomes and engagement.

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Appendix A

Emergent Life Events Coding System (Guan et al., 2017)

This observational coding system was used to identify ELEs, characteristics of the ELEs, and provider responses to the ELEs. Identification of ELEs and provider responses to ELEs had excellent interrater reliability (κ > .60 [substantial or above agreement; Landis & Koch, 1977]). Provider responses were coded into four broad categories. Refer to Table A1 for detailed descriptions of when codes were applied as well as examples.

ELECS – Provider Response to ELE

Code	Applied when
Unstructured activity related to the ELE	Provider gave one of 12 specific responses: 1. Supportive or empathic statements 2. Relating the ELE to past life experiences 3. Information gathering about the event 4. Information gathering about the subjective impact of the ELE on client 5. Informal advice giving 6. Informal problem solving 7. Psychoeducation related to the ELE 8. Informal reframing statement 9. Safety protocol required by the agency and not from MATCH 10. Provision of supportive resources outside of therapy 11. Provision of supportive resources by provider Other
Unstructured activity unrelated to ELE	Session activities that were not related to the ELE, or any structured protocol, lasted longer than 2 minutes e.g., Provider asks client about what they did at their friend's house
Structured activity related to ELE	Provider responded with a "teaching moment", in which they addressed the ELE 1. Used the module to demonstrate why MATCH may be helpful (e.g., psychoeducation) 2. Demonstrate a skill as a way of handling the ELE (e.g., problem solving) e.g., Provider might cover the MATCH skill of Quick Calming if a client reported getting into a fight at school
Structured activity unrelated to ELE	Provider covered a MATCH module or other structured skills without relating them to the ELE e.g., Provider continues to cover original Fear Ladder module after the client reports an ELE, without explaining how the Fear Ladder could address the ELE

Appendix B

Description of Attendance Measures

Short-term Attendance

MATCH Client Consultation Record. The MATCH Client Consultation Record is a checklist completed by study consultants during weekly semi-structured consultation meetings with providers to record if providers implemented MATCH in the most recent therapy session and to plan future treatment practices (Ward et al., 2013). In addition to the checklist, it also tracks the date of the most recent therapy session between the provider and the client. In the present study, we first referred to the MATCH Client Consultation Record to find when the next session with the client was held immediately following the report of an ELE.

No-Show or Cancellation Record. The No Show or Cancellation Record is a record completed by providers if clients missed their planned treatment sessions. Providers were asked to specify whether the session was missed due to a no-show, family-initiated cancellation, provider-initiated cancellation, missed attempt, or other reason. In the present study, the No Show or Cancellation Record was used determine if a planned session was missed immediately following the session in which an ELE was reported.

Long-term Attendance

Consolidated Standards for Research Trial (CONSORT) Status Instrument. The CONSORT Status Instrument recorded the nature of the client's termination from treatment as reported by each provider, according to criteria outlined by the CONSORT Workgroup (Campbell, Elbourne, Altman, & the CONSORT Group, 2004). The information was then confirmed by agreement of study personnel, including study consultants and the principal investigator.

Laura A. Pazos, BS

The University of Southern Mississippi

Laura graduated from The University of Southern Mississippi in 2019 with a Bachelor of Science in biology and a minor in psychology. In the fall, she will be attending graduate school to pursue a Master of Arts in psychology, with research interests mainly in social cognition. In her free time, she likes hanging out friends, playing with her dog, trying new recipes, and reading.

Contact: lap070@SHSU.edu

Was there a particular experience that sparked your research interests?

To complete my Honors curriculum, I was required to do a research-based thesis. Writing a thesis pushed me to join a research lab early, and my experience with that lab truly sparked a love for research I didn't know I had. Upon finishing my thesis, I realized that I wanted to continue researching, writing manuscripts, and pursuing academia!

Who has been the most influential person in your life?

My sister is honestly the most influential person in my life. As identical twins, we have felt pressured in the past to be super competitive with each other. However, she always uses this competition to better herself, which in turn makes me want to better myself. She faces challenges fearlessly and relentlessly, and she inspires me to work just as diligently and persistently towards my goals.

What is your greatest accomplishment?

While I don't feel I have a "greatest" accomplishment, one of my top three is the completion of my thesis. From the data collection to the manuscript writing, the process was not easy. However, once I saw the completed product, I finally realized all the time, energy, and copious amounts of data collection was so incredibly worth it. I'm still incredibly proud of it!

Where do you see yourself in 10 years?

In ten years, I hope to have already gotten my doctorate and be working as a professor. I would love to be actively doing research, contributing to the field, and mentoring students. I'm not sure what else is in my future, including what type of research I want to do, as I have so many differing interests! I also hope that in ten years I can finally convince myself to become a frequent runner.

Contagious or Not Contagious: Is that the Question? Evaluating the Effects of Disease Contagion on Memory

Laura A. Pazos[1] and Mark J. Huff[1]

Researchers have suggested that individuals possess a disease-avoidance system designed to detect and remember potential sources of harmful pathogens, a system termed the behavioral immune system. Consistent with this system, evidence has shown an increase in memory for objects that are physically touched by individuals who are contaminated with a contagious disease versus individuals with a non-contagious disease or who are healthy. We further extend these findings by examining correct and false memory using the Deese/Roediger-McDermott (DRM) paradigm in which individuals study lists of associates (e.g., bed, rest, tired, etc.) that converge upon a single critical lure (e.g., sleep), which is often falsely recalled and/or recognized at a later test. Participants studied associative lists that were presented auditorily by an individual described as either infected with a contagious disease (influenza), infected with a noncontagious disease (cancer), or healthy. On final recall and recognition tests, neither correct nor false memory were found to differ across disease groups, suggesting that disease-related information may not affect memory processes for words presented auditorily, and that have not been physically contacted by an infected individual.

Exposure to potential sources of disease is common. Fortunately, disease exposure is rarely fatal, which is partially attributable to well-tuned biological processes designed to eliminate threats that can harm the body. Specifically, the biological immune system has evolved over time to retaliate against pathogens that enter internally to stave off illness (Schaller & Park, 2011). While the immune system is generally effective at thwarting pathogenic threats, its operation is not cost free. In response to pathogens, for instance, individuals may show an increase in mucus production and develop a cough to quarantine and clear the respiratory system of foreign particles. Furthermore, individuals often develop a fever to create an inhospitable environment for infectious pathogens. In these cases, symptoms are uncomfortable and require considerable energy to rid the body of pathogens.

Given the cost of the biological immune system, researchers have suggested that individuals may have evolved another way to detect and avoid pathogenic sources through the behavioral immune system (BIS; Schaller, 2006; Schaller & Duncan, 2007). An effective BIS requires a high-functioning cognitive system to encode, store, and retrieve stimuli associated with a diseased source that may be harmful to the self. The purpose of this study is to provide an additional test of whether memory processes are indeed more sensitive to information across different sensory domains associated with potential pathogens, consistent with the BIS. To this end, the present experiment will examine memory performance for lists of words when audibly presented by individuals who are described as infected by a contagious or non-contagious disease versus a healthy individual.

1. The University of Southern Mississippi

Disease-Avoidant Effects on Memory

Disease-avoidant behaviors have been well documented in humans and other animals. For example, animals have been shown to avoid other members of their own species who are perceived as contaminated with pathogens (Behringeret al., 2006; Loehle, 1995), and engage in grooming behaviors to remove potential pathogens from themselves and others (Eckstein & Hart, 2000; Zhukovskaya et al., 2013). Humans show similar avoidant behaviors. For example, individuals have shown greater repelling arm movements towards faces when primed with disease-related information (Mortensen et al., 2010), and exhibit disgust responses towards infectious sources (Schaller & Duncan, 2007; Schaller & Park, 2011). Disgust responses are triggered by a variety of stimuli including bodily functions that are often a byproduct of illness (e.g., sneezing, itching, coughing, etc.), foods that have spoiled, and animals that may be carriers of pathogens (e.g., ticks, fleas, mosquitos, etc.; Tybur et al., 2009; Tybur et al., 2013). Therefore disgust may reflect activation of the BIS which would encourage individuals to avoid pathogenic sources.

Consistent with behavioral-avoidance systems, accumulating evidence suggests that cognitive systems have adapted to process and retain information relevant to genetic longevity. For instance, females show greater memory for male faces in a long-term dating context versus a long-term worker context with whom they would establish a "long-term contract," such as by creating a team to develop important projects (Pandeirada et al., 2017). Furthermore, there is evidence that processing information based on its perceived relevance towards survival improves memory relative to information that has not been processed based on survival relevance. This memory improvement has been termed the survival-processing effect (Nairne et al., 2007; Nairne & Pandeirada, 2016) and has been suggested to be the result of an evolutionary process in which the cognitive system has been selectively "tuned" to remember information that can benefit survival and increase the likelihood of reproduction—consistent with the natural selection process.

To evaluate whether cognitive processes are sensitive to survival-related information, Nairne et al. (2007) asked participants to study lists of words using a survival-processing task. In this task, participants were asked to imagine that they were stranded in the grasslands of a foreign land and would need to sustain their own survival. Participants then rated words based on their relevance to the survival scenario. When tested, processing words based on survival relevance increased correct memory relative to a control task in which participants imagined that they were moving to a new city and rated the words based on their relevance for thriving in a new location. Importantly, this control task mimicked many of the elements of the survival task but lacked the survival component.

Subsequent experiments have revealed that the survival-processing effect is robust. It holds relative to powerful deep study tasks such as pleasantness ratings and self-referential encoding (Craik & Lockhart, 1972; Kang et al., 2008), and under survival scenarios outside of the grasslands scene (e.g. surviving a zombie apocalypse; Soderstrom & McCabe, 2011; Nairne & Pandeirada, 2010), and being socially isolated or around potential attackers (Kostic et al., 2012). Given the broad and reliable benefits for processing information based on survival relevance, an important question is whether information that could potentially compromise survival, such as sources of disease, may also be highly memorable to avoid contamination, potentially through activation of the BIS.

To evaluate the effects of diseased sources on memory, Fernandes et al. (2017) presented participants with pictures of objects that were paired with a face of an individual who presumably interacted with the object. Critically, the faces were either paired with a description of the individual that communicated the presence of disease (e.g., "constant cough") or did not communicate disease information (e.g., "green eyes"). According to the law of contagion, disease-connoting objects transfer pathogens to individuals who encounter these objects, thereby inflicting harm (Frazer, 1922). Therefore, if individuals perceive objects as infectious, they will be more likely to remember them later. Consistent with this possibility, object recall was found to be greater when objects were paired with faces with a disease-related description than with a non-disease description. Thus, sources associated with disease may be processed more deeply and thus

better remembered than non-threatening sources due to BIS activation.

An important factor for whether disease knowledge will affect memory processes may be whether the disease is perceived as contagious and consequently threatening. In a separate study, Gretz and Huff (2019) examined whether association with disease alone is sufficient for enhancing memory, or if the disease needs to be perceived as contagious. Participants viewed a set of household videos in which a single actor interacted with a series of objects. Prior to viewing, participants were informed that the actor was either diagnosed with influenza (an infectious disease), cancer (a noninfectious disease), or that the actor was healthy. In addition, the influenza actor (but not the cancer or healthy actors) sneezed prior to touching objects in the videos to enhance the salience of the disease to viewers. Following the presentation of the videos, participants recalled objects presented in the videos with instructions to identify both touched and non-touched objects, followed by a source-recognition test. In the source-recognition test, participants were presented with a list of objects and were asked to classify each object as being one that was touched, not touched, or not presented in the videos. Correct recall and source recognition were found to be greater for items that were touched versus not; however, source recognition was particularly high for touched items in the influenza videos, but not for the cancer or healthy videos. Thus, knowledge of the actor having an infectious disease appears to facilitate contextual memory for objects that have been touched, presumably because participants can avoid these objects later and be less likely to contract a potential illness.

False Memory Errors and the Effects of Distinctiveness

In addition to examining correct memory, researchers have also been interested in memory errors which could negatively affect overall accuracy. Memory errors have generally been classified into two broad types: errors of omission and errors of commission. Omission errors refer to a retrieval failure, possibly due to a failure in encoding memory initially. Commission errors refer to remembering events that did not happen or remembering them differently than how they originally occurred (Roediger & McDermott,1995; Schacter, 1999). Given that commission errors are common and highly problematic due to their introduction of false details, it is important to determine whether methods that facilitate correct memory also enhance false memory. In particular, the present study examines whether disease salience may operate to improve memory accuracy by increasing correct memory while reducing memory errors.

A powerful method for inducing commission errors in a laboratory setting is the Deese/Roediger-McDermott (DRM) paradigm (Deese, 1959; Roediger & McDermott, 1995). In this paradigm, participants study lists of strongly related words that are presented auditorily (e.g., bed, rest, tired, dream, etc.) that all converge upon a single non-presented critical lure (e.g., sleep). This critical lure is an item that is related to the presented list of associates but does not appear in the initial study list. After studying the list, participants then complete a memory test in which false recall and recognition of critical lures often meet or even exceed correct memory rates for presented items. The robust pattern of false recall and recognition is termed the DRM illusion. Given the power of the DRM illusion, researchers have explored several ways to reduce it. The DRM illusion has been reduced (but not eliminated) when participants had been warned about it, especially before studying (Gallo et al., 1997; Gallo et al., 2001), and when participants had been given more time to study list words (McDermott & Watson, 2001). Relevant to our study, the DRM illusion has also been reduced following distinctive item-specific encoding, occurring when participants focus on unique characteristics of list items. Item-specific encoding increases correct recognition while producing a concomitant reduction in false recognition—a pattern termed a mirror effect since correct and false are inversely correlated (Glanzer & Adams, 1990; Gunter et al., 2007; Huff et al., 2015; McCabe et al., 2004). Given Gretz and Huff's (2019) findings that pathogenic concerns associated with influenza facilitate memory for item-specific source details, it was expected that influenza pathogenicity would produce a reduction in the DRM illusion.

In the present study, participants studied a set of DRM lists presented auditorily by a female speaker. An auditory rather than visual modality was chosen to be consistent with the standard DRM paradigm (Roediger & McDermott, 1995), and to test whether disease-related

effects on memory could be detected with non-visual stimuli. Critically, prior to the presentation of each study list, participants were informed that the speaker had either influenza (a contagious disease), cancer (a non-contagious disease), or was healthy and not afflicted with ailments (based on Gretz & Huff, 2019). Following study of each list, participants completed a free-recall test for the list of words followed by a final recognition test. Disease conditions were manipulated using a between-subject design.

According to the BIS account, correct memory should be enhanced for the influenza group over the cancer and healthy groups. Avoidance of this contagious influenza source should be associated with an increase in the likelihood of survival, therefore facilitating correct memory. False memory was expected to decrease when correct memory increases, if consistent with mirror effect patterns reported in the literature following item-specific encoding (e.g., Huff & Bodner, 2013).

To more effectively characterize the effects of the BIS on memory accuracy, participants in both experiments further completed the Perceived Vulnerability to Disease Scale (PVD; Duncan et al., 2009). The PVD is a dispositional rating scale that assesses an individual's concerns towards pathogens. The scale is composed of two subscales: one that assesses participants' beliefs concerning their susceptibility to infectious diseases, termed perceived infectability, and another that assesses emotional discomfort concerning pathogen transmission, termed germ aversion. Based on responses to this scale, it is possible that individuals who show greater concerns towards their own infectability and/or are more averse to germs may possess a more sensitive BIS and, therefore, more exaggerated memory effects. If so, then responses on the PVD and the two subscales will be positively correlated with correct memory but negatively correlated with false memory across conditions.

Method

Participants

Sixty-seven University of Southern Mississippi Psychology undergraduates participated for partial fulfillment of course credit. Six were removed for failure to follow experimental instructions, with the remaining participants randomly assigned to the influenza (N = 21), cancer (N = 18), or healthy (N = 22) groups. Participants ranged in age from 18 to 59, with a mean age of 22.77 (8.1) years. Most participants were female (68%) and of those who reported ethnicity, 54% of participants were Caucasian, 38% were African American, and less than 1% were Asian. All were proficient English speakers and reported normal or corrected-to-normal vision.

Materials

Twenty DRM lists containing the highest levels of mean backward associative strength (BAS) from the list items to the critical lure were taken from Roediger et al. (2001). BAS refers to the magnitude of association between the list items and the critical lure and has a strong positive correlation with false recall and recognition of critical lures (e.g., Roediger et al.). These DRM lists were divided into two sets of 10 lists to create two versions which were counterbalanced across participants. Each list contained 15 items that were presented in descending order of BAS. Due to experimenter error, two lists (the "Car" and "Chair" lists) were presented in a random BAS order instead. Lists were presented via audio recordings featuring two female speakers. Both speakers spoke in a plain, controlled manner, lacking any distinctive indicators of illness. Each word was read aloud at an approximate rate of one word every two seconds.

An 80-item recognition memory test was constructed and consisted of 30 items from study lists (from list positions 1, 8, and 10 in each list), 30 non-studied items from the lists in the non-studied version (from the same list positions), 10 critical lures from studied lists, and 10 critical lures from the lists in the non-studied version. The recognition test was randomized once and presented in the same order across participants.

The 15-item PVD scale (Duncan et al., 2009) was also administered. The PVD contains two subscales: perceived infectability and germ aversion, which correspond to separate dispositional responses. The perceived infectability subscale contains seven items to assess susceptibility to diseases (e.g., "I have a history of susceptibility to diseases."), whereas the germ aversion subscale consists of eight items to assess an individual's aversion to pathogenic threats (e.g., "It really bothers me

when people sneeze without covering their mouths."). A 7-point Likert scale was used to make responses ranging from strongly disagree (1) to strongly agree (7). Higher scores indicate greater perceptions of disease vulnerability. Six items were reverse scored. The overall PVD (M = 3.73; range = 1.87-5.80; α = .79), the germ aversion subscale (M = 4.23; range = 1.50-6.50; α = .74), and the perceived infectability subscale (M = 3.16; range = 1.57-6.71; α =.71) had acceptable reliabilities.

Procedure

Following informed consent, participants were tested individually via a computer using Microsoft PowerPoint and were instructed that they would be presented with lists of words auditorily and that their memory for these words would be tested. At this time, participants were presented with one of the condition-specific disease instructions. The influenza group was informed that "the individual reading this list has recently been diagnosed with influenza, a highly contagious disease that can result in fever, sore throat, and muscle or body aches." The cancer group was informed that "the individual reading the list has recently been diagnosed with cancer, a non-contagious disease that can result in anemia, the development of tumors, and changes in digestive movements." The healthy group was informed that "the individual reading this list is healthy and not afflicted with ailments." Additionally, each group was presented with a photograph of a female who visually matched the description presented in each disease group to better portray the disease status of the speaker reading the word lists. Specifically, the photograph in the influenza group depicted a female who was blowing her nose next to bottles of medicine. The photograph in the cancer group depicted a female with no hair. The photograph in the healthy group depicted a female who was smiling at the camera (Appendix).

After listening to each list, participants then completed a one minute arithmetic filler task followed by a one minute free-recall test. Using a filler task is a standard procedure for testing the DRM paradigm (e.g., Huff et al., 2011; Roediger & McDermott, 1995). The free-recall test instructed participants to write down as many words as possible from the list in any order on a provided sheet of paper. Immediately following the free-recall test, participants then completed another study/recall cycle until all 10 lists were tested. Disease information was repeated prior to each study list to ensure participants were aware of the disease status of the speaker.

After the final study/recall cycle, participants then completed an old/new recognition test. They were presented with a sheet of paper with 80 words and were instructed to determine whether each word was "old" and studied on a previous list, or "new" and not studied on a previous list by placing a checkmark into the old or the new column. The recognition test was untimed, and participants were required to make a response for every item. Following the recognition test, participants completed the PVD, a brief demographics questionnaire, and were then debriefed regarding the purpose of the study. The experimental session lasted approximately 60 minutes.

Results

All data were analyzed using SPSS statistics software. Table 1 reports recall and recognition performance as a function of disease group. For recognition analyses, a signal-detection measure of discriminability (d') was computed. False alarm rates of 0 and hit rates of 1 were adjusted using Macmillan and Creelman's (1991) 1/2n correction. For correct recognition, d' was computed by taking the z-score for the list item hit rate minus the z-score for the false alarm rate for list item controls. Similarly, for false recognition, d' was computed by taking the z-score for "hit" rates to critical lures minus the z-score for false alarms to critical lure controls1[1] (see Huff & Bodner, 2013; Schacter et al., 1999, for an identical application of signal detection to critical lures).

An alpha level of .05 was used for all results reported unless otherwise noted. All non-significant effects were further tested using a Bayesian estimate of evidence supporting the null hypothesis (Masson, 2011; Wagenmakers, 2007).

1 1For completeness, we include adjusted correct and adjusted false recognition scores in Table 1. Adjusted scores were taken by subtracting raw false alarm rates to control items from the respective raw recognition rates for studied list items and critical lures. Analyses using adjusted recognition scores showed identical statistical patterns as the d' analysis and are therefore not discussed further.

Table 1

Mean (SE) Recall and Recognition Proportions for Studied List Items, Critical Lures, and Extra-List Intrusions per List as a Function of Influenza, Cancer, and Healthy Disease Groups

Disease Group/ Test Type	Influenza	Cancer	Healthy
N	21	18	22
Recall Test			
List Items	.50 (.02)	.47 (.02)	.45 (.02)
Critical Lures	.48 (.04)	.59 (.05)	.50 (.05)
Extra-List Intrusions	.76 (.13)	.73 (.13)	.67 (.12)
Recognition Test			
List Items	.81 (.02)	.85 (.02)	.83 (.02)
List Item Controls	.09 (.02)	.12 (.02)	.11 (.02)
List Item *d'*	**2.45 (.16)**	**2.55 (.18)**	**2.40 (.13)**
Adjusted List Items	.72 (.03)	.74 (.04)	.72 (.03)
Critical Lures	.79 (.04)	.74 (.04)	.72 (.03)
Critical Lure Controls	.19 (.03)	.21 (.05)	.13 (.03)
Critical Lure *d'*	**1.87 (.19)**	**2.09 (.19)**	**2.39 (.12)**
Adjusted Critical Lures	.60 (.06)	.66 (.05)	.76 (.03)

Note. Boldface indicates *d'* values included in the reported analyses. Adjusted recognition proportions reflect corrected scores (i.e., List Items and Critical Lures minus Control Items) and analyses are included in Footnote 1.

The Bayesian analysis compares the probabilities for two models: one that assumes an effect and one that assumes no effect, given the observed data. For this Bayesian analysis, we assumed that the two models had equal prior probabilities. This analysis yields a probability estimate that the null effect is retained, a p-value termed pBIC (the posterior probability given the Bayesian Information Criterion). Thus, for all null effects reported, we include a pBIC analysis which improves our confidence that the null effect is reliable. Additionally, a pBIC analysis is highly sensitive to sample size and can therefore serve as a proxy for a power analysis.

Free Recall

The three disease groups (healthy vs. cancer vs. influenza) were compared using a one-way ANOVA. Correct recall, false recall, and mean number of extra-list intrusions were not found to differ across disease groups, $F(2, 58) = 1.20$, $MSE = .01$, $p = .31$, $pBIC = .95$; $F(2, 58) = 0.80$, $MSE = .05$, $p = .45$, $pBIC = .96$; and $F(2, 58) = 0.30$, $MSE = .34$, $p = .74$, $pBIC = .98$, respectively. Therefore, disease status of the individual presenting auditory word lists produced no effect on any of the recall measures.

Recognition

Recognition analyses were conducted on d′ values as reported above. For correct recognition of studied list items, the one-way ANOVA yielded no effect of disease group on d′ , $F(2, 58) = .24$, $MSE = .50$, $p = .79$, $pBIC = .98$. For false recognition d′, a marginal difference was found across groups based on a standard null-hypothesis significance testing, but, importantly, evidence from the Bayesian analysis indicated fairly strong evidence in support of the null effects, $F(2, 58) = 2.50$, $MSE = .59$, $p = .09$, $pBIC = .81$. Given strong support of the null, we did not further analyze individual groups. Thus, consistent with correct and false recall, disease conditions appear to affect neither correct recognition for studied list items nor false recognition for critical lures[2].

Table 2

Perceived Vulnerability to Disease Scale Correlations

	1	2	3	4	5	6	7
1. Correct Recall	-						
2. False Recall	-.09	-					
3. Correct RGN	.71**	-.01	-				
4. False RGN	.07	.34**	.39**	-			
5. PVD	-.11	-.06	.05	-.04	-		
6. Infectability	-.07	.08	-.09	-.12	.71**	-	
7. Germ Aversion	-.09	-.14	.13	.03	.85**	.23^	-

Notes. ** Correlation is significant at the 0.01 level (2-tailed). * Correlation is significant at the 0.05 level (2-tailed). ^ Correlation is marginal ($p = .05$-$.10$). RGN = recognition.

Correlations with the PVD Scale

Correlation analyses were then conducted to examine the relationship between memory responses and the PVD. These correlations, including the two subscales (infectability and germ aversion) are reported in Table 2. Given the relatively low number of participants in each disease group, correlation analyses collapsed across groups in order to maximize sensitivity and reliability. No significant relationships were found between the overall PVD scale and subscales, and correct or false recall and recognition, $rs < .14$, $p > .29$. Therefore, responses on the PVD were not related to memory performance on either

2 Analyses were similarly conducted on criterion c, a response bias estimate that often accompanies signal-detection analyses. Although we did not have any a priori reason to expect bias to differ as a function of disease condition, we conducted a separate analysis on c estimates. No difference was found across groups for c for studied list items, $F(2, 58) = 1.04$, $MSE = .12$, $p = .36$, $pBIC = .96$, nor for critical lures, $F(2, 58) = 0.53$, $MSE = .16$, $p = .59$, $pBIC = .97$. Thus, response biases were similarly unaffected by disease instructions.

the recall or recognition tests.

Discussion

The experimental findings failed to mimic patterns found in prior literature. Correct and false recall were equivalent across the disease groups and the healthy control, and this pattern was echoed on correct and false recognition. Disease-related effects on memory were similarly absent when correlations were computed between recall and recognition performance and the PVD scale. Here, no relationships were found, suggesting that individual dispositional responses towards disease vulnerability were not related to memory performance when diseased sources provided memory information auditorily.

A possible reason for these null effects may be a lack of direct physical contact between the diseased source and memory items. As mentioned above, an auditory modality was chosen in part to be consistent with the standard DRM paradigm; however, this presentation type has not been used in past literature and may have limited disease-related effects on memory.

For instance, in Fernandes et al. (2017), participants were explicitly told that memory objects were touched by individuals with characteristics consistent with diseases, thereby producing a physical "vector" allowing disease to infect studied objects which may have been perceived as threatening to participants. Similarly, in Gretz and Huff (2019), videos included actors who physically interacted with objects which also established a disease vector. In the present experiment, participants were auditorily provided with word lists and descriptions of the speakers' disease states, but a direct vector between the disease state and the studied item was not created. Physical interaction between the diseased speaker and the memory item might therefore be critical for demonstrating disease-related effects on memory.

Additionally, another reason why this study failed to find disease-related effects on memory could have been that participants did not believe or were not heavily affected by the disease manipulation. According to Nairne et al. (2007), only information that is relevant to an individual's survival chances will enhance retention. In this experiment, participants may not have perceived the disease state of the speaker as threatening to their well-being. Indeed, word lists were presented through computer speakers, and the speakers spoke with clear voices that were likely incongruent with the expectations of a diseased state. The information provided about influenza and cancer disease states may therefore have been rendered ineffective. Future research could examine this possibility by presenting word lists read aloud by speakers who better match the appropriate disease condition. For example, a healthy person would have the control voice used in this experiment, while the cancer or influenza speakers would be frail or nasally to better emulate illness auditorily.

Disease potency could also have been a key player. In Fernandes et al. (2017), the diseases presented to participants were not specified. Without this detail, subjects may have perceived the disease characteristics to be extremely potent. Our experiments clearly stated the disease state of each presenter, leaving little room for imagination. Influenza was used as the contagious disease state due to its common occurrence in the population and would therefore have been experienced by most participants. While symptoms associated with influenza may be easily recognizable, the actual term of the illness might not have been, as the word "flu" is more readily recognized and used in the common vernacular. Disease-related effects of memory may have occurred if the disease was more severe, such as Ebola, measles, or coronavirus—possibilities that are currently being explored.

As mentioned above, future studies could examine different contagious illnesses with varying degrees of severity. A reasonable extension of this study could also study a different population (e.g., older population), as the participants used in this study were college students. In summary, the present study further tested the role of adaptive memory and how it may be moderated by the effects of the BIS when individuals are faced with potential disease-related threats. In an experiment modeled after prior work from Fernandes et al. (2017) and Gretz and Huff (2019), participants were presented with word lists read by healthy individuals or those with an infectious or non-infectious disease. Memory for these word lists showed no differences as a function of disease state, and the use of Bayesian analyses indicated strong support for the null effect. This study suggests that findings reported

previously for the visual modality do not generalize to the auditory modality. The discrepancy with prior literature could be due to a variety of the methodological differences discussed above; however, the present study demonstrates that disease-related effects on memory may not always occur consistently.

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Appendix

Photographs of Disease States

Cancer

Healthy

Influenza