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Neurobehavioral Responses to Ambiguity and Exploratory Behaviors Following Early Life Adversity

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Neurobehavioral Responses to Ambiguity and Exploratory Behaviors Following Early Life Adversity

A dissertation submitted in partial satisfaction of the

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by

Natalie Saragosa-Harris

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ABSTRACT OF THE DISSERTATION

Neurobehavioral Responses to Ambiguity and Exploratory Behaviors

Following Early Life Adversity

by

Natalie Saragosa-Harris

Doctor of Philosophy in Psychology

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Professor Jennifer Ashley Silvers, Chair

Early life adversity (ELA) is a potent and common risk factor for a number of mental health challenges. ELA is thought to increase risk for psychopathology in part by sensitizing threat-responsive neural circuitry and heightening vigilance to potential threat. This hypervigilance is thought to result in a tendency to overestimate threat in the face of ambiguity or uncertainty, a core feature of several internalizing disorders. However, few studies have examined how ELA shapes neural or behavioral responses to ambiguous and uncertain stimuli. Across three studies, this dissertation integrates neuroimaging, behavioral, and self-report data to examine how ELA shapes responses to ambiguity and uncertainty. We examine these associations in children, adolescents, and emerging adults with varying histories of caregiving adversity. In Study 1 and Study 2, we use representational similarity analysis to evaluate whether similarity in neural representations of ambiguity and threat varies depending on adversity history. In Study 1, we find that emerging

adults who experienced higher levels of abuse and neglect demonstrate greater representational similarity between ambiguous and threatening stimuli within threat-sensitive neurocircuitry. These results indicate that ELA may predispose an individual to represent ambiguity as threatening at the neural level. In Study 2, we sought to replicate these findings in a population of adopted youth who had experienced institutionalization in orphanage care, a rare and extreme form of caregiving adversity. However, we find that the degree of similarity in neural representations of ambiguity and threat does not significantly differ between previously institutionalized and control youth. In Study 3, we demonstrate that emerging adults who experienced higher levels of abuse and neglect exhibit less avoidance of uncertainty in an explore-exploit task. Together, these three studies provide novel insights into how ELA shapes neural and behavioral functioning in the face of the unknown and how these processes relate to wellbeing following caregiving adversity.

The dissertation of Natalie Saragosa-Harris is approved.

Adriana Galván

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2024

This dissertation is about the importance of caregiving. My cousin Darcie was the most natural caregiver I have ever met. She made every child in her life feel valued, safe, and loved.

This dissertation is dedicated to her.

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Study 1 is a version of Saragosa-Harris, N.M., Guassi Moreira, J.F., Waizman, Y., Sedykin, A., Peris, T.S., & Silvers, J.A. (2024). Early life adversity is associated with greater similarity in neural representations of ambiguous and threatening stimuli. *Development and Psychopathology*, 1-13. 10.1017/S0954579424000683. For Study 1, N.M. Saragosa-Harris, J.F. Guassi Moreira, Y. Waizman, and A. Sedykin collected and maintained the data. N.M. Saragosa-Harris analyzed the data and wrote the manuscript. J.F. Guassi Moreira, Y. Waizman, A. Sedykin, T.S. Peris, and J.A. Silvers edited the manuscript. T.S. Peris and J.A. Silvers were the principal investigators of the project. Study 2 is part of a larger project with contributions in data collection by N.M. Saragosa-Harris, J.F. Guassi Moreira, A.S. Méndez Leal, Y. Waizman, E. Ninova, W.J. Meredith, E.M. Gaines, and J.A. Silvers. N.M. Saragosa-Harris analyzed the data and wrote the manuscript. J.A. Silvers was the principal investigator of the project. Study 3 is a version of Saragosa-Harris, N.M., Nussenbaum, K., Hartley, C.A., and Silvers, J.A. (in preparation). The effects of novelty and uncertainty on exploratory behaviors following early life adversity. For Study 3, N.M. Saragosa-Harris analyzed the data with guidance from K. Nussenbaum, C.A. Hartley, and J.A. Silvers. N.M. Saragosa-Harris wrote the manuscript. J.A. Silvers was the principal investigator of the project.

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SELECTED PUBLICATIONS

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General Introduction.

Background and significance.

Exposure to early life adversity (ELA), including experiences of abuse, neglect, and institutional care, is a potent risk factor for impaired psychosocial functioning that is estimated to account for between 30 to 45% of psychopathologies worldwide (J. G. Green et al., 2010; Kessler et al., 2010; McLaughlin et al., 2012). The implications of ELA are wide-reaching, increasing the risk of delinquency (Ford et al., 2010; Turner et al., 2016), behavioral problems (Choi et al., 2019; Schroeder et al., 2020), social dysfunction (McCrory et al., 2022; Salzinger et al., 1993), and psychopathology (Baldwin et al., 2023; J. G. Green et al., 2010; Kessler et al., 2010; McLaughlin et al., 2012). Notably, studies suggest that responses to ambiguous and uncertain stimuli are linked to mental health (Carleton, 2016; Constans et al., 1999; Lissek et al., 2010) and may play a role in psychosocial functioning following adversity exposure (Hayward et al., 2020; Vantieghem et al., 2017), although research in this area is limited. This dissertation leverages behavioral, neuroimaging, and self-report data to investigate how responses to ambiguous stimuli and engagement with uncertainty vary as a function of early life adversity. This research examines these processes in children, adolescents, and emerging adults from both community samples and in a sample specifically recruited based on exposure to extreme ELA in the form of institutional orphanage care. Additionally, these studies integrate multimethod analyses, including multivariate pattern analyses of neuroimaging data and statistical modeling of behavior, to capture how these processes manifest across neural and behavioral domains. Across three studies, this dissertation provides insight into how ELA shapes neural representations of ambiguity and behavior in the face

of the unknown and, crucially, how these neurobehavioral profiles relate to risk for psychopathology.

Does early life adversity shape responses to ambiguity?

ELA is hypothesized to disrupt healthy functioning in part by sensitizing neural circuitry to motivationally salient and threat-relevant cues (Callaghan & Tottenham, 2016; McLaughlin & Sheridan, 2016), resulting in heightened vigilance for potential threat (McLaughlin & Lambert, 2017; Nusslock & Miller, 2016; Silvers et al., 2017). This sensitization may result in a tendency to overestimate threat in ambiguous situations (E. Chen & Matthews, 2001, 2003; Lange et al., 2019; McLaughlin et al., 2019). Critically, in samples not selected for ELA exposure, the tendency to assume threat in the face of ambiguity has been linked to psychosocial challenges (Carleton, 2016; J. T.-H. Chen & Lovibond, 2020; Dodge, 2006; Taghavi et al., 2000). Moreover, positive evaluations of ambiguity have been shown to mitigate risk for psychosocial challenges following ELA (Lange et al., 2019; Troller-Renfree et al., 2015, 2017; Vantieghem et al., 2017). Although an extensive literature has demonstrated ELA-based differences in neural responses to objectively negative cues (da Silva Ferreira et al., 2014; Doretto & Scivoletto, 2018; Herzberg & Gunnar, 2020; Saarinen et al., 2021), few studies have examined neural responses to ambiguous stimuli as a function of adversity exposure. Notably, work in clinical populations suggests that responses to ambiguous stimuli are more predictive of psychosocial health than responses to explicitly threatening stimuli (Lissek et al., 2010). Examining how ELA shapes responses to ambiguity stands to transform our understanding of how early experiences contribute to psychosocial outcomes and to eventually identify modifiable protective factors in vulnerable populations.

Prior behavioral studies suggest that ELA is associated with developmental differences in processing ambiguity. For instance, Bick et al. (2017) found that children with a history of

institutional orphanage care differed from age-matched comparisons in recognition accuracy for ambiguous, but not unambiguous, facial expressions (Bick et al., 2017). Further research has demonstrated that ELA-exposed youth tend to interpret ambiguity as threatening more often than age-matched peers (Dodge et al., 1990) (although see VanTieghem et al., 2017, which finds the opposite). For instance, Chen & Matthews (2001, 2003) demonstrated that low socioeconomic status (SES) youth were more likely than high SES youth to interpret ambiguous scenarios as threatening, whereas no group differences were observed when presented with explicitly threatening scenarios. Similarly, Pollak & Kistler (2002) found that, relative to comparison youth, abused children overidentified anger in morphed facial expressions. At present, little is known about how ELA exposure impacts ambiguity processing in adulthood, limiting our understanding of how enduring the effects of ELA are on interpretations of ambiguity.

Although several studies suggest that, on average, ELA-exposed individuals overestimate threat when evaluating ambiguity, there is marked heterogeneity amongst ELA-exposed individuals. Such individual differences may be particularly important for psychosocial functioning in ELA-exposed individuals. For example, VanTieghem et al. (2017) found that the tendency to evaluate ambiguous facial expressions positively mitigated risk for internalizing symptoms in previously institutionalized (PI), but not comparison, youth, suggesting that a positivity bias may be a uniquely protective factor for ELA-exposed populations. Ambiguous stimuli may thus be useful for probing hypersensitivity to potential threats (Neta et al., 2017; Pollak & Kistler, 2002) and more broadly indexing individual differences relevant to psychosocial functioning (Lissek et al., 2010; Neta & Brock, 2021; Petro et al., 2021; Puccetti et al., 2020; Vantieghem et al., 2017). However, few studies have examined how evaluations of ambiguity relate to experiences of ELA or moderate associations between ELA and mental health. Study 1

and Study 2 of this dissertation assess whether responses to ambiguous stimuli vary as a function of adversity history, and Study 1 examines whether differences in appraisals of ambiguity moderate links between ELA and psychosocial wellbeing.

Neural representations of ambiguity following early life adversity.

The tendency to appraise ambiguity as threatening may stem in part from difficulty distinguishing between ambiguous and threatening stimuli. At the neural level, this may manifest in the brain representing ambiguous and threatening information similarly (Lecei & van Winkel, 2020) — particularly within affective neural circuitry that responds to threatening and valenced stimuli. While this possibility has received theoretical support (Lecei & van Winkel, 2020), prior empirical work examining neural discrimination among affective cues following ELA has largely relied on univariate analyses to capture average BOLD responses to affective stimuli (S. A. Green et al., 2016; Tottenham et al., 2011; van Harmelen et al., 2013). While useful, univariate approaches rely on averaging brain activity over several units to distill a single index of activity. As a result, univariate analyses cannot capture more detailed, distributed patterns of representations of ambiguity — or, crucially, how similar these distributed patterns are to representations of threat.

Multivariate tools offer a unique opportunity to examine more detailed, distributed patterns of neural activity. Such methods are particularly sensitive to subtle variations in social and affective stimuli (Weaverdyck et al., 2020). For example, representational similarity analysis (RSA) is a technique that assesses representational overlap between stimulus types (e.g., ambiguous versus threatening) based on distributed patterns of voxelwise neural activity (Dimsdale-Zucker & Ranganath, 2018; Kriegeskorte, 2008). Using RSA, studies in community samples demonstrate that multivariate representations within the amygdala track subtle variations

in perceived trustworthiness of ambiguous social stimuli (FeldmanHall et al., 2018; Tashjian et al., 2019). RSA may similarly provide insight into whether similarity between multivariate representations of ambiguity and threat differs as a function of adversity history. Study 1 and Study 2 leverage RSA to examine whether individuals with a history of early caregiving adversity demonstrate greater similarity between representations of ambiguous and threatening affective cues within threat-sensitive neural circuitry. Study 1 (Saragosa-Harris et al., 2024) examines these processes in a community sample of emerging adults (ages 18 to 19) who provided retrospective reports of experiences of adversity during childhood. Study 2 builds upon Study 1 by employing a similar research methodology and analyses in data collected from youth (ages 9.99 to 22.90 years; mean age = 16.33) with a history of extreme ELA in the form of orphanage care, in addition to a comparison group.

Early life adversity and exploratory behaviors.

While Study 1 and Study 2 examine how ELA shapes initial responses to ambiguity, Study 3 seeks to understand the behavioral manifestations of such patterns. Study 3 employs a task in which participants actively choose whether to explore unfamiliar, novel options or exploit familiar, known options — what researchers refer to as the "explore-exploit dilemma" (Addicott et al., 2017). By focusing on exploratory decision-making, Study 3 seeks to test whether in addition to negative responses to *ambiguity* — "here and now" situations characterized by vagueness or equivocality (the focus of Study 1 and Study 2) — individuals with a history of ELA may similarly exhibit negative responses to *uncertainty* — future-oriented scenarios involving unpredictability or obscurity (see Grenier et al., 2005, for discussion of ambiguity versus uncertainty). Given the association between exploratory behaviors and mental health (Addicott et al., 2017; Heller et al., 2020; Saragosa-Harris et al., 2022), understanding how ELA shapes exploratory decision-making

has implications for functioning in ELA-exposed individuals, who are at heightened risk for developing psychopathology (Kessler et al., 2010).

Although prior work has demonstrated differences in exploratory decision-making as a function of ELA (Humphreys, Lee, et al., 2015; Lloyd et al., 2022; Y. Xu et al., 2023), this work has relied on tasks that are unable to distinguish between two important components of exploratory decision-making: stimulus novelty and reward uncertainty. In the context of decision-making tasks, "novelty" refers to the extent to which a given choice option has been encountered previously, whereas "uncertainty" refers to the variance or unpredictability in the reward payout associated with that choice option. Given the structure of many decision-making tasks, these two attributes are often linked. A choice option that has not been selected previously has both high novelty and high uncertainty, as its reward structure is unknown. Selecting the same choice option over time minimizes both its novelty and the uncertainty, as one learns the structure of its reward payout over the course of many trials. Despite being positively linked — wherein highly novel stimuli tend to also have high uncertainty — novelty is generally conceptualized as an appetitive or rewarding property of a stimulus (Houillon et al., 2013; Krebs et al., 2009; Wittmann et al., 2007, 2008) whereas uncertainty is often considered to be aversive (Blankenstein et al., 2016; de Berker et al., 2016; Herry et al., 2007). As a result, exploratory choices depend on a balance between novelty-seeking and uncertainty-avoidant tendencies (Cockburn et al., 2022; Nussenbaum et al., 2023). Although many commonly used tasks confound novelty and uncertainty, recent work suggests that these two components have unique effects on exploratory behaviors, underscoring the importance of decoupling these two motivators of behavior (Cockburn et al., 2022; Nussenbaum et al., 2023).

Prior work suggests that ELA could affect sensitivity to both novelty and uncertainty. Although research has demonstrated an association between ELA and novelty-seeking tendencies, the directionality of this association is inconsistent, even within studies (De Carvalho et al., 2015; Schouw et al., 2020). For instance, Schouw et al. (2020) found that while physical abuse predicted greater self-reported novelty-seeking, maternal rejection was associated with lower self-reported novelty-seeking. Similarly, de Carvalho et al. (2015) found that experiences of abuse, but not neglect, were associated with heightened self-reported novelty-seeking, suggesting that associations may depend on the type of adversity considered. Research has also demonstrated lower tolerance for uncertainty in individuals who experienced high levels of ELA (Hayward et al., 2020; Shen et al., 2024) and chronic stress (Raio et al., 2022). Results from Study 1 further suggest that individuals with a history of ELA may be more likely to evaluate uncertainty negatively. It is thus possible that ELA will be associated with a greater tendency to avoid highly uncertain choice options during exploratory decision-making. This pattern of results would align with a number of empirical studies (Humphreys, Lee, et al., 2015; Lloyd et al., 2022; Loman et al., 2014; Y. Xu et al., 2023) and theoretical models (Frankenhuis & Gopnik, 2023) linking ELA to decreased exploration. However, research in anxious individuals suggests that intolerance for uncertainty can actually increase engagement with uncertain options in explore-exploit tasks in an effort to reduce uncertainty (Aberg et al., 2021). Although prior work has examined the association between ELA and exploration, it remains unclear how ELA specifically shapes sensitivity to novelty and uncertainty during exploratory decision-making. Study 3 leverages a task that decomposes the unique effects of novelty and uncertainty in explore-exploit decision-making to examine how these distinct components relate to exploration following childhood adversity.

Examining how two distinct motivators of behavior, novelty and uncertainty, shape exploratory choices will provide integral insight into the mechanisms linking ELA to potentially suboptimal decision-making in adulthood. In addition to their unique effects on exploratory decision-making, sensitivity to novelty and uncertainty also have distinct associations with mental health challenges (Castellanos-Ryan et al., 2016; McEvoy & Mahoney, 2012). Understanding how these two components of exploratory decision-making differ as a function of ELA may also shed light on mechanisms linking ELA to psychopathology.

Specific Aims and Hypotheses.

Study 1 aims.

In a sample of 41 emerging adults (18 to 19-year-olds), **Study 1** aims to examine whether ELA relates to neural representations of ambiguity within threat-sensitive regions and whether behavioral responses to ambiguity moderate links between ELA and wellbeing.

Study 1 hypotheses.

Hypothesis 1a. Individuals with higher ELA will demonstrate greater sensitivity to threat, indicated by greater similarity (i.e., less differentiation) in their representations of ambiguous and threatening images within the four regions of interest (the amygdala, nucleus accumbens, anterior insula, and vmPFC) but not in the tested control region (V1).

Hypothesis 1b. Individuals exposed to greater levels of ELA will be more likely to appraise the ambiguous images negatively and will exhibit worse global functioning.

Hypothesis 1c. Individual differences in behavioral responses to ambiguity processing will moderate links between ELA and global functioning, such that positive evaluations of ambiguity will mitigate the negative association between ELA and global functioning.

Hypothesis 1d. Based on prior work demonstrating that taking longer to evaluate ambiguity is associated with more positive evaluations — potentially reflecting an adaptive regulatory process (Neta & Tong, 2016) — we hypothesize that longer response times to ambiguous images will mitigate the negative association between ELA and global functioning.

Study 2 aims.

In a sample of 81 youth (ages 9.99 to 22.90 years; mean age = 16.33), **Study 2** builds upon Study 1 by applying a similar analytical framework to a sample of youth who were exposed to extreme ELA in the form of orphanage care (N = 36) and comparison youth (N = 45). Based on Study 1, Study 2 tests four regions of interest (the amygdala, nucleus accumbens, anterior insula, and vmPFC) and one control region (V1). Study 2 tests two competing hypotheses regarding how similarity in neural representations of ambiguous and threatening cues may vary with ELA history and evaluates whether links between ELA and anxiety are moderated by neural responses to ambiguity.

Study 2 hypotheses.

Based on findings from Study 1 and previous literature, we expect to see group differences in neural representations of ambiguity between PI and control groups. However, contradicting findings from the few studies examining responses to ambiguity as a function of ELA suggest that these differences could unfold in several ways. Here, we consider two possibilities.

Threat sensitivity hypothesis. Results from Study 1 suggest that ELA is associated with greater similarity (i.e., less differentiation) in neural representations of ambiguous and threatening images — potentially reflecting hypersensitivity to potential threat. Based on these results, the *threat sensitivity hypothesis* posits that, relative to the comparison group, the PI group will demonstrate greater similarity in representations of ambiguous and threatening stimuli within the regions of interest but not the control region.

Accelerated maturation hypothesis. Behavioral work in PI youth, however, presents an alternative possibility. VanTieghem et al. (2017) found that, relative to comparison youth, six- to fourteen-year-old PI youth were more likely to interpret ambiguous cues positively (i.e., exhibit a

positive valence bias), a behavioral phenotype the authors consider to reflect more "adult-like" processing and potentially indicate accelerated development. Given the older age range of our sample (ages 9 to 22), group differences arising from putative differences in maturation will likely be more difficult to detect. That said, it is still possible that this observed tendency for PI youth to respond more positively to ambiguous cues may be similarly evident on the neural level even in our older sample. The *accelerated maturation hypothesis* therefore posits that, relative to the comparison group, the PI group will demonstrate greater similarity in representations of ambiguous and nonthreatening stimuli within the regions of interest but not the control region.

Anxiety hypotheses. We hypothesize that individuals in the PI group will exhibit higher anxiety levels. Based on prior work (Lange et al., 2019), we also will test whether representational overlap between ambiguous and threatening, or ambiguous and nonthreatening, stimuli within the amygdala moderate the relationship between ELA group (PI or control) and anxiety levels.

Study 3 aims.

While Study 1 and Study 2 aim to examine immediate neural responses to ambiguous cues, **Study 3** focuses on how ELA relates to exploratory behaviors. In a sample of 554 emerging adults (ages 18 to 25 years), this study investigates how novelty and uncertainty of choice options affect exploratory decision-making and tests whether the effects of novelty and uncertainty on exploratory choices differ as a function of caregiving adversity.

Study 3 hypotheses.

Hypothesis 3a. Individuals with higher cumulative ELA (indicated by total CTQ score) will demonstrate lower sensitivity to reward (i.e., their choices will be less value-driven) in an explore-exploit decision-making task.

Hypothesis 3b. Individuals with higher cumulative ELA will exhibit lower novelty-seeking behavior (i.e., a lower tendency to explore novel options).

Hypothesis 3c. Individuals with higher cumulative ELA will exhibit greater aversion to reward uncertainty (i.e., a greater tendency to avoid choice options associated with greater reward uncertainty).

Hypothesis 3d. In exploratory analyses, we hypothesize that the unique effects of novelty and reward uncertainty on exploration will differ based on the type of adversity experienced. In these analyses, we will consider the effects of childhood abuse, childhood neglect, and unpredictability in the caregiving environment.

Study 1: Neurobehavioral responses to ambiguity following early life adversity in emerging adults.

Introduction.

Exposure to early life adversity (ELA) is hypothesized to sensitize threat-responsive neural circuitry (Callaghan & Tottenham, 2016; Hein & Monk, 2017; McLaughlin & Sheridan, 2016; Nusslock & Miller, 2016). This may lead individuals to overestimate threat in the face of ambiguity (E. Chen & Matthews, 2001, 2003; Lange et al., 2019; McLaughlin et al., 2019), a cognitive-behavioral phenotype linked to poor mental health (Carleton, 2016; Constans et al., 1999; Lissek et al., 2010). The tendency to process ambiguity as threatening may stem in part from difficulty distinguishing between ambiguous and threatening cues (Lecei & van Winkel, 2020). However, it is unknown how exposure to ELA relates to neural representations of ambiguous and threatening stimuli, or how processing of ambiguity following ELA relates to psychosocial functioning.

In this study, we used RSA to investigate similarity in neural representations of ambiguous and threatening images as a function of ELA history. We chose to focus on the transition from adolescence to adulthood (i.e., "emerging adulthood") (Arnett et al., 2014) based on prior work suggesting that individual differences in responses to ambiguity are particularly important for shaping wellbeing during this period of development (Bardi et al., 2009; Silvers & Peris, 2023). This developmental stage is characterized by a number of ambiguous challenges (e.g., moving to a new and unfamiliar city for college or a first job, choosing a career path, living independently for the first time). The uncertainties associated with emerging adulthood are thought to be especially stressful during the earliest stages of this transitional period, when these novel stressors are the most unfamiliar and ambiguous (Bardi et al., 2009). For this reason, we recruited freshmen college students in order to capture this initial transition period in which ambiguity is thought to

be most closely linked to wellbeing (Bardi et al., 2009). Our decision to focus on this developmental stage was additionally motivated by work demonstrating heightened risk for psychopathology during the transition to adulthood (Arnett et al., 2014), especially within populations with a history of caregiving adversity (van der Vegt et al., 2009).

A sample of 41 emerging adults with varying levels of ELA exposure underwent fMRI while viewing ambiguous, threatening, and nonthreatening images. Outside of the scanner, participants rated the images. We hypothesized that individuals with higher ELA would demonstrate greater sensitivity to threat, indicated by greater similarity (i.e., less differentiation) in their representations of ambiguous and threatening images. We expected this pattern to be specific to ambiguity and threat — that is, we did not expect to see ELA-based differences in representational overlap between ambiguous and nonthreatening, or between threatening and nonthreatening, images. These hypotheses were tested in four a priori regions of interest, selected based on (1) their sensitivity to motivationally salient stimuli, especially ambiguous and potentially threatening signals, and (2) research demonstrating ELA-related differences in function within these regions: the amygdala (Fareri & Tottenham, 2016; FeldmanHall et al., 2018; Tashjian et al., 2019; P. Xu et al., 2021), nucleus accumbens (Fareri & Tottenham, 2016; Gee et al., 2018; Ray et al., 2020; P. Xu et al., 2021), anterior insula (Hein & Monk, 2017; Menon & Uddin, 2010; Tanovic et al., 2018; P. Xu et al., 2021), and ventromedial prefrontal cortex (vmPFC) (Chavez & Heatherton, 2015; Cohodes et al., 2021; Hart et al., 2018; P. Xu et al., 2021).

Given that ELA is associated with impairments across a broad range of domains, we also assessed global functioning, a construct that encapsulates mental health as well as other features of psychosocial functioning (Pirkis et al., 2005; Wing et al., 1998). We hypothesized that individuals exposed to greater levels of ELA would be more likely to appraise the ambiguous

images negatively and exhibit worse global functioning. While prior work has demonstrated robust effects of ELA on emotional outcomes, it has also revealed marked heterogeneity among ELA-exposed groups (Callaghan et al., 2019; Gee, 2021; Lange et al., 2019; Silvers et al., 2017; Stevens et al., 2021). Thus, we also tested whether individual differences in behavioral responses to ambiguity processing moderated links between ELA and global functioning. Based on prior work, we hypothesized that positive evaluations of ambiguity would be associated with better global functioning in high ELA individuals (Lange et al., 2019; Troller-Renfree et al., 2015, 2017; Vantieghem et al., 2017). Lastly, prior work demonstrates that taking longer to evaluate ambiguity is associated with more positive evaluations — potentially reflecting an adaptive regulatory process (Neta & Tong, 2016). We sought to replicate this finding and determine whether ELA moderates links between time spent evaluating ambiguity and global functioning, which ostensibly encompasses aspects of self-regulation.

Methods.

Code availability.

All task and analysis code for this study are available on GitHub (https://github.com/nsaragosaharris/earlylifeadversity_ambiguity_study).

Participants.

We recruited healthy participants via flyers and online recruitment. An a priori, planned sample size of 40 was selected based on prior neuroimaging studies that used similar multivariate modeling techniques to the planned analyses (Dimsdale-Zucker & Ranganath, 2018; FeldmanHall et al., 2018; Stolier & Freeman, 2016). In total, 41 participants completed neuroimaging and the

post-scan behavioral task (N = 29 females, age = 18 to 19 years old, $\underline{X}_{age}$ = 18.34, SD_{age} = 0.48). Three participants did not complete the questionnaire assessing global functioning (see *Questionnaires*). Sample demographics and summary statistics for questionnaire data can be found in *Table 1*. Participants provided written consent. All study procedures were completed in accordance with the University of California Los Angeles Institutional Review Board (IRB# 19-001000).

Participants completed questionnaires at an initial lab session and subsequently underwent fMRI testing within two weeks of their lab session. Immediately after fMRI testing, participants completed a behavioral task (described below). Participants were compensated for participation.

Variable	N = 41[1]
Age	
18	27 (66%)
19	14 (34%)
Sex	
Female	29 (71%)
Male	12 (29%)
Race	
Asian	20 (49%)
Black/African American	4 (9.8%)
Caucasian/White	12 (29%)
Multiracial	3 (7.3%)
Not Reported	1 (2.4%)
Other	1 (2.4%)
Hispanic	
Hispanic	8 (20%)
Not Hispanic	33 (80%)
Negativity bias (proportion ambiguous trials categorized negatively)	0.69 (0.54, 0.77)
CTQ Score	38 (32, 45)
(Missing)	1
HoNOS Score	14 (7, 19)
(Missing)	3

[1] n (%); Median (Q1, Q3)

Table 1. Sample demographics and summary statistics for questionnaire data.

Participant inclusion criteria.

Data were collected as part of a larger study investigating mental health in individuals transitioning from adolescence to adulthood. Eligibility for inclusion in the study was based on the

following criteria and assessed via brief in-person interview and MRI screening form: (1) individuals in their freshman year of college who were at least 18 years old; (2) no medical or psychiatric conditions contraindicating study participation (e.g., psychosis); (3) no current use of a psychiatric medication; (4) no current treatment for anxiety or depression; (5) no presence of metal in the body; (6) no current report of pregnancy; (7) no pressing mental health concern requiring immediate follow up (e.g. psychosis); and (8) no fear of enclosed spaces (claustrophobia).

Questionnaires.

Early life adversity. Early life adversity was measured using the Childhood Trauma Questionnaire Short Form (CTQ-SF) (Bernstein et al., 2003), a 28-item scale that assays experiences of emotional abuse, emotional neglect, physical abuse, physical neglect, and sexual abuse before age fourteen. The CTQ-SF has been validated in clinical and non-clinical samples and corresponds well to therapists' interview-based ratings of abuse and neglect (Bernstein et al., 2003). For each item, participants rated on a scale of 1 to 5 (1 = never true, 5 = very often true) how much they agreed with various statements (e.g., "I believe that I was physically abused"). Responses were totaled across subtypes of abuse and neglect, with higher scores indicating greater experiences of childhood trauma. Total scores were log-transformed and then z-scored to meet the assumptions of the planned statistical tests (i.e., normality).

Self-reported ambiguity tolerance. Self-reported ambiguity tolerance was measured using the Multiple Stimulus Types Ambiguity Tolerance Scale-II (MSTAT-II), a 13-item self-report questionnaire that has been validated in adults (McLain, 2009). The MSTAT-II assesses reactions to five types of ambiguous stimuli: generally ambiguous stimuli ("I prefer a situation in which

there is some ambiguity"), complex stimuli ("I enjoy tackling problems that are complex enough to be ambiguous"), uncertain stimuli ("I find it hard to make a choice when the outcome is uncertain" (reverse scored)), new/unfamiliar/novel stimuli ("I generally prefer novelty over familiarity"), and insoluble/illogical/irreducible/internally inconsistent stimuli ("I try to avoid problems that don't seem to have only one 'best' solution" (reverse scored)). Participants rated their level of agreement with each statement on a five-point Likert scale (1 = strongly disagree, 5 = strongly agree). Scores across all items were totaled, with greater scores indicating greater tolerance for ambiguity (McLain, 2009).

Global functioning. Global functioning was measured by the self-rated version of the Health of the Nation Outcomes Scale for Children and Adolescents (HoNOSCA-SR) (Gowers et al., 2002), a 13-item measure based on the Health of the Nation Outcomes Scale (Wing et al., 1998) that assesses functioning across four domains of symptoms and functioning: behavioral problems (aggressive/antisocial, overactivity/attention, self-harm, substance misuse), impairment (scholastic/language skills, physical disability), symptomatic problems (hallucinations and delusions, non-organic somatic symptoms, emotional and related symptoms), and social problems (peer relationships, self-care and independence, family life and relationships, poor school attendance) (Pirkis et al., 2005). The HoNOSCA-SR has been validated (Pirkis et al., 2005) and correlates with a number of other mental health scales (Gowers et al., 2002). For each item on the HoNOSCA, participants used a 5-point Likert scale to indicate the degree to which they were affected by a given symptom or experience (e.g., "Have you been troubled by your disruptive behavior, physical or verbal aggression?") in the last two weeks (0 = "Not at all", 1= "Insignificantly", 2 = "Mild but definitely", 3 = "Moderately", 4 = "Severely"). Responses across the 13 items were totaled, with higher scores indicating poorer functioning.

fMRI task and analyses.

fMRI paradigm. The fMRI task used an event-related design coded in PsychoPy2 (Peirce et al., 2019). Stimuli were drawn from the racially diverse affective expression (RADIATE) dataset (Conley et al., 2018). Participants viewed a set of faces with 99 unique actors from the RADIATE dataset while undergoing fMRI scanning. Actors in the selected images were 22% Asian, 32% Black/African American, 19% Hispanic or Latinx, and 26% White. 51% were female. Each of the 99 actors had three unique images, each with a different facial expression: angry, happy, and surprised. Based on prior work, angry, happy, and surprised faces were considered the threatening, nonthreatening, and ambiguous stimuli, respectively (Neta et al., 2017; Pine et al., 2005; Pollak & Kistler, 2002; Vantieghem et al., 2017).

Participants viewed a single image per trial. Within each run (three total), participants viewed 33 threatening (angry), 33 nonthreatening (happy), and 33 ambiguous (surprised) faces in addition to 9 blurred images (a composite of all face images), for a total of 108 trials per run and 324 total trials (*Figure 1A*). Each stimulus was presented for 500 ms. Every actor was shown three times (once per run), each time with a different facial expression (threatening, nonthreatening, or ambiguous). Participants were asked to press the button box only when they saw the blurred image (attention check trials). Between trials, there was a jittered fixation cross. Jitter times were created in OptSeq2 (https://surfer.nmr.mgh.harvard.edu/optseq/; mean length = 3 seconds, range = 1.5 to 8 seconds). Each run lasted 6 minutes and 36 seconds in total. Images within each of the three runs were shown in a randomized order and the order of runs was counterbalanced across participants.

fMRI acquisition. Data were acquired on a 3T Siemens Magnetom Prisma scanner using a 32-channel head coil. Functional data were acquired using the following parameters: voxel size = 2.0 × 2.0 × 2.0 mm, slices = 60 (interleaved), slice thickness = 2.0 mm, repetition time (TR) =

1000 ms, echo time (TE) = 37 ms, flip angle = 60°, field of view = 208 mm, multiband acceleration = 6x. AutoAlign was used to position and align slices. Structural images were acquired using a high-resolution MPRAGE sequence (voxel size = 0.8 × 0.8 × 0.8 mm; TR = 2400 ms, echo time = 2.22 ms, field of view = 256 mm, slice thickness = 0.8 mm, 208 slices).

fMRI preprocessing. Processing of fMRI data was carried out using FEAT (FMRI Expert Analysis Tool) Version 6.00, part of FSL (FMRIB's Software Library, www.fmrib.ox.ac.uk/fsl). Functional data was registered to participants' high resolution structural images using boundary based registration (BBR) (Greve & Fischl, 2009). High resolution structural images were registered to standard space (MNI 2.0 x 2.0 x 2.0 mm stereotaxic space) with 12 degrees of freedom using FLIRT (FMRIB's Linear Image Registration Tool) (Jenkinson et al., 2002; Jenkinson & Smith, 2001). Preprocessing included motion correction using MCFLIRT (Jenkinson et al., 2002) using 24 standard and extended regressors, non-brain extraction using BET (Brain Extraction Tool) (Smith, 2002), grand-mean intensity normalization, and high-pass temporal filtering (Gaussian-weighted least-squares straight line fitting, with sigma = 50.0s). Based on similar multivariate pattern analysis (MVPA) and RSA work (Glenn et al., 2020; Harry et al., 2013; Jin et al., 2015; Lee et al., 2020; Liang et al., 2017; Tashjian et al., 2019) and current recommendations (Dimsdale-Zucker & Ranganath, 2018; Misaki et al., 2013; Weaverdyck et al., 2020), in order to maintain fine-grained spatial details across voxels for RSA, we did not apply smoothing for multivariate analyses. For univariate analyses only, we used 3.5 mm full-width half maximum smoothing. Analyses were carried out using FILM (FMRIB's Improved Linear Model) prewhitening with local autocorrelation correction (Woolrich et al., 2001).

Our a priori, preregistered exclusion criteria required that (1) runs in which a participant responded to fewer than 5 of the 9 of the catch trials in the fMRI task (i.e., button presses in

response to blurred images) were to be excluded and (2) any participants with less than two usable runs (based on this response criterion) were to be excluded. However, no participants met exclusionary criteria for lack of responding.

First level modeling. BOLD response patterns were modeled separately by trial expression type (threatening, nonthreatening, or ambiguous) in FSL using first level (i.e., within-participant, within-run) models, each of which included a regressor for each expression type. Blurred face trials (attention checks) were modeled but not further analyzed. Between-trial fixation crosses served as implicit baseline (i.e., were not explicitly modeled). This resulted in three general linear models (GLMs) per participant (one per run), each of which included BOLD estimates for threatening, nonthreatening, and ambiguous trials. Temporal derivatives for all regressors were included as covariates. Regressors were modeled using a double-gamma hemodynamic response function (HRF). To account for head motion, individual volumes with a framewise displacement greater than 0.9 mm were included as regressors (spike regressors created using 'fsl_motion_outliers'). Motion regressors and their derivatives were included as regressors of no interest.

Regions of interest. Four regions of interest (ROIs; amygdala, nucleus accumbens, anterior insula, and vmPFC) were selected a priori based on (1) their hypothesized role in responding to motivationally salient stimuli, especially ambiguous and potentially threatening signals (Tanovic et al., 2018) and (2) research demonstrating ELA-related functional differences within these regions (Fareri & Tottenham, 2016). An additional region, V1, was tested as a control region expected to respond to the affective visual stimuli (Kragel et al., 2019) but not expected to differ in functional activity based on ELA. The amygdala and nucleus accumbens were defined based on FSL's Harvard-Oxford atlas and were thresholded in MNI space using Harvard-Oxford's

probabilistic masks, which specify the probability that a given voxel falls within the specified brain region. The amygdala was thresholded at $p = 0.50$ and the nucleus accumbens was thresholded at $p = 0.25$ based on prior work (Guassi Moreira et al., 2021; Tashjian et al., 2019) and visual inspection of anatomical alignment. V1 was defined based on FSL's Juelich atlas (Amunts et al., 2000) and thresholded at $p = 0.75$. For the anterior insula and vmPFC, which are less structurally defined than the amygdala and nucleus accumbens, masks from Xu et al. (2021), a meta-analysis of regions involved in processing facial expressions (including angry, happy, and surprised faces), were used. All masks were originally defined in MNI space and transformed into functional space in FSL for each participant prior to multivariate (RSA) analyses. Because masks were participant-specific and in native functional space, there was variability in ROI size. In cases in which an ROI-based statistical estimate was significant, we conducted sensitivity analyses in which we controlled for the number of voxels within the ROI to ensure that differences in ROI size across participants did not affect statistical estimates. Because the univariate analyses (*Supplemental Figure 2*) used the estimates from second level models, which are provided by FSL in MNI space, no additional transformations were applied for these analyses.

Representational similarity analysis. The function 'NiftiMasker' in the Python package 'nilearn'(Abraham et al., 2014) was used to extract vectors of voxel-level coefficients within each ROI. All vectors were participant-specific, run-specific, ROI-specific, and condition-specific: Each vector corresponded to a regressor of interest (ambiguous, threatening, or nonthreatening) from the aforementioned GLMs for a given ROI per run (e.g., run 1 ambiguous vector, run 1 threatening vector, run 1 nonthreatening vector). These vectors were used to compute three pairwise Pearson correlations (ambiguous/threatening, ambiguous/nonthreatening, threatening/nonthreatening) for each run. Next, these correlations were averaged across runs,

resulting in three correlations per ROI for a given participant (*Figure 1B*). Fisher's r-to-z transformation was then applied to the averaged Pearson correlation values (Dimsdale-Zucker & Ranganath, 2018). These z-transformed values represent similarity in patterns of representations between (1) ambiguous and threatening, (2) ambiguous and nonthreatening, and (3) threatening and nonthreatening facial expressions within a given ROI, with greater values indicating relatively greater similarity in voxelwise patterns of activation. Parallel analyses were run in a control region (V1). We hypothesized that individuals with higher ELA would demonstrate greater similarity ("overlap") in their representations of ambiguous and threatening images within the four ROIs (but not V1), and did not expect to see ELA-based differences in representational overlap between ambiguous and nonthreatening, or between threatening and nonthreatening, images.

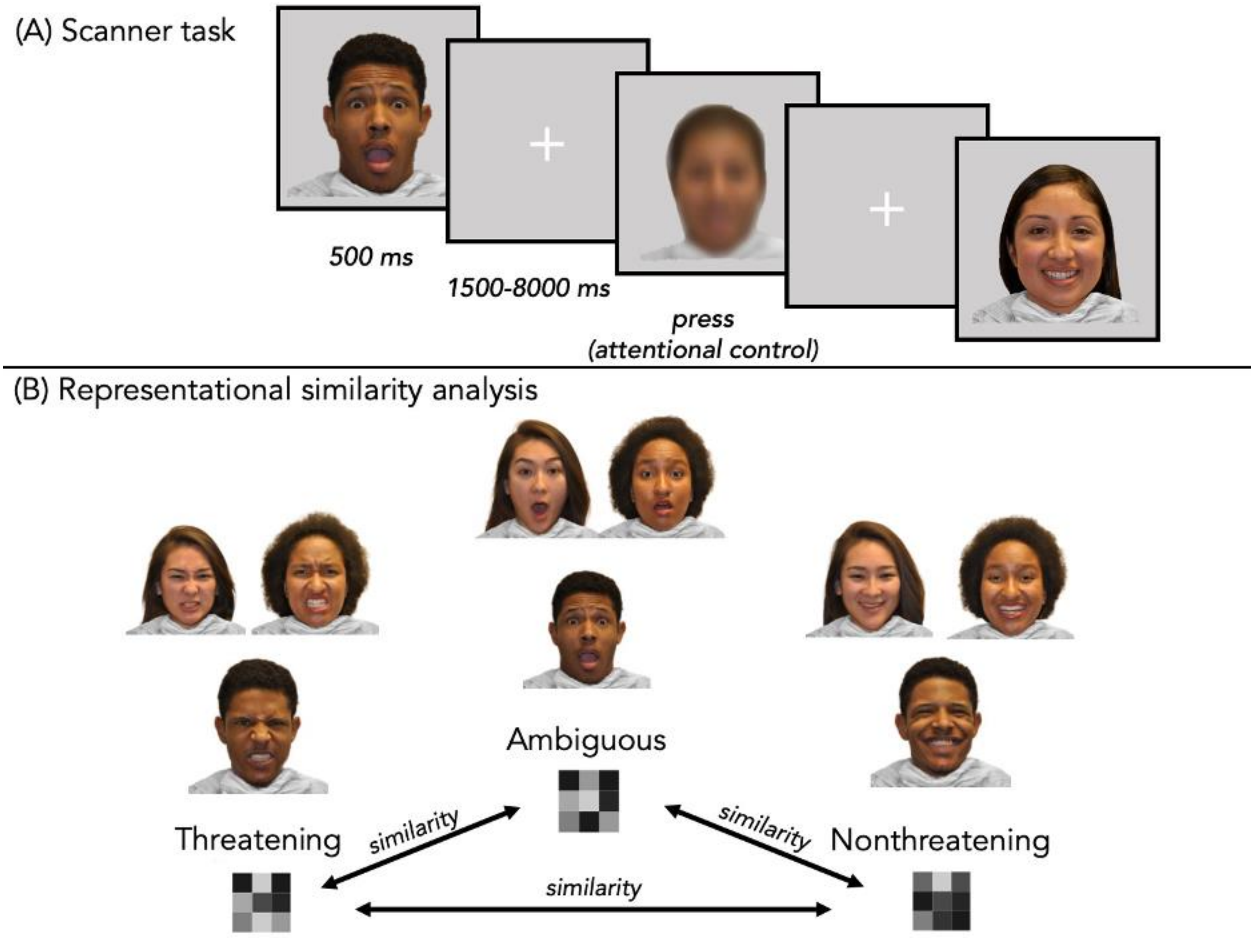


Figure 1. Study 1 task and analysis design. During the MRI task (A), participants passively viewed threatening, nonthreatening, and ambiguous faces. Catch trials included a blurred image and required a button box response. In representational similarity analyses (B), each expression type was modeled to create three multivoxel, vectorized patterns (within participant, run, and ROI). Pairwise correlations (indicated by arrows) were computed to index relative similarity between patterns of responses.

Post-scan categorization task.

Paradigm. Participants completed a surprise, post-scan task in which they were shown a subset of images seen in the fMRI task. After completing six practice trials, participants were shown 200 images (100 ambiguous) over ten blocks (ten ambiguous, five threatening, and five nonthreatening faces per block). Block order was randomized and faces within each block task were shown in a randomized order. More ambiguous faces (N = 100) were shown because this was

the primary condition of interest for this study. On each trial, participants pressed a button to indicate whether the person in the image "feels good" or "feels bad" (Vantieghem et al., 2017) by pressing a button on the keyboard (1 or 0, counterbalanced across participants). Each face was presented for 500 ms, followed by a screen with text requesting their response, which lasted for 1500 ms regardless of when they responded (*Figure 2*). Early responses (during the initial 500 ms presentation screen) were accepted and included in analyses. If participants made more than one response, their final appraisal was used in analysis to minimize the possibility of analyzing responses made in error. A 200ms fixation cross was included between trials (*Figure 2*). In between blocks, there was a ten second fixation screen.

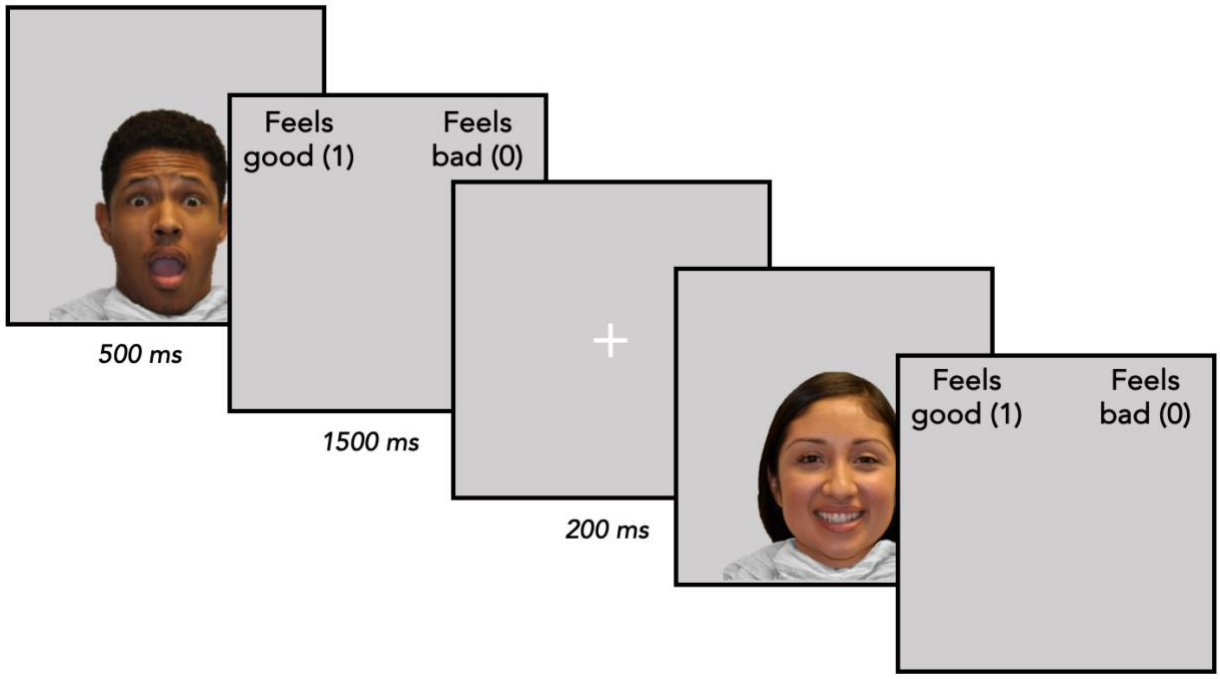


Figure 2. Study 1 post-scan behavioral categorization task. During the post-scan behavioral categorization task, participants categorized a subset of the previously seen threatening (angry), nonthreatening (happy), and ambiguous (surprised) faces as "feels good" or "feels bad" (0 or 1, counterbalanced across participants) outside of the scanner. The stimulus was presented for 500 ms, followed by a screen with text requesting their response, which lasted for 1500 ms regardless of when they responded.

Behavioral data analysis. To index an individual's propensity to interpret ambiguous faces negatively ("negativity bias"), we computed the percent of ambiguous trials in which participants selected the "feels bad" option. Based on prior work examining responses to ambiguity (Neta & Tong, 2016), we also computed average response times (RTs) by expression type (threatening, nonthreatening, ambiguous), as well as RT differences by expression type.

Sensitivity analyses of post-scan behavioral task. One participant demonstrated a decline in performance partway through the post-scan task, which resulted in five blocks in which this participant had low accuracy on angry trials due to repeated button presses. To account for these blocks in which this participant appeared not to be engaging with the task, we conducted sensitivity analyses for all statistical models involving data from the post-scan task. In these analyses, we excluded this participant's response data from the five blocks in which their accuracy on angry and happy trials was less than 80% (N = 100 usable trials). Unless otherwise stated, all reported results from behavioral analyses remained after excluding this participant's low-accuracy blocks.

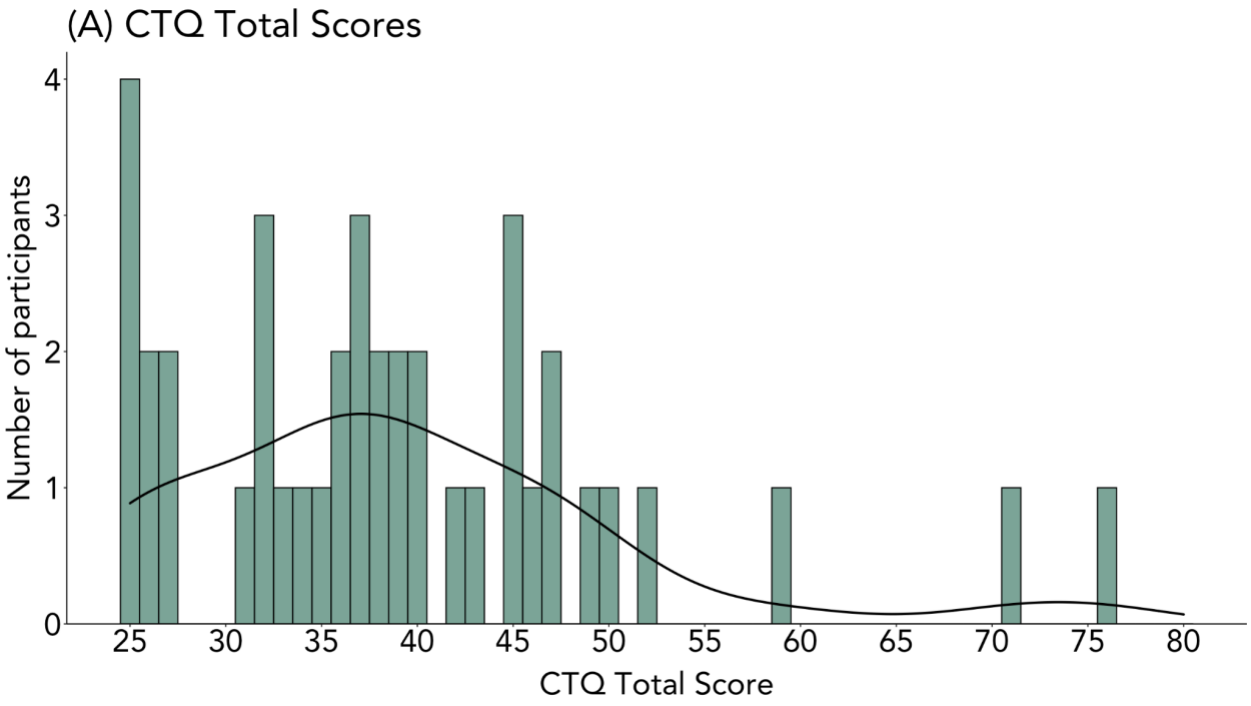
Results.

ELA, global functioning, and post-scan task behavior.

ELA and global functioning. As hypothesized, individuals with greater self-reported ELA reported poorer global functioning (i.e., higher HoNOS scores; $\beta = 0.32$, 95% CI [0.02, 0.63], $t(35) = 2.19$, $p = 0.04$).

ELA and self-reported ambiguity tolerance. We expected ELA to predict decreased self-reported ambiguity tolerance (i.e., lower MSTAT scores). Contrary to our hypothesis, we did not observe a significant association between ELA and self-reported ambiguity tolerance ($\beta = -0.05$; $t(98) = -0.49$; $p = 0.63$).

Post-scan task behavior. We conducted one-tailed t-tests to ensure that accuracy was significantly above chance performance (50%) on the threatening and non-threatening (i.e., unambiguous) trials in the post-scan task. These analyses were conducted in order to verify that participants understood the task instructions. Results confirmed that participants correctly rated angry facial expressions negatively (mean accuracy = 0.93; $t(40) = 30.6$; $p < 0.001$) and happy facial expressions positively (mean accuracy = 0.96; $t(40) = 71.5$; $p < 0.001$). This pattern of high accuracy and agreement in ratings also verified that the valences of these two types of images were indeed unambiguous. In line with prior work (Neta et al., 2009), participants took longer on average to evaluate surprised faces than angry ($t(40) = 8.23$, mean difference = 0.069 ms, 95% CI [0.05, 0.09], $p < 0.001$) or happy ($t(40) = 9.85$, mean difference = 0.097 ms; 95% CI [0.08, 0.12], $p < 0.001$) faces, supporting the idea that that surprised facial expressions are more ambiguously valenced. In line with prior work (Neta & Tong, 2016), across participants, surprised trials were interpreted negatively more often than positively (*Figure 3C*).



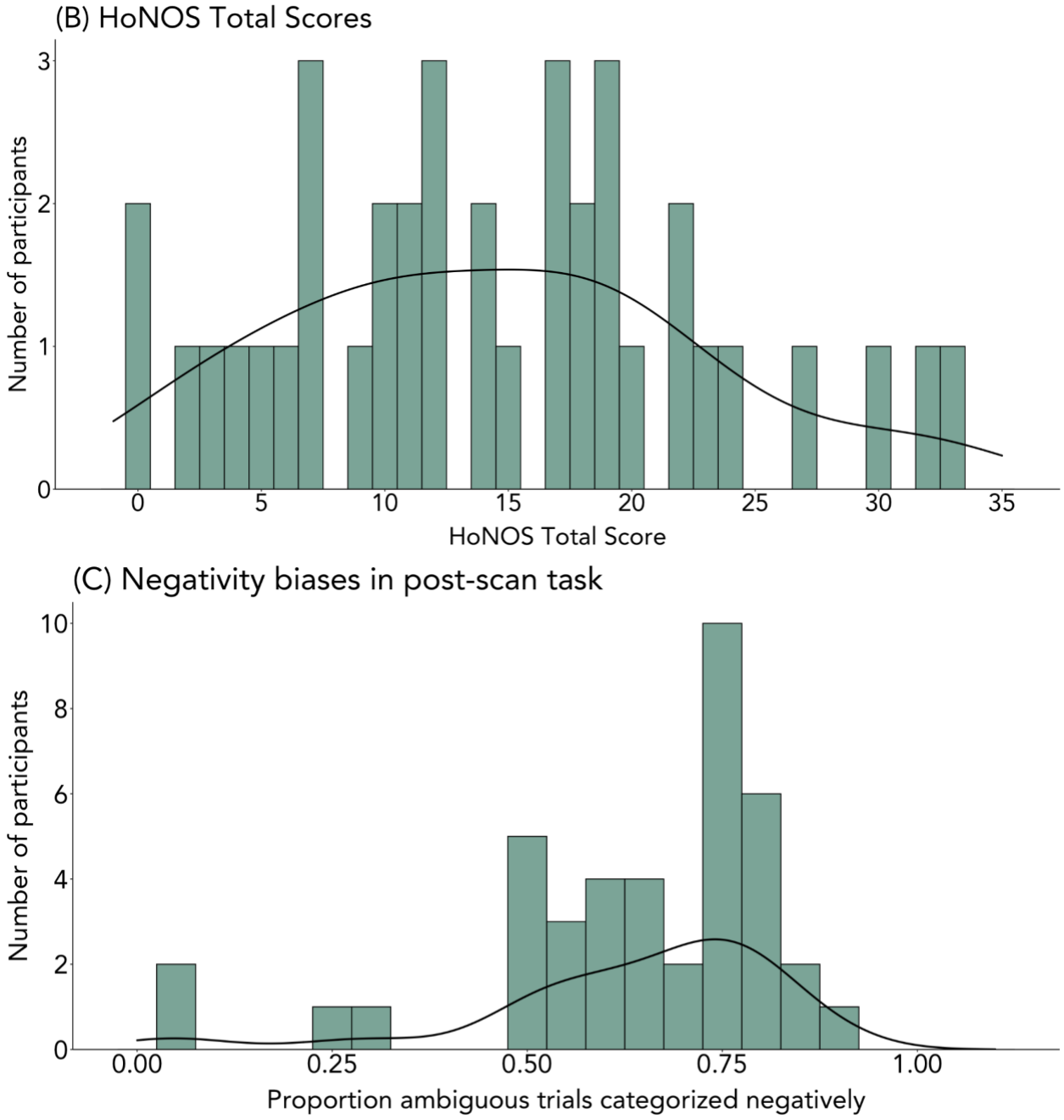


Figure 3. Distributions of questionnaire scores and behavioral data. (A) Distribution of Childhood Trauma Questionnaire (CTQ) total scores. (B) Distribution of Health of the Nation Outcomes Scale (HoNOS) total scores. Note that greater scores indicate greater impairment in global functioning.(C) Distribution of negativity biases, or percent of surprised trials (N = 100 total) interpreted negatively in the behavioral task.

ELA, negativity biases, and global functioning. We next tested whether ELA or global functioning related to negativity biases (i.e., the percent of ambiguous trials categorized negatively). After controlling for global functioning, individuals with greater ELA scores demonstrated a greater negativity bias (categorized a greater number of ambiguous faces negatively; β = 0.34, 95% CI [0.002, 0.68], $t(34) = 2.04$, $p = 0.049$). After excluding one participant's low-accuracy blocks in a sensitivity analysis (see *Sensitivity analyses of post-scan behavioral task* for description), this association was trending (β = 0.34, 95% CI [-0.005, 0.68], $t(34) = 2.00$, $p = 0.05$). Based on this sensitivity analysis and given that, on their own, neither ELA (*Supplemental Table 1*) nor global functioning (*Supplemental Table 2*) was associated with negativity biases, we caution against strong interpretation of this finding. Contrary to our hypothesis, ELA and negativity biases did not interact to predict psychosocial functioning (β = 0.10, 95% CI [-0.20, 0.41], $t(33) = 0.69$, $p = 0.50$; *Supplemental Table 3*).

Task reaction times and evaluations of ambiguous stimuli. We next examined the relationship between reaction time (RT) and evaluations of the stimuli. Between-subject average RTs to ambiguous images did not predict negativity biases (*Supplemental Table 4*). However, in line with prior work (Neta & Tong, 2016), longer within-subject, trial-level RTs predicted more positive ratings of ambiguous stimuli in a multilevel model (OR = 1.95; 95% CI [1.44, 2.65], z = 4.29, $p < 0.01$).

Based on prior work suggesting that taking time to evaluate ambiguity may engage emotion regulation processes (Neta et al., 2022), we sought to determine whether ELA moderated association between time spent evaluating ambiguous (relative to unambiguous) stimuli and global functioning. We observed an interaction between RT differences and ELA exposure, such that taking more time on average to evaluate ambiguous, relative to threatening (b = 5.88, 95% CI

[0.81, 10.95], *t*(33) = 2.36, *p* = 0.02; *Figure 4A*) and nonthreatening (b = 6.86, 95% CI [0.73, 12.99], *t*(33) = 2.28, *p* = 0.03; *Figure 4B*), images was associated with better global functioning, specifically in individuals with lower ELA scores.

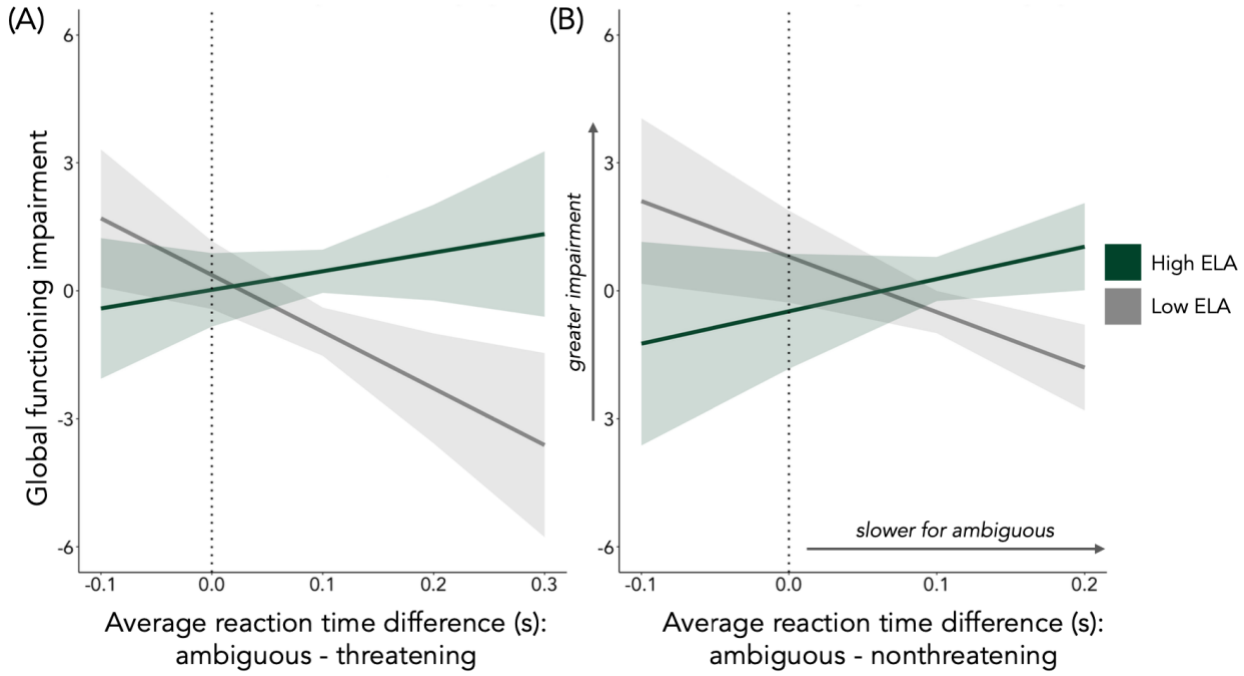


Figure 4. ELA interacted with reaction time to ambiguous cues to predict global functioning. For individuals exposed to lower levels of ELA, taking more time on average to evaluate ambiguous, relative to threatening (A) and nonthreatening (B) images was associated with better global functioning. The simple slopes for the association between ambiguous vs. threatening reaction difference and global functioning (A) are *b* = 4.36 and *b* = -13.28 for high and low ELA, respectively. The simple slopes for the association between ambiguous vs. nonthreatening reaction difference and global functioning (B) are *b* = 7.58 and *b* = -13.01 for high and low ELA, respectively. ELA was measured continuously, but is plotted categorically, at high (*z* = 1.5, in green) and low (*z* = -1.5, in gray) levels for visualization purposes only. Shaded regions represent 95% confidence intervals.

ELA and similarity in neural representations of nonthreatening, threatening, and ambiguous stimuli.

Using RSA, we tested our hypothesis that individuals with higher self-reported ELA would demonstrate greater similarity ("overlap") in representations of ambiguous and threatening stimuli within the regions of interest. We expected this association to be specific to ambiguous/threatening overlap — that is, we hypothesized no association between ELA and ambiguous/nonthreatening overlap or threatening/nonthreatening overlap.

Representational overlap: Ambiguous and threatening stimuli. As hypothesized, individuals exposed to higher levels of ELA demonstrated greater similarity ("overlap") in multivariate representations of ambiguous and threatening stimuli bilaterally within the amygdala, nucleus accumbens, anterior insula, and vmPFC, but not within the control region, V1 (*Table 2*; *Figure 5*). All associations remained significant after controlling for the number of voxels within a participant's ROI and after adjusting for multiple comparisons across different ROIs by using false discovery rate (FDR)-corrected *q* values (Benjamini & Hochberg, 1995).

Region	**Standardized beta value**	**95% CI**	***t* value**	***p* value**	***q* value**	**Adjusted for ROI size**
Amygdala						
Right	β = 0.05	[0.02, 0.08]	$t(38) = 3.31$	$p < 0.01$	$q = 0.01$	β = 0.05 [0.02, 0.08], $t(37) = 3.26$, $p < 0.01$
Left	β = 0.05	[0.02, 0.08]	$t(38) = 3.07$	$p < 0.01$	$q = 0.01$	β = 0.05 [0.02, 0.08], $t(37) = 3.00$, $p < 0.01$
Nucleus accumbens						
Right	β = 0.03	[0.01, 0.06]	$t(38) = 2.44$	$p = 0.02$	$q = 0.04$	β = 0.03 [0.01, 0.06], $t(37) = 2.43$, $p = 0.02$
Left	β = 0.04	[0.01, 0.07]	$t(38) = 3.16$	$p < 0.01$	$q = 0.01$	β = 0.04 [0.02, 0.07], $t(37) = 3.20$, $p < 0.01$
Anterior insula						
Right	β = 0.04	[0.01, 0.07]	$t(38) = 2.78$	$p < 0.01$	$q = 0.02$	β = 0.04 [0.01, 0.07], $t(37) = 2.52$, $p = 0.02$
Left	β = 0.04	[0.003, 0.08]	$t(38) = 2.20$	$p = 0.03$	$q = 0.04$	β = 0.04 [0.0003, 0.08], $t(37) = 2.04$, $p = 0.049$
vmPFC						
Right	β = 0.04	[0.01, 0.07]	$t(38) = 2.36$	$p = 0.02$	$q = 0.04$	β = 0.04 [0.01, 0.08], $t(37) = 2.38$, $p = 0.02$
Left	β = 0.04	[0.003, 0.07]	$t(38) = 2.24$	$p = 0.03$	$q = 0.04$	β = 0.03 [0.003, 0.07], $t(37) = 2.18$, $p = 0.04$
V1 (control region)						

Right	β = -0.01	[-0.07, 0.05]	$t(38) = -0.27$	$p = 0.79$	$q = 0.88$	β = -0.01 [-0.07, 0.05], $t(37) = -0.24$, $p = 0.81$
Left	β = 0.005	[-0.06, 0.07]	$t(38) = 0.15$	$p = 0.88$	$q = 0.88$	β = 0.01 [-0.06, 0.07], $t(37) = 0.24$, $p = 0.81$

Table 2. ELA was positively associated with greater similarity in multivariate representations of ambiguous and threatening stimuli in the four regions of interest. The same pattern was not evident in V1, the control region tested. Table includes the standardized beta coefficients and test statistics from a linear regression with z-scored log-transformed CTQ scores as the predictor and Fisher z-transformed ambiguous/threatening RSA values as the outcome. Table includes false discovery rate (FDR)-corrected *q* values that adjust for multiple comparisons across different regions. Column on the right includes the same statistics after participant-specific ROI size was added as a covariate in the model.

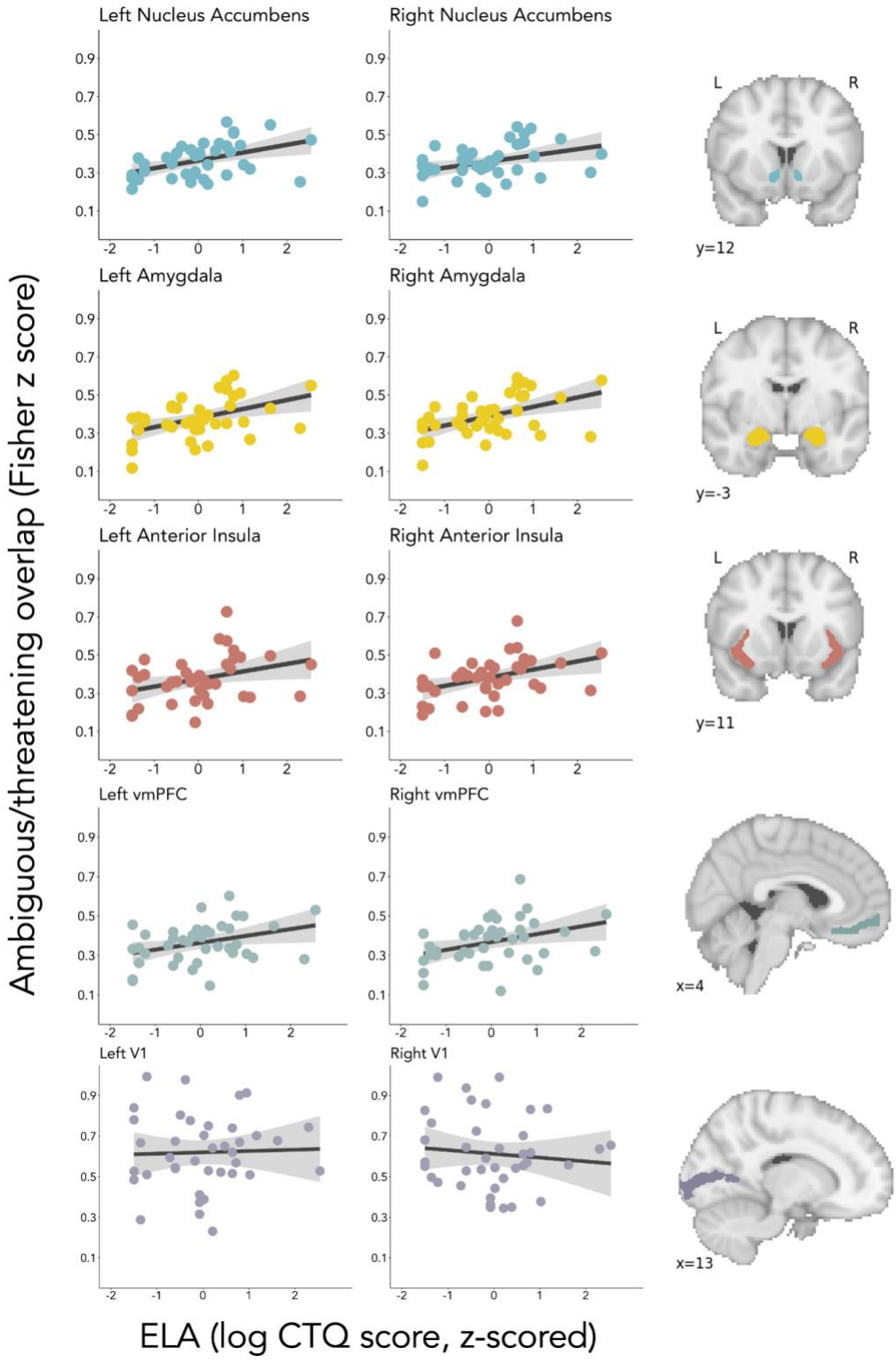


Figure 5. ELA and representational overlap between ambiguous and threatening stimuli. As hypothesized, individuals exposed to higher levels of ELA demonstrated greater representational overlap between ambiguous and threatening stimuli bilaterally within the nucleus accumbens, amygdala, anterior insula, and vmPFC, but not within V1 (control region).

Representational overlap: Ambiguous and nonthreatening stimuli. We next tested whether ELA was associated with representational overlap between ambiguous and nonthreatening stimuli. Contrary to our hypothesis, we found that ELA was positively associated with greater similarity in multivariate representations of ambiguous and nonthreatening stimuli in the right amygdala (β = 0.03; 95% CI [0.01, 0.06]; $t(38) = 2.56$, $p = 0.01$), even after controlling for participant-specific number of voxels within the region (β = 0.03, 95% CI [0.01, 0.06], $t(37) = 2.51$, $p = 0.02$). However, this was no longer significant following FDR-corrected adjustments for multiple comparisons across different ROIs (FDR-adjusted $q = 0.14$; *Supplemental Table 7*). Although a similar pattern was observed in the right anterior insula, this association did not reach significance (β = 0.03; 95% CI [0.00, 0.06]; $t(38) = 1.96$, $p = 0.06$). This association was not evident within any of the other regions tested (*Supplemental Table 6*).

Representational overlap: Threatening and nonthreatening stimuli. We next tested whether ELA was associated with representational overlap between threatening and nonthreatening stimuli. Contrary to our hypothesis, we found that individuals with higher ELA scores evidenced greater similarity in representations of threatening and nonthreatening stimuli within the right anterior insula (β = 0.03, 95% CI [0.003, 0.06], $t(38) = 2.23$, $p = 0.03$), even after controlling for the number of voxels within the region (β = 0.04, 95% CI [0.01, 0.06], $t(37) = 2.51$, $p = 0.02$). However, this was no longer significant following FDR-corrected adjustments for multiple comparisons across different ROIs (FDR-adjusted $q = 0.22$; *Supplemental Table 9*). This association was not evident in the left anterior insula or within any of the other regions tested (*Supplemental Table 8*).

Associations between brain, behavior, and global functioning.

Representational overlap between ambiguous and threatening stimuli and global functioning. We hypothesized that greater representational overlap between ambiguous and threatening stimuli would be associated with poorer global functioning. However, we did not observe any significant associations between global functioning and representational similarity between ambiguous and threatening stimuli (*Supplemental Table 10*).

Representational overlap between ambiguous and threatening stimuli and post-scan task behavior. We hypothesized that greater representational similarity between ambiguous and threatening stimuli would predict greater negativity biases in the post-scan task, but we did not observe this hypothesized association (*Supplemental Table 11*).

Discussion.

Exposure to ELA impacts the development of threat-sensitive neural circuitry (Fareri & Tottenham, 2016; Herzberg & Gunnar, 2020). Altered functioning within these networks may underlie hypersensitivity to potential threat in the face of ambiguity, potentiating risk for impaired psychosocial functioning (Lecei & van Winkel, 2020; Nusslock & Miller, 2016). Leveraging RSA to characterize multivariate representations of affective stimuli, we find that emerging adults exposed to ELA demonstrated greater similarity ("overlap") in their representations of ambiguous and threatening images within affective and threat-sensitive circuitry. Notably, rather than a general effect in which individuals with a history of ELA simply exhibited general impairments in differentiating among affective cues, we found that ELA specifically related to attenuated discrimination between ambiguity and threat. These results were not evident in the tested control region (V1), suggesting specificity of the effect to threat-sensitive affective circuitry commonly

found to be affected by ELA exposure (Cohodes et al., 2021; Fareri & Tottenham, 2016; Hein & Monk, 2017).

These results provide support for Lecei and van Winkel's (2020) theoretical model, which stipulates that ELA results in impaired pattern separation (i.e., impaired differentiation, or greater similarity) of emotional information, specifically in the presence of negative or ambiguous stimuli. In turn, this impairment is hypothesized to result in increased fear generalization, threat anticipation, and psychopathological symptoms. Our behavioral findings suggest that individual differences in processing ambiguity relate to global functioning, and that this association varies as a function of ELA exposure. Crucially, we examined these processes in individuals experiencing the transition from adolescence to adulthood. During this developmental stage, risk for psychopathology is heightened (Solmi et al., 2022) — especially within populations with a history of caregiving adversity (van der Vegt et al., 2009) — and responses to ambiguity are believed to have an increased effect on mental health (Bardi et al., 2009; Silvers & Peris, 2023). Results from the current study have implications both for basic models regarding how ELA shapes neural representations of threat and ambiguity, as well as for the role that ambiguity processing may play in psychosocial functioning following early life adversity.

Effects of ELA on representations of threat and ambiguity.

The tendency to represent ambiguity similarly to threat following ELA may reflect an adaptive, learned response stemming from childhood experiences (Lecei & van Winkel, 2020). When repeatedly faced with threatening experiences, it is rational to infer threat when presented with an ambiguous scenario (Dunsmoor & Paz, 2015). Furthermore, having a low threshold for threat detection is an adaptive response that serves to protect an individual living in a high-threat environment from further harm (Boyce & Ellis, 2005; Chaby et al., 2015; Pollak & Kistler, 2002).

The observed pattern of results, in which ELA-exposed individuals demonstrate impaired neural differentiation between ambiguous and threatening social cues, could stem from hypersensitive threat detection mechanisms. Notably, associations with ELA were only robustly observed when comparing neural representations of ambiguous and threatening cues, suggesting that ELA-exposed individuals do not simply exhibit general impairments in differentiating among affective cues. This specificity in observed results dovetails with existing theoretical models of hypersensitivity to threat (McLaughlin & Lambert, 2017), especially in the face of ambiguity (Lecei & van Winkel, 2020), following early life adversity. However, given that representational similarity did not predict subsequent appraisals of the ambiguous stimuli, it is possible that while rapid, initial responses to ambiguity are highly similar to responses to threat in ELA-exposed individuals, top-down compensatory mechanisms regulate responses in the decision-making phase. The role of potential regulatory mechanisms is especially important to consider given that participants were from a sample of college students with relatively healthy psychosocial functioning. Further research on how initial representations of ambiguity and regulatory processes interact to shape behavior is warranted.

Ambiguity processing and psychosocial functioning after ELA exposure.

Contrary to our hypothesis, we did not observe a robust association between ELA and negativity biases in interpretations of ambiguity. Replicating prior work (Neta & Tong, 2016), we found that taking longer to evaluate ambiguous, relative to unambiguous, stimuli predicted subsequent positive appraisals, lending support to the idea that positive evaluations of ambiguity may require top-down regulatory mechanisms (Neta et al., 2022; Neta & Tong, 2016). Based on research linking responses to ambiguous stimuli to psychosocial outcomes (Lissek et al., 2010; Williams et al., 2015), we tested whether behavioral responses to ambiguity related to global

functioning, and whether this differed as a function of ELA exposure. In line with the notion that slower responses to ambiguity reflect regulatory processes, taking longer to evaluate ambiguous relative to unambiguous images was associated with better global functioning, specifically in individuals with lower ELA levels. Research suggests that more deliberative and regulated responses are more advantageous in predictable environments (Kidd et al., 2013). In line with this reasoning, the observed interaction suggests that reliance on slower and ostensibly more calculated evaluations of ambiguity are associated with better functioning in individuals with low exposure to adversity. Investigation in a larger sample is needed to understand how this effect differs at various levels of ELA exposure and whether these group differences are driven by variations in self-regulation or other relevant mechanisms.

Strengths and limitations.

The current study offers novel insights into the associations between ELA and neural processing of emotional information by leveraging multivariate pattern analyses. Our analytic approach enabled us to examine distributed patterns of brain activity within affective circuitry and, crucially, test similarity between multivariate representations of ambiguity and threat. This study design also allowed us to demonstrate specificity in our findings in that we provide evidence that these effects primarily pertain to ambiguity and threat, and within putatively affective, threat-sensitive circuitry. That said, given the limited sample size, the results from this study should be treated as provisional. Future studies replicating the current findings in a larger longitudinal sample could provide greater clarity into how ELA shapes representations of ambiguity.

Prior research suggests that negative responses to ambiguity may reflect hypersensitivity in the affective processes that govern rapid threat detection (J. T.-H. Chen & Lovibond, 2016; Grupe & Nitschke, 2013; Mathews et al., 1997). Based on this work, we designed a task to probe

rapid, uninstructed representations of ambiguity while participants were in the scanner. To this end, we asked participants to simply view the images while in the scanner and measured explicit categorizations of the images during the post-scan task. An important next step for future research is to characterize neural representations during the interpretation stage in which participants explicitly evaluate the valence of ambiguous stimuli. Moreover, based on similar prior work (Vantieghem et al., 2017), and to avoid biasing responses, participants rated whether the person in the image "feels good" or "feels bad". As a result, we did not capture explicit ratings of threat. Future work may benefit from a more precise measurement of the extent to which participants interpret the images as threatening.

Lastly, we measured ELA by incorporating retrospective reports of abuse and neglect into a broader summary measure. Examining ELA continuously via CTQ scores enabled us to demonstrate a linear relationship between severity of adversity history and the degree of similarity in representations of ambiguity and threat. While we did not have adequate power to investigate how different dimensions of experiences (e.g., threat or unpredictability in the caregiving environment) may differentially shape representations of ambiguity, this is an important avenue for future research.

Conclusion.

Exposure to ELA, including experiences of abuse and neglect, is estimated to account for between 30 to 45% of psychopathologies worldwide (J. G. Green et al., 2010; Kessler et al., 2010; McLaughlin et al., 2012). Using multivariate pattern analysis, we provide novel insight into how ELA shapes threat-sensitive neural circuitry, evidencing reduced neural differentiation between ambiguous and threatening cues in ELA-exposed individuals, and link behavioral responses to ambiguity to psychosocial wellbeing during the transition to adulthood. Interventions that target

responses to ambiguity may be particularly powerful in mitigating the detrimental effects of adverse early experiences.

Study 2: Neurobehavioral responses to ambiguity following early life adversity in previously institutionalized youth.

Introduction.

In Study 1, we examined multivariate representations of threatening and ambiguous social cues in a community sample of 41 emerging adults (aged 18 to 19 years). Using representational similarity analysis, we assessed neural representations of ambiguous and threatening images within affective neural circuitry (amygdala, nucleus accumbens, anterior insula, and vmPFC) and tested whether similarity in these representations varied by early life adversity (ELA) exposure (self-reported abuse and neglect during childhood). Results from Study 1 suggest that emerging adults with greater ELA demonstrate greater similarity ("overlap") in their representations of ambiguous and threatening images within affective and threat-sensitive circuitry. Study 2 built upon these findings by testing similar associations (within the same ROIs and control region) in a sample of youth specifically recruited based on history of extreme ELA in the form of institutionalized orphanage care. This study tested two competing hypotheses regarding how similarity in neural representations of ambiguous and threatening cues varies between previously institutionalized (PI) and comparison youth and evaluated whether links between ELA and anxiety are moderated by neural responses to ambiguity.

Study 2 shares many similarities with Study 1 but diverges methodologically in several crucial ways. Firstly, Study 1 examined these processes in a sample of emerging adults (18- to 19-year-olds) who retrospectively reported experiences of neglect and abuse during childhood (before the age of fourteen). Based on these retrospective accounts, cumulative ELA was examined as a continuous variable within this community sample. Study 2 expands this research by comparing representations of ambiguity and threat between a specialized sample of previously

institutionalized (PI) youth and a group of comparison youth, ranging from ages 9.99 to 22.90 years (mean age = 16.33). In doing so, this work not only tests these processes in a unique sample with a specific history of ELA, but also expands the age range in question to include a broader range of adolescents and emerging adults. Secondly, whereas Study 1 operationalized threatening and ambiguous social cues as angry and surprised faces respectively, Study 2 uses fearful and neutral faces as the threatening and ambiguous cues. Prior work in PI samples has similarly used fearful and neutral faces to probe processing of threat-related and emotional cues (Silvers et al., 2017; Tottenham et al., 2011). Moreover, prior work in developmental samples has compared reactions to surprised and neutral faces as ambiguous stimuli and found that, for both expression types, individuals vary in their interpretations (suggesting that these stimuli do have ambiguous properties), with a bias toward negative interpretations in children and adolescents (Tottenham et al., 2013). This suggests that both surprised and neutral facial expressions can be used to probe reactions to ambiguous stimuli in developmental samples (Tottenham et al., 2013). Therefore, unlike Study 1 (which used angry and surprised faces), in Study 2, fearful and neutral faces serve as the threatening and ambiguous cues. This difference in task design enabled us to examine whether the previously observed associations replicate in a task with similar, but distinct stimuli. If so, this would suggest that prior findings do not simply reflect an artifact of the visual properties of the previously used stimuli and are not specifically linked to the specific emotions portrayed (i.e., angry and surprised faces). In doing so, this would lend support for the hypothesis that the ambiguous nature of expressions with unclear valence (i.e., surprised or neutral faces), coupled with the threatening nature of negatively valenced stimuli (i.e., angry or fearful faces), are the central component linking ELA to differences in representational similarity — that is, rather than depending on a specific emotion type (such as anger), the observed effects more broadly reflect

neural representations of ambiguous and threatening cues. Lastly, although differences in ambiguity tolerance are linked to several forms of psychopathology (Boswell et al., 2013; Einstein, 2014; McEvoy & Mahoney, 2012), negative interpretations of ambiguity are most consistently linked to anxiety disorders (J. Chen et al., 2020; Norr et al., 2013). Given the heightened risk for anxiety in PI youth (Silvers et al., 2017; Tottenham et al., 2010), Study 2 examined wellbeing in terms of anxiety, rather than the more general measure of global functioning examined in the Study 1 sample.

Given the unique experiences of the PI youth in this sample, a group exposed to a rare and extreme form of adversity, and the age differences between the two samples we expected that findings might differ from Study 1 findings. Based on Study 1 and previous literature, we expected to see group differences in neural representations of ambiguity between PI and control groups. However, contradicting findings from the few studies examining responses to ambiguity as a function of ELA suggest that these differences could unfold in several ways. Here, we consider two possibilities, which we refer to as the *threat sensitivity hypothesis* and the *accelerated maturation hypothesis*. Results from Study 1 suggest that ELA is associated with greater similarity in neural representations of ambiguous and threatening images — potentially reflecting hypersensitivity to potential threat. Based on these results, the *threat sensitivity hypothesis* posits that, relative to the comparison group, the PI group would demonstrate greater similarity in representations of ambiguous and threatening stimuli within the regions of interest but not the control region. Behavioral work in PI youth, however, presents an alternative possibility. VanTieghem et al. (2017) found that, relative to comparison youth, six-to fourteen-year-old PI youth were more likely to interpret ambiguous cues positively (i.e., exhibit a positive valence bias), a behavioral phenotype the authors consider to reflect more "adult-like" processing and potentially

indicate accelerated development. This could suggest that different forms of ELA elicit different developmental consequences with regards to ambiguity processing. Given the older age range of our sample (ages 9 to 22), group differences arising from putative differences in maturation will likely be more difficult to detect. That said, it is still possible that this observed tendency for PI youth to respond more positively to ambiguous cues may be similarly evident on the neural level even in our older sample. The *accelerated maturation hypothesis* therefore posits that, relative to the comparison group, the PI group would demonstrate greater similarity in representations of ambiguous and nonthreatening stimuli within the regions of interest but not the control region.

Based on several studies demonstrating heightened anxiety in PI youth (Silvers et al., 2017; Tottenham et al., 2010), we hypothesized that individuals in the PI group would exhibit higher anxiety levels. We also tested whether representational overlap between ambiguous and threatening or ambiguous and nonthreatening stimuli within the amygdala moderated the relationship between group (PI vs. control) and anxiety levels. Based on prior work, we hypothesized that greater overlap between representations of ambiguous and nonthreatening stimuli within the amygdala would buffer anxiety (Saragosa-Harris et al., 2023), and that this buffering effect would be pronounced in the PI group (Lange et al., 2019).

Methods.

Participants. Data from this study are part of a larger longitudinal study examining brain development and mental health following early life adversity. The final sample size was determined by the number of participants with usable fMRI data who completed the task and did not exceed motion thresholds. Participants who had 20% or more of individual volumes across the task with a framewise displacement greater than 0.9 mm were excluded. After this criteria, 81

participants were included in analyses (*N* = 47 female; ages 9.99 to 22.90 years; mean age = 16.33). This sample includes previously institutionalized (PI) youth (*N* = 36 total; *N* = 25 female; mean age = 17.50) who were exposed to extreme ELA in the form of orphanage care and comparison youth (*N* = 45 total; *N* = 22 female; mean age = 15.38). The mean age of the PI group was significantly higher than the mean age of the control group (*t*(78.83) = 2.88, 95% CI [0.66, 3.59], *p* = 0.01). Participant demographics are included in *Table 3* below.

All study procedures were completed in accordance with the University of California Los Angeles Institutional Review Board (IRB 19-000001). Methods and analysis plans were preregistered on Open Science Framework prior to analyses (https://osf.io/2793f/).

Variable	Control N = 45[1]	PI N = 36[1]
Sex assigned at birth		
Female	22 (49%)	25 (69%)
Male	23 (51%)	11 (31%)
Age	15.4 (3.8)	17.5 (2.9)
Race		
African American/Black	6 (14%)	1 (2.8%)
Asian	5 (12%)	16 (44%)
Multiracial	5 (12%)	5 (14%)
Native Hawaiian or Other Pacific Islander	1 (2.4%)	0 (0%)
Other	4 (9.5%)	3 (8.3%)
White	21 (50%)	11 (31%)
(No data)	3	0
Hispanic or Latino	6 (13%)	0 (0%)
(No data)	0	6

[1] n (%); Mean (SD)

Table 3. Participant self-reported demographics.

Questionnaires.

Self-reported anxiety. To assess self-reported anxiety symptomatology, participants ages 18 and older (N = 30) were administered the State-Trait Anxiety Inventory (STAI) Form Y (C. Spielberger et al., 1983), which measures state and trait anxiety symptoms. For the 20 items on the state anxiety subscale, participants are asked to describe the extent to which they agree each statement indicates how they feel "right now, at this moment" using a four-point Likert scale (1 = not at all, 2 = somewhat, 3 = moderately so, 4 = very much so). Similarly, for the 20 items on the trait anxiety subscale, participants use the same Likert scale to rate the extent to which they agree each statement indicates how they generally feel. The STAI is a commonly used anxiety measure that has been validated in adults and the state and trait subscales have been shown to have high internal consistency (C.D. Spielberger et al., 1971). Scores for the trait subscale, which we analyzed in this study, have been shown to be stable over time (C.D. Spielberger et al., 1971). Scores are totaled within each subscale to indicate overall state and trait anxiety, with higher scores indicating higher anxiety.

Participants younger than age 18 (N = 51) were administered the child version of the Screen for Child Anxiety Related Disorders (SCARED), a 41-item questionnaire assaying anxiety symptoms. Their parent or caregiver was also administered a version of the questionnaire in which they answered the questions about their child. For each item on the scale, participants are asked to rate the extent to which they agree each statement describes how they have (or their child has) felt in the last three months using a three point Likert scale (0 = not true or hardly ever true, 1 = somewhat true or sometimes true, 2 = very true or often true). The SCARED has been validated in children and adolescents (Birmaher et al., 1997, 1999; Monga et al., 2000) and corresponds well to the STAI trait subscale (Monga et al., 2000). The SCARED measures anxiety symptoms across

five factors: panic/somatic, generalized anxiety, separation anxiety, social anxiety, and significant school avoidance. Item responses yield scores for each of the five subscales. A total score is calculated by totaling responses across all items.

In order to include child and adult self-reported anxiety scores in the same model, anxiety scores were normalized (z-scored) by age group (corresponding to which questionnaire they completed) in order to put the SCARED and STAI total scores on the same scale.

fMRI task and analysis plan.

fMRI paradigm. Participants completed an emotional go/no-go task (Hare et al., 2008) while undergoing fMRI imaging. In the task, participants were shown a series of neutral, fearful, and happy facial expressions from four female actors from the NimStim dataset (Tottenham et al., 2009). Here, neutral faces are considered the ambiguous stimulus, fearful faces are considered the threatening stimulus, and happy faces are considered the nonthreatening stimulus. There were two runs in the task, each of which had 48 trials total. In both runs, there were 24 neutral image trials. One run had 24 fearful image trials and the other had 24 happy image trials (*Figure 6*). Run order was counterbalanced across participants. On each trial, participants were shown an image on the screen for 500 ms. A fixation cross was presented in between trials with a jitter between 300 to 1000 ms. Participants were instructed to press the button box when they saw a neutral face.

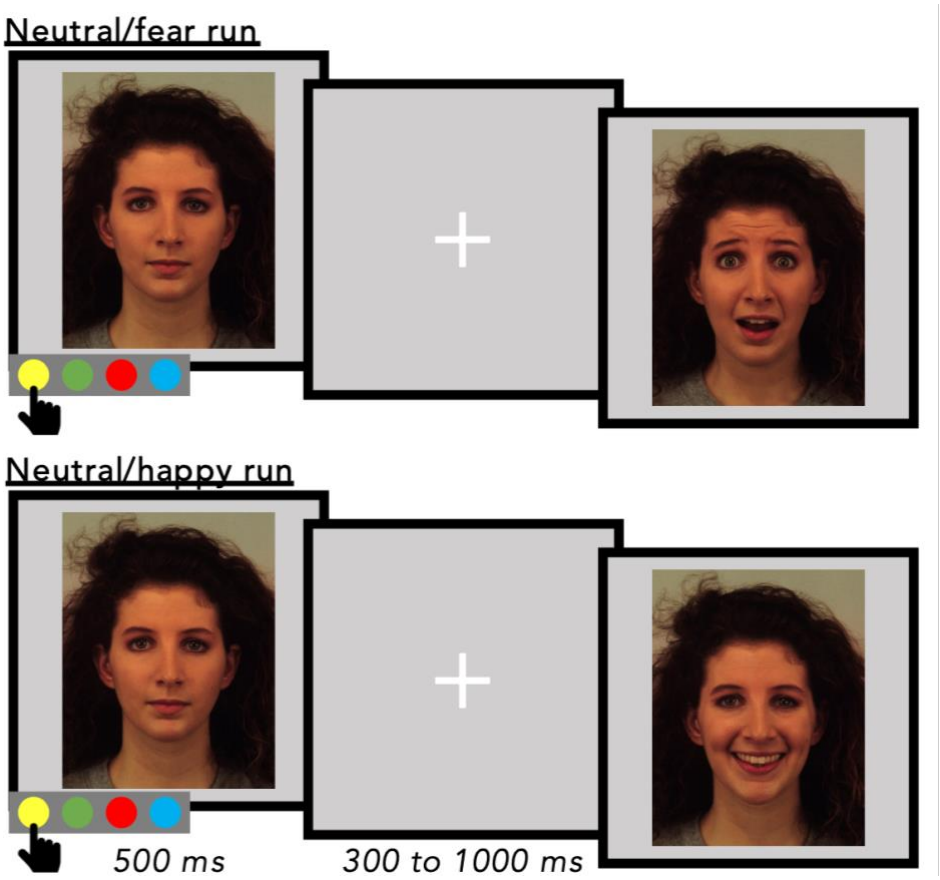


Figure 6. Study 2 task design. Participants viewed ambiguous (neutral), threatening (fearful), and nonthreatening (happy) faces in the fMRI task and were instructed to press the button box when they saw a neutral face. Same actress shown here for illustrative purposes.

fMRI acquisition. Data were acquired on a 3T Siemens Magnetom Prisma scanner using a 32-channel head coil. Functional data were acquired using the following parameters: voxel size = 3.0 x 3.0 x 4.0 mm, slices = 33 (interleaved), slice thickness = 4.0 mm, repetition time (TR) = 2000 ms, echo time (TE) = 30 ms, flip angle = 75°, field of view = 192 mm. AutoAlign was used to position and align slices. Structural images were acquired using a high-resolution MPRAGE sequence (voxel size = 0.8 x 0.8 x 0.8 mm; TR = 2400 ms, echo time = 2.22 ms, field of view = 256 mm, slice thickness = 0.8 mm, 208 slices).

fMRI preprocessing. Processing of fMRI data was carried out using FEAT (FMRI Expert Analysis Tool) Version 6.00, part of FSL (FMRIB's Software Library, www.fmrib.ox.ac.uk/fsl). Functional data were registered to participants' high resolution structural images using boundary based registration (BBR) (Greve & Fischl, 2009). High resolution structural images were registered to standard space (MNI 2.0 x 2.0 x 2.0 mm stereotaxic space) with 12 degrees of freedom using FLIRT (FMRIB's Linear Image Registration Tool) (Jenkinson et al., 2002; Jenkinson & Smith, 2001) and FNIRT nonlinear registration (J. Andersson et al., 2007; J. L. Andersson et al., 2007). Preprocessing included motion correction using MCFLIRT (Jenkinson et al., 2002) using 24 standard and extended regressors, non-brain extraction using BET (Brain Extraction Tool) (Smith, 2002), grand-mean intensity normalization, and high-pass temporal filtering (Gaussian-weighted least-squares straight line fitting, with sigma = 50.0s). As in Study 1, we did not apply smoothing for multivariate analyses. For univariate analyses only (*Supplemental Figure 4*), we used 3.5 mm full-width half maximum smoothing. We used FILM (FMRIB's Improved Linear Model) prewhitening with local autocorrelation correction (Woolrich et al., 2001) in analyses.

First level modeling. As in Study 1, BOLD response patterns were modeled in FSL using first level (i.e., within-participant, within-run) models. There were two general linear models (GLMs) per participant (one per run). One run GLM included a regressor for threatening (fearful) and ambiguous (neutral) trials and the other included a regressor for nonthreatening (happy) and ambiguous (neutral) trials. Regressors were modeled using a double-gamma hemodynamic response function (HRF). Fixation crosses presented between trials were not explicitly modeled and served as implicit baseline. Temporal derivatives for all regressors were included as covariates. To account for head motion, individual volumes with a framewise displacement greater than 0.9

mm were included as regressors (spike regressors created using 'fsl_motion_outliers'). Motion regressors and their derivatives were included as regressors of no interest.

Regions of interest. We applied representational similarity analyses in the same four regions of interest (ROIs; amygdala, nucleus accumbens, anterior insula, and vmPFC) in Study 1, which were chosen based on (1) their hypothesized role in responding to motivationally salient stimuli, especially ambiguous and potentially threatening signals (Tanovic et al., 2018) and (2) research demonstrating ELA-related functional differences within these regions (Fareri & Tottenham, 2016). As in Study 1, we tested V1 as a control region expected to respond to the affective visual stimuli (Kragel et al., 2019). We used the same procedures as in Study 1 to define these five regions (see *Regions of Interest* in Study 1 for a detailed description).

Representational similarity analysis. We used the same procedures as in Study 1 to conduct representational similarity analysis. The primary difference is that, while Study 1 had three runs of the task (and thus three first level models per participant), Study 2 only had two runs of the task (and thus two first level models per participant). As in Study 1, we used the function 'NiftiMasker' in the Python package 'nilearn' (Abraham et al., 2014) to extract vectors of voxel-level coefficients within each ROI. Each vector corresponded to a regressor of interest (ambiguous, threatening, or nonthreatening) from the aforementioned first level model for a given ROI per run. Thus, each vector was participant-specific, run-specific, ROI-specific, and condition-specific. We used these vectors to compute two pairwise Pearson correlations between stimulus conditions (ambiguous/threatening and ambiguous/nonthreatening), resulting in two correlations per ROI for a given participant. We then applied Fisher's r-to-z transformation to the averaged Pearson correlation values (Dimsdale-Zucker & Ranganath, 2018) to represent ROI-specific similarity in patterns of representations between (1) ambiguous and threatening and (2) ambiguous and

nonthreatening facial expressions, with greater values indicating relatively greater similarity in voxelwise patterns of activation.

Statistical analyses.

To test the *threat sensitivity hypothesis*, we used a linear regression to test whether, after controlling for age, relative to the comparison group, the PI group demonstrates greater similarity in representations of ambiguous and threatening stimuli within the regions of interest but not the control region. To test the *accelerated maturation hypothesis*, we used a linear regression to test whether, after controlling for age, relative to the comparison group, the PI group demonstrates greater similarity in representations of ambiguous and nonthreatening stimuli within the regions of interest but not the control region. Given the significant difference in age between the PI and control group, we also performed sensitivity analyses in which we controlled for linear age when testing these associations.

We used a linear regression to test whether there are group differences in anxiety levels. We hypothesized that individuals in the PI group would exhibit higher anxiety levels. Additionally, we tested interactions to determine whether representational overlap between ambiguous and nonthreatening, or ambiguous and nonthreatening, stimuli within the amygdala moderate the relationship between group (PI vs. control) and anxiety levels.

Results.

ELA group and anxiety. Using a linear regression, we examined whether, after controlling for age group (child or adult), ELA group (PI or control) predicted z-scored self-reported anxiety scores. In order to include child and adult self-reported anxiety scores in the same model, anxiety

scores were normalized (z-scored) by age group in order to put the SCARED and STAI total scores on the same scale. Neither age group (b = 0.09, 95% CI [-0.387, 0.57], $t(77) = 0.40$, $p = 0.69$) nor ELA group (b = 0.35, 95% CI [-0.11, 0.81], $t(77) = 1.53$, $p = 0.13$) predicted self-reported anxiety scores. We then examined the relationship between ELA group and total anxiety scores separately by age group. Among participants 18 years or older, ELA group was not significantly associated with self-reported STAI anxiety scores (b = 0.42, 95% CI [-0.36, 1.20], $t(27) = 1.10$, $p = 0.28$). Among participants younger than 18 years old, ELA group was not significantly associated with self-reported SCARED anxiety scores (b = 0.31, 95% CI [-0.28, 0.90], $t(49) = 1.07$, $p = 0.29$). For participants younger than 18 years old, we also examined caregiver-reported SCARED total scores. Although caregiver-reported anxiety was higher on average in the PI group, there was not a significant group difference in scores (b = 0.51, 95% CI [-0.07, 1.08], $t(47) = 1.77$, $p = 0.08$). Thus, although the PI group demonstrated greater mean anxiety scores, there were no significant group differences in total self-reported anxiety scores between the PI and control groups (*Figure 7*).

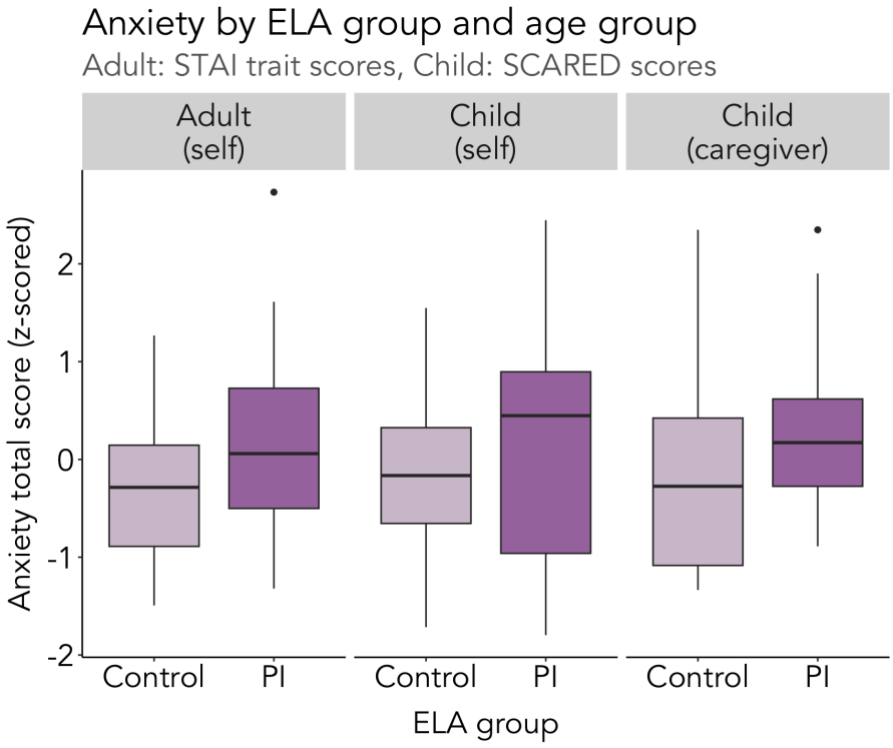


Figure 7. Anxiety by ELA group and age group. Adult participants (ages 18 and older) were administered the State-Trait Anxiety Inventory (STAI) Form Y, while child participants (younger than 18 years) were administered the self-report Screen for Child Anxiety Related Disorders (SCARED) questionnaire, and their caregivers were administered the caregiver-report SCARED questionnaire to answer on their behalf. Reporter for a given questionnaire is indicated in parentheses. For both the STAI and SCARED questionnaires, total scores were normalized (z-scored) by age group in order to put the total scores from the separate questionnaires on the same scale.

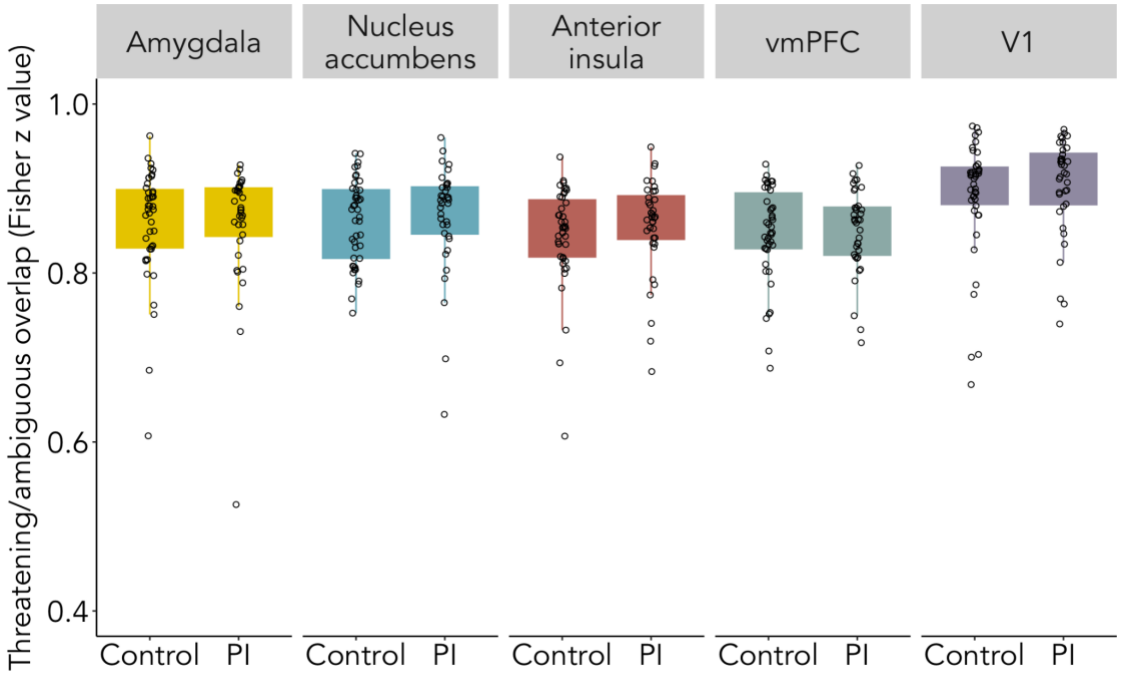
Average representational similarity values. For descriptive purposes, we calculated the average representational overlap values (Fisher z-transformed correlations) between threatening (fearful) and ambiguous (neutral) images and between nonthreatening (happy) and ambiguous (neutral) images in the five regions of interest. Here, we report averages and standard deviations of the Fisher z-transformed correlations within each region across the entire sample. Average Fisher z scores corresponding to representational overlap between threatening and ambiguous representations were as follows: amygdala ($\mu = 0.86$; sd = 0.07), nucleus accumbens ($\mu = 0.86$; sd

= 0.06), anterior insula (μ = 0.85; sd = 0.06), vmPFC (μ = 0.85; sd = 0.05), and V1 (μ = 0.90; sd = 0.07). Average Fisher z scores corresponding to representational overlap between nonthreatening and ambiguous representations were as follows: amygdala (μ = 0.84; sd = 0.06), nucleus accumbens (μ = 0.84; sd = 0.06), anterior insula (μ = 0.84; sd = 0.07), vmPFC (μ = 0.84; sd = 0.07), and V1 (μ = 0.87; sd = 0.07).

ELA group and representational similarity between threatening and ambiguous images. We next tested whether ELA group predicted representational overlap between threatening (fearful) and ambiguous (neutral) images in the five regions of interest. In these models, ELA group (PI or control) was the predictor variable and Fisher z-transformed correlations between angry and neutral images within a given region of interest (ROI) was the outcome variable. To account for between-participant differences in the size of a given ROI, participant-specific number of voxels within a given region was included as a control variable. Contrary to the threat sensitivity hypothesis, ELA group was not significantly associated with representational similarity between threatening and ambiguous images within the amygdala (b = -0.01, 95% CI [-0.05, 0.02], $t(76)$ = -0.80, p = 0.43), nucleus accumbens (b = 0.01, 95% CI [-0.02, 0.03], $t(76)$ = 0.50, p = 0.62), anterior insula (b = 0.02, 95% CI [-0.01, 0.04], $t(76)$ = 1.17, p = 0.25), or vmPFC (b = -0.001, 95% CI [-0.03, 0.02], $t(75)$ = -0.04, p = 0.97). There was also not a significant association between ELA group and representational similarity between threatening and ambiguous images within V1 (b = 0.02, 95% CI [-0.01, 0.06], $t(75)$ = 1.36, p = 0.18), the control region (*Figure 8a*). These associations remained nonsignificant after controlling for linear age (*Supplemental Table 12*). Average representational similarity values (i.e., Fisher z-transformed correlations) between threatening and ambiguous images by ELA group and region are provided in *Table 4*.

ELA group and representational similarity between nonthreatening and ambiguous images. We next tested whether ELA group predicted representational overlap between nonthreatening (happy) and ambiguous (neutral) images in the five regions of interest. In these models, ELA group (PI or control) was the predictor variable and Fisher z-transformed correlations between happy and neutral images within a given region of interest (ROI) was the outcome variable. Participant-specific number of voxels within a given region was included as a control variable. Contrary to the accelerated maturation hypothesis, ELA group was not significantly associated with representational similarity between nonthreatening and ambiguous images within the amygdala (b = 0.01, 95% CI [-0.02, 0.04], $t(77)$ = 0.79, p = 0.43), nucleus accumbens (b = -0.004, 95% CI [-0.03, 0.02], $t(77)$ = -0.28, p = 0.78), anterior insula (b = -0.01, 95% CI [-0.04, 0.02], $t(77)$ = -0.49, p = 0.63), or vmPFC (b = 0.01, 95% CI [-0.02, 0.04], $t(77)$ = 0.41, p = 0.68). There was also not a significant association between ELA group and representational similarity between nonthreatening and ambiguous images within V1 (b = 0.005, 95% CI [-0.03, 0.04], $t(76)$ = 0.28, p = 0.78), the control region (*Figure 8b*). These associations remained nonsignificant after controlling for linear age (*Supplemental Table 13*). Average representational similarity values (i.e., Fisher z-transformed correlations) between nonthreatening and ambiguous images by ELA group and region are provided in *Table 4*.

(A)



(B)

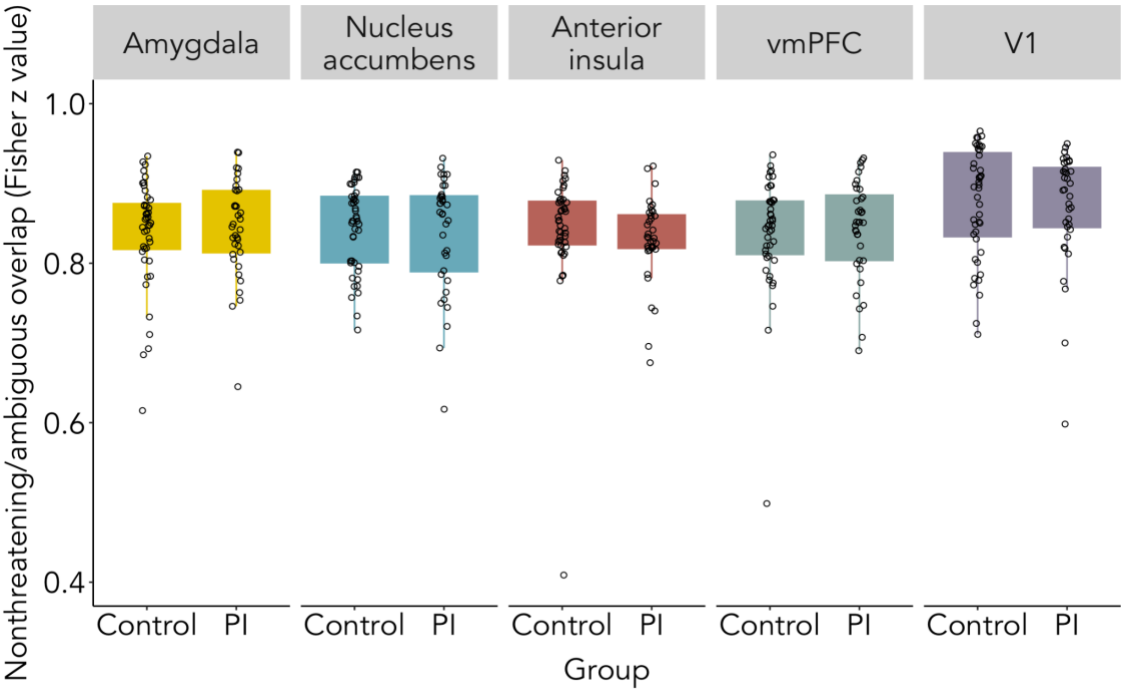


Figure 8. Representational similarity by ELA group. Representational similarity (i.e., overlap), corresponding to Fisher z-transformed correlations, between (A) threatening and ambiguous images and (B) nonthreatening and ambiguous images by ELA group and region.

	Threatening/ambiguous overlap		Nonthreatening/ambiguous overlap	
Region	Control[1]	PI[1]	Control[1]	PI[1]
Amygdala	0.86 (0.07)	0.86 (0.07)	0.84 (0.07)	0.84 (0.06)
Anterior insula	0.84 (0.06)	0.86 (0.06)	0.84 (0.08)	0.83 (0.05)
Nucleus accumbens	0.86 (0.05)	0.87 (0.06)	0.84 (0.05)	0.84 (0.07)
vmPFC	0.85 (0.06)	0.85 (0.05)	0.84 (0.07)	0.84 (0.06)
V1	0.89 (0.07)	0.90 (0.06)	0.88 (0.07)	0.87 (0.07)

[1] Mean (SD)

Table 4. Average and standard deviation of representational similarity (i.e., overlap), corresponding to Fisher z-transformed correlations, between threatening and ambiguous images and nonthreatening and ambiguous images by ELA group and region.

Interactions between ELA group and representational similarity in the amygdala in predicting anxiety. In a previous study (Saragosa-Harris et al., 2023), we found that greater representational overlap between nonthreatening and ambiguous images within the amygdala buffered anxiety symptoms in emerging adults. We tested interactions to evaluate whether ELA group and representational similarity between threatening and ambiguous images (*Supplemental Table 14*), or nonthreatening and ambiguous images (*Supplemental Table 15*), within the amygdala interact to predict anxiety symptoms. Age group, which corresponded to which anxiety questionnaire participants completed, was included as a control variable. Contrary to our hypotheses, we did not observe a significant interaction between ELA group and representational overlap between threatening and ambiguous images (b = 0.15, 95% CI [-6.17, 6.48], $t(73)$ = 0.05, p = 0.96) or between ELA group and representational overlap between nonthreatening and ambiguous images (b = -2.32, 95% CI [-9.41, 4.76], $t(74)$ = -0.65, p = 0.52) in predicting self-reported anxiety.

Discussion.

Early life adversity is estimated to affect approximately over 60% of American youth (Merrick et al., 2018). Institutionalization in orphanage care, however, is an exceedingly rare and extreme form of adversity. Individuals adopted from orphanages represent an incredibly unique group: These youth not only had the rare experience of institutional rearing during infancy, but they also experienced an uncommon and significant shift in their caregiving environment early in development in the form of adoption to a stable home. Prior work in PI youth has linked this form of caregiving deprivation to a number of psychopathologies (Humphreys, Gleason, et al., 2015; Tottenham et al., 2010; Wiik et al., 2011; Zeanah et al., 2009), as well as broader difficulties with attention (Gunnar et al., 2007) and emotion regulation (Tottenham et al., 2010). Research within this population offers key insights into how severe caregiving deprivation — specifically during infancy and early toddlerhood — has persistent effects on mental health into adulthood. In Study 2, we examined how previous institutionalization shapes multivariate neural representations of ambiguity and threat. Using representational similarity analysis (RSA), we compared similarity in neural representations of ambiguous and threatening, and ambiguous and nonthreatening, images in previously institutionalized (PI) and comparison youth. Contrary to our hypotheses, representational similarity did not significantly differ by ELA group. Moreover, neural similarity patterns did not relate to anxiety symptomatology. Although these patterns do not mirror those observed in Study 1, there are notable differences in study design between the two studies that may account for differences in observed results.

Prior work suggests that neurobehavioral responses to ambiguity are predictive of mental health challenges (Carleton, 2016; Taghavi et al., 2000). Given the robust links between previous institutionalization and mental health challenges (Humphreys, Gleason, et al., 2015; Tottenham et

al., 2010; Wiik et al., 2011; Zeanah et al., 2009), Study 2 aimed to characterize representations of ambiguity in this unique population to test whether this might form a mechanistic link between experiences and risk for psychopathology. In Study 1, we found that individuals with greater ELA history demonstrated greater similarity in representations of ambiguity and threat, patterns that could reflect hypervigilance to potential threat. Based on these findings and other work linking ELA to threat hypervigilance (Pollak & Kistler, 2002), the *threat sensitivity hypothesis* posited that relative to the comparison group, the PI group would demonstrate greater similarity in representations of ambiguous and threatening stimuli. However, we did not observe any significant group differences in representational similarity between ambiguous and threatening images within any of the regions of interest.

Although some studies link ELA to more negative or threatening evaluations of ambiguous social cues (i.e., decreased ambiguity tolerance), others evidence seemingly opposite patterns. For instance, prior research has demonstrated unusually trusting behavior toward unfamiliar adults in youth who have experienced caregiving adversity, patterns that could suggest greater tolerance for ambiguous social cues. Specifically, prior work has noted high levels of "indiscriminate friendliness" in PI youth (Chisholm, 1998) and maltreated foster youth (Pears et al., 2010). In these cases, children exhibit affectionate or friendly behavior toward unfamiliar adults, including strangers, without exhibiting the fearful or cautious behaviors considered typical for their developmental stage. The tendency to respond to strangers as though they are a trusted adult rather than exhibiting a fear response typical for their developmental stage could reflect more optimistic evaluations of ambiguous social cues. In line with this work, VanTieghem et al. (2017) found that PI youth were more likely than comparison youth to interpret ambiguous facial expressions positively. VanTieghem et al. (2017) considered this pattern to reflect more "adult-like" processing

and potentially indicate accelerated development in the PI group. Although our sample included an older age range of participants — making it difficult to assess whether between-group differences indicate accelerated development — it is still possible that this observed tendency for PI youth to respond more positively to ambiguous cues could be similarly evident on the neural level in older samples. Based on this reasoning, the *accelerated maturation hypothesis* posited that, relative to the comparison group, the PI group would demonstrate greater similarity in representations of ambiguous and nonthreatening stimuli. I describe this prior work to illustrate the conflicting evidence in the literature for how ELA shapes representations of ambiguity but underscore that we do not find evidence in the present study for ELA altering representations of ambiguity in one way or another.

There are a number of methodological differences between the tasks used in Study 1 and Study 2 that may account for the differences in observed results. The stimuli used in the two studies differed in multiple ways. While Study 1 used angry faces as the threatening stimulus and surprised faces as the ambiguous stimulus, Study 2 used fearful faces as the threatening stimulus and neutral faces as the ambiguous stimulus. Moreover, Study 1 used 99 unique actors, each shown once per expression type, while Study 2 showed only four unique actors. By averaging responses from trials using a greater number of unique actors, patterns from Study 1 may have provided more reliable or generalized estimates for representations of each image type (threatening, nonthreatening, or ambiguous). The actors in Study 1 were diverse in race and gender identity, while in Study 2, the four actors were all female with similar skin color, features, and hair color. These visual similarities could in part explain why the average representational overlap values in Study 2 (*Figure 8*; *Table 4*) were higher than those in Study 1 (*Supplemental Figure 1*) within the regions of interest. In Study 2, subtle differences in multivariate responses to the emotions expressed across the different

images may have been overshadowed by the many visual similarities shared across the images. It is also worth noting that the MRI sequences differed between the two studies. Study 1 used a multiband sequence whereas Study 2 did not. While functional images in Study 1 were collected at 2.0 × 2.0 × 2.0 mm voxel resolution, Study 2 data were collected at 3.0 x 3.0 x 4.0 mm voxel resolution. Greater spatial resolution may have enabled heightened sensitivity to subtle variations in patterns of voxelwise activity in Study 1, compared to Study 2 (note, however, that smaller voxel sizes introduce concerns about noise) (Wall, 2023).

In addition to task design differences, differences between the populations studied may have contributed to discrepancies in results. While Study 1 included a community sample of young adults with a restricted age range (18-to 19-year-olds) with ranging ELA experiences, Study 2 included a wider age range (9-to 22-year-olds) of youth specifically recruited based on a history of one type of adversity. It is possible that the effect observed in Study 1 — wherein individuals with a greater history of ELA demonstrate greater overlap in representations of ambiguity and threat — is simply not evident in PI youth. Given how specific and extreme institutionalization is as a form of early adversity, it is not surprising that this group would not exhibit the same patterns observed in a community sample with a range of adverse experiences. Moreover, in Study 1 we examined ELA linearly, accounting for varied experiences of abuse and neglect across the sample. In Study 2, we operationalized ELA categorically based on group (PI or control). Other than this binary distinction, we did not assay other measures of ELA in either group. This design enabled us to isolate the effects of a specific adversity type rather than general adversity. However, it is also possible that within-group heterogeneity in the PI sample (due to pre-or post-adoption experiences, genetic variance, or other individual differences) or in the control sample (due to other forms of ELA experiences) contributed to the lack of statistical differences between the

groups in MRI analyses. This could also in part explain why the anticipated group differences in anxiety, though in the expected direction, were not statistically significant. Future work would benefit from examining these processes in larger samples and incorporating measures of continuous ELA as well as categorical, specific adverse experiences. Lastly, it is possible that age of exposure to ELA is an important factor to consider. In our sample, PI youth were typically adopted by the age of two. It will be important for future research to account for age of adoption or age of adversity exposure when examining representations of ambiguity.

A number of studies have examined emotion processing and valence biases in PI youth. To our knowledge, this was the first study to compare neural representations of ambiguity to those of threat in this specialized population of youth. Future research is needed to understand how this specific type of adversity shapes processing of ambiguity, and how this confers risk or resilience for psychopathology.

Study 3: Early life adversity and exploratory behaviors in emerging adults.

Introduction.

While Study 1 and Study 2 primarily examine rapid neural responses to ambiguous stimuli, Study 3 focuses on behavior in the presence of uncertain or unfamiliar stimuli. Results from Study 1 suggest that early life adversity (ELA) is associated with a heightened tendency to respond to ambiguous cues in the environment as though they are threatening. In line with this reasoning, individuals with a history of ELA may overrepresent likelihood of negative outcomes in ambiguous situations and consequently may be less likely to engage with situations in which the future outcomes are unknown. Recent work provides support for this possibility by demonstrating a negative association between ELA and exploration of novel, unfamiliar environments in a computerized foraging task (Lloyd et al., 2022). Both theoretical (Spear, 2000) and empirical accounts (Heller et al., 2020; Saragosa-Harris et al., 2022) suggest that exploratory behaviors are linked to emotional wellbeing in everyday life. Moreover, research highlights the potential for interventions that target learning mechanisms, including those subserving exploratory decision-making, to promote healthy outcomes in youth with a history of caregiving adversity (McLaughlin et al., 2019). Identifying how early experiences shape exploratory behaviors thus has the potential to provide integral insight for clinical work in high-risk youth.

Recent work highlights the importance of distinguishing the unique effects of stimulus novelty and reward uncertainty on exploratory decision-making, particularly when examining group or individual differences in exploration (Cockburn et al., 2022; Nussenbaum et al., 2023). Although prior work has demonstrated an association between ELA and attenuated exploration (Humphreys, Lee, et al., 2015; Lloyd et al., 2022; Loman et al., 2014; Y. Xu et al., 2023), it remains unclear whether these two distinct motivators of exploratory behavior differentially shape

exploratory decision-making following early adversity. Study 3 seeks to elucidate whether ELA affects sensitivity to novelty and uncertainty in the context of exploratory decision-making. Importantly, this study examines these processes in a sample of emerging adults. Prior work suggests that real-world exploratory behaviors increase during the transition from adolescence to adulthood (Saragosa-Harris et al., 2022). Exploratory and novelty-seeking behaviors may be particularly adaptive during this transitional period of development in which individuals transition toward independence and navigate novel environments (Spear, 2000). Moreover, given the heightened risk for psychopathology during this stage (Arnett et al., 2014), especially in high ELA groups (van der Vegt et al., 2009), understanding how ELA relates to healthy exploration during the transition to adulthood has important clinical implications.

In addition to examining the unique role of novelty and uncertainty in ELA-related exploratory behaviors, a secondary goal of the study is to examine whether these patterns differ based on the type of adversity experienced. Although prior work has showcased a general association between ELA and attenuated exploration (Lloyd et al., 2022), it remains unclear how specific types of adversities shape exploratory behaviors. The broad construct of "early life adversity" often functions as a catch-all term that encapsulates many disparate adverse experiences, ranging from extreme poverty to parental incarceration to emotional abuse (Bellis et al., 2019; Felitti et al., 1998; McLaughlin et al., 2014; McLaughlin & Sheridan, 2016; Spinhoven et al., 2014). Given the high cooccurrence of these lifetime experiences (Felitti et al., 1998), a general construct of ELA is sometimes warranted as it captures the complex nature of lifetime adversity. However, distinguishing among different types of early life adversity is important for investigating mechanisms and tailoring interventions based on individual experiences (Cohodes et al., 2021; McLaughlin & Sheridan, 2016). It is possible that effects of novelty and uncertainty

differentially affect exploratory behaviors depending on the specific dimension of adversity considered. One recent theoretical framework, the threat-deprivation model, suggests that ELA may be classified in terms of threat (e.g., abuse) and deprivation (e.g., neglect) and that different types of adversities have distinct effects on neural and behavioral development (McLaughlin et al., 2014; McLaughlin & Sheridan, 2016). Other models highlight the importance of unpredictability of the early caregiving environment in shaping later behavior (Baram et al., 2012; Ellis et al., 2009, 2022). We thus examine whether abuse, neglect, and caregiving unpredictability differentially relate to the effects of novelty and uncertainty on exploratory decision-making.

Methods.

Participants.

Recruitment. We recruited two samples of 18-to 25-year-olds (N = 600 total). One sample was recruited using Prolific (N = 300) and one sample was recruited using the University of California Los Angeles Sona Subject Pool (N = 300). All participants completed the study online. Participants completed a series of questionnaires on Qualtrics and a behavioral task on Pavlovia, a platform for hosting behavioral tasks online. Prolific participants received monetary compensation and Sona participants received course credit. All study procedures were completed in accordance with the University of California Los Angeles Institutional Review Board (IRB 23-000386).

Inclusion criteria. Participants were required to be between the ages of 18 and 25, be fluent in English, and reside in the United States to enroll in the study. Participants whose Qualtrics location or browser time zone data indicated they were located outside of the United States were excluded from analyses. We included several attention check questions within Qualtrics to assess

participant attention and filter potential bots. Additional attention checks were added for the Prolific participants given concerns with bots or server farms (Simone et al., 2023). Participants who answered two or more attention checks incorrectly were excluded from all analyses. After applying these inclusion criteria, a total of 554 participants (N = 267 Sona participants and N = 287 Prolific participants) completed the questionnaires and the exploration task.

For analyses of a given questionnaire, only participants who answered every item of that questionnaire were included in analyses. For analyses of the exploration task, choice trials in which participants did not respond or respond faster than 200 ms were excluded from task analyses (Nussenbaum et al., 2023). After excluding trials with no responses and trials with reaction times 200 milliseconds or faster, participants needed to have at least 120 remaining trials to be included in task analyses. The final sample of participants included in task analyses consisted of 270 Prolific participants and 248 Sona participants (N = 518 total participants).

Participant demographics. Participants recruited through Prolific ranged from 18 to 25 years old (mean age = 21.61 years) and participants recruited through Sona ranged from 18 to 24 years old (mean age = 20.27 years). Within the Prolific sample, gender identity was 47% female, 46% male, 5% non-binary/gender non-conforming (N = 4 participants chose "other" or "prefer not to say"). Within the Sona sample, gender identity was 75% female, 24% male, and 1% other. Participants in the Prolific sample self-reported their racial identity as 17% Asian, 15% Black or African American, 50% Caucasian or White, <1% Native Hawaiian or other Pacific Islander, 12% multiracial, and 5% other, with 21% identifying as Hispanic or Latinx. Participants in the Sona sample self-reported their racial identity as 1% American Indian or Alaska Native, 39% Asian, 3% Black or African American, 35% Caucasian or White, <1% Native Hawaiian or other Pacific Islander, 10% multiracial, and 11% other, with 24% identifying as Hispanic or Latinx.

Questionnaires.

Early life adversity. Early life adversity was measured using the Childhood Trauma Questionnaire Short Form (CTQ-SF) (Bernstein et al., 2003), a 28-item scale that assays retrospective accounts of experiences of emotional abuse, emotional neglect, physical abuse, physical neglect, and sexual abuse before age fourteen. The CTQ-SF has been validated in clinical and non-clinical samples and corresponds well to therapists' interview-based ratings of abuse and neglect (Bernstein et al., 2003). For each item, participants rate on a scale of 1 to 5 (1 = never true, 5 = very often true) how much they agree with various statements (e.g., "I believe that I was physically abused"). Responses to items regarding emotional, physical, and sexual abuse are added together into an abuse subscale score, while items regarding emotional and physical neglect are added together into a neglect subscale score. Additionally, responses across all items are added to create a total CTQ score, with higher scores indicating greater cumulative experiences of childhood trauma. Prior to inclusion in regression models, abuse subscale scores, neglect subscales scores, and total scores were log-transformed and then z-scored to meet the assumptions of the planned statistical tests (i.e., normality).

Unpredictability of early caregiving environment. Unpredictability of the early caregiving environment was measured using the Questionnaire of Unpredictability in Childhood (QUIC), a 38-item questionnaire that assays five subscales of unpredictability in early caregiving environments: parental involvement, parental predictability, parental environment, physical environment, and safety and security (Glynn et al., 2019). The QUIC has been validated in adults and shown to have high internal and test-retest reliability. For each item, participants respond "yes" or "no" to indicate whether a statement applies to their experiences. For some items, participants are asked to reflect on their experiences before the age of twelve. On other items, participants are

asked to answer based on their experiences before the age of eighteen. Example items include "I experienced changes in my custody arrangement" and "I had a bedtime routine (e.g., my parents tucked me in, my parents read me a book, I took a bath)". Scores on the QUIC can range from 0 to 38, with higher scores indicating greater exposure to unpredictability in the environment during childhood.

Anxiety. Self-reported anxiety was measured using the Screen for Adult Anxiety Related Disorders (Angulo et al., 2017). In this questionnaire, participants rate how well 44 statements describe them now or within the past three months ("not true or hardly ever true", "somewhat true or sometimes true", or "very true or often true"). Example items include "I worry about being as good as other people" and "I am a worrier". The questions assess experiences of panic disorder or significant somatic symptoms, generalized anxiety, separation anxiety, and social phobia. Total scores, summed across these four subscales, indicate overall anxiety symptoms. Higher total scores indicate greater anxiety.

Self-reported ambiguity tolerance. Self-reported ambiguity tolerance was measured using the Multiple Stimulus Types Ambiguity Tolerance Scale-II (MSTAT-II), a 13-item self-report questionnaire that has been validated in adults (McLain, 2009). The MSTAT-II assesses reactions to five types of ambiguous stimuli: generally ambiguous stimuli ("I prefer a situation in which there is some ambiguity"), complex stimuli ("I enjoy tackling problems that are complex enough to be ambiguous"), uncertain stimuli ("I find it hard to make a choice when the outcome is uncertain" (reverse scored)), new/unfamiliar/novel stimuli ("I generally prefer novelty over familiarity"), and insoluble/illogical/irreducible/internally inconsistent stimuli ("I try to avoid problems that don't seem to have only one 'best' solution" (reverse scored)). Participants rated their level of agreement with each statement on a five-point Likert scale (1 = strongly disagree, 5

= strongly agree). Scores across all items were totaled, with greater scores indicating greater tolerance for ambiguity (McLain, 2009).

Self-reported intolerance of uncertainty. Self-reported intolerance of uncertainty was measured using the Intolerance of Uncertainty Scale (Buhr & Dugas, 2002), a 27-item scale that measures an individual's opinions and feelings about uncertainty. Example items include "Uncertainty makes me uneasy, anxious, or stressed" and "It frustrates me not having all the information I need". Participants rate items on a five-point Likert scale (1 = not at all characteristic of me, 5 = entirely characteristic of me). Items are totaled in a single score, with higher scores indicating greater intolerance (i.e., lower tolerance) for uncertainty.

Self-reported novelty-seeking tendencies. Self-reported novelty-seeking tendencies were measured using the novelty subscale from the Personal Expansion Questionnaire (Gordon & Luo, 2011). The novelty subscale of this questionnaire consists of 5 statements regarding novelty-seeking behaviors and feelings about novelty. Participants are asked to respond to using a five-point Likert scale (1 = strongly disagree, 5 = strongly agree). Example items include "I usually seek out new opportunities or experiences" and "Trying new things is important for me to stay happy". The novelty subscale of this questionnaire has been validated and shown to relate to other psychological constructs including personality traits and positive affectivity (Gordon & Luo, 2011).

Explore-exploit task.

We used an explore-exploit task designed by Nussenbaum, Martin et al. (2023), which was adapted from Cockburn et al. (2022). We translated the original task from MATLAB to PsychoPy version 2022.2.5 (Peirce et al., 2019) in order to host the task on Pavlovia (pavlovia.org) for online

data collection. The PsychoPy task is available on GitLab (https://gitlab.pavlovia.org/nsaragosaharris/enchanted-world-task-public). In the task, participants are told that they are collecting coins from different territories of an enchanted world. Each territory is owned by its own magical creature who hides coins in three different hiding spots within that territory. Each block of the task corresponds to a different territory (N = 10). At the beginning of each block, participants are told that they have entered a new territory in which a new creature has hidden coins. On each trial (N = 15 per block), participants are shown two hiding places and are given four seconds to select one of the hiding places in order to search for coins (*Figure 9*). After a screen highlighting their response (500 ms), a screen indicating whether or not a coin was found in the chosen location is shown for 1.5 seconds.

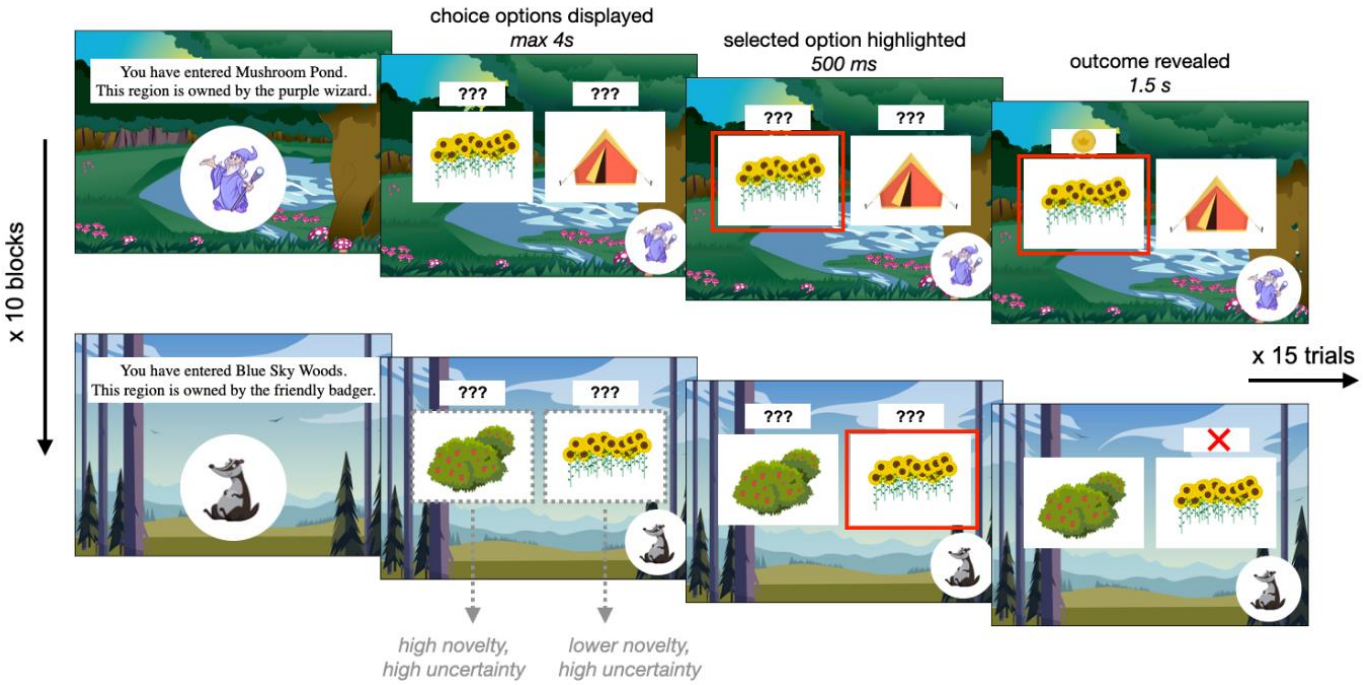


Figure 9. Study 3 task design. Figure from Nussenbaum, Martin et al. (2023). The task has 10 blocks and 15 trials in each block. Throughout a given block, the current territory is indicated by the background image, and the creature owning that territory is pictured in the corner of the screen.

Each territory (block) has three hiding spots. Two hiding spots are shown on each trial. All three hiding spots shown within the first block of the task are novel as the participant has not encountered them previously. For each subsequent block, two hiding spots are familiar (i.e., seen in a previous block) and one is novel. Familiar hiding spots are randomly selected from all hiding spots the participant encountered in any previous block. Given this randomization, some hiding spots are presented more often than others across blocks. Therefore, in addition to having one completely novel hiding spot in each block, the novelty of the two familiar options (i.e., how many times the hiding spot had been encountered in previous blocks) can also vary.

In "easy" blocks (N = 5), the three possible hiding spots reveal a coin on 20%, 50%, and 80% of trials. In "hard" blocks (N = 5), the three possible hiding spots reveal a coin on 30%, 50%, and 70% of trials. Participants were not told these reward probabilities and had to learn through trial and error which options most often yielded a reward. Difficulty of each block (i.e., territory) is randomly assigned. Within each block, hiding spots are randomly assigned a reward probability. Thus, the payout structure of each hiding spot is independent of previous blocks. That is, familiar hiding spots do not necessarily have the same payout structure across different territories, so participants must learn the unique payout structure of each option for every new territory visited. With this design, the task separates stimulus novelty from reward uncertainty; at the beginning of each block, all hiding spots have high reward uncertainty but varying novelty. In the instructions for the task, participants are told that reward probabilities of each hiding spot were reset on each block ("Every region is owned by a magical creature that has its own favorite spots to hide coins"; "You will [..] have to choose which hiding spot the creature likes best").

Analyses.

We used R version 4.3.3 (2024) for statistical analyses (R Core Team, 2024). In analyses of self-report data, we used Spearman rank correlations to examine whether cumulative ELA (total CTQ scores) or childhood unpredictability scores (total QUIC scores) related to self-reported ambiguity tolerance, self-reported intolerance of uncertainty, or self-reported novelty-seeking tendencies. In these analyses, we used the 'DescTools' (Signorell et al., 2024) and 'stats' (R Core Team, 2024) R packages. We used the R packages 'lme4' (Bates et al., 2024) and 'afex' (Singmann et al., 2024) for multilevel models and 'sjPlot' (Lüdecke et al., 2024) and 'ggplot2' (Wickham et al., 2024) for plots. Methods and analysis plans were preregistered on Open Science Framework prior to data collection (https://osf.io/237fx).

ELA and choice behavior: Logistic regression. Following the analyses in Nussenbaum, Martin et al. (2023) and Cockburn et al. (2022), we calculated the expected value, reward uncertainty, and stimulus novelty of each option (hiding spot) for every trial, as well as differences in these values between the right and left choice option for each trial. Expected value was calculated as the mean of a beta distribution defined by Beta [α,β], where α = number of wins from that choice option (in the current block) + 1 and β = number of losses from that choice option (in the current block) + 1. Reward uncertainty for each choice option was calculated as the variance of the same beta distribution. Stimulus novelty was calculated as the variance of a beta distribution Beta [α,β], where α = the number of times the participant had previously seen the given option (hiding spot) + 1 and β = 1. In the primary model of interest, we used a multilevel logistic regression to model the probability participant *j* chose the left option on a given trial *i* (see statistical model below). This model included random intercepts for each participant, with trials nested within participant. The differences in expected value (EV), reward uncertainty (RU), and

stimulus novelty (SN) between the left and right choice option for trial *i* were included as fixed and random effects in the model. Additionally, this model tested how these differences interact with ELA (total CTQ score) in predicting choice behavior. In doing so, this model tested whether the extent to which expected value, reward uncertainty, and stimulus novelty affect choice behavior differs as a function of early life adversity.

$$Y_{ij} = b_{0j} + b_{1j}((left\ EV - right\ EV)_{ij}) +$$
$$b_{2j}((left\ RU - right\ RU)_{ij}) +$$
$$b_{3j}((left\ SN - right\ SN)_{ij}) +$$
$$b_4((left\ EV - right\ EV)_{ij})(ELA_j) +$$
$$b_5((left\ RU - right\ RU)_{ij})(ELA_j) +$$
$$b_6((left\ SN - right\ SN)_{ij})(ELA_j) + \varepsilon_{ij}$$

In addition to this statistical model, in exploratory analyses we also fit participant data with three computational models to formalize the mental processes supporting trial-level decisions (see *Supplemental Text*).

Results.

ELA and questionnaires. As hypothesized, Spearman rank correlations demonstrated that cumulative experiences of ELA (CTQ total scores) were positively correlated with self-reported experiences of unpredictability in childhood (QUIC scores; $r_s(552) = 0.74$, 95% CI [0.70, 0.78], $p < 0.001$). Relations among ELA and self-reported anxiety, tolerance of uncertainty and ambiguity,

and novelty-seeking behaviors were all in the hypothesized direction. On average, individuals who reported greater ELA indicated more anxiety symptoms ($r_s(552) = 0.4$, 95% CI [0.33, 0.47], $p < 0.001$), lower tolerance of uncertainty (greater Intolerance of Uncertainty Scale scores; $r_s(550) = 0.35$, 95% CI [0.28, 0.42], $p < 0.001$) and ambiguity (lower MSTAT scores; $r_s(551) = -0.18$, 95% CI [-0.26, -0.10], $p < 0.001$), and fewer novelty-seeking tendencies ($r_s(552) = -0.17$, 95% CI [-0.25, -0.08], $p < 0.001$). In line with these patterns, individuals who experienced greater unpredictability during childhood reported higher anxiety ($r_s(552) = 0.42$, 95% CI [0.35, 0.48], $p < 0.001$), lower tolerance of uncertainty ($r_s(550) = 0.33$, 95% CI [0.25, 0.40], $p < 0.001$) and ambiguity ($r_s(551) = -0.17$, 95% CI [-0.25, -0.09], $p < 0.001$), and fewer novelty-seeking tendencies ($r_s(552) = -0.13$, 95% CI [-0.20, -0.04], $p = 0.003$). Relations among anxiety, intolerance of uncertainty, tolerance of ambiguity, and novelty-seeking tendencies can be found in the correlation matrix (*Figure 10*). These same associations with the abuse and neglect subscales of the CTQ separated can be found in *Supplemental Figure 13*.

Figure 10. Correlation matrix summarizing Spearman rank correlations (rho values) among all questionnaires. Color indicates direction of association and shading indicates strength of association. All associations are significant ($p < 0.01$).

Overall task behavior.

Overall task performance. To model performance across blocks of the task, we used a multilevel linear model that predicted the total number of coins won within a block based on block number and block difficulty. Controlling for block difficulty, block number was negatively associated with total coins won (b = -0.14, 95% CI [-0.16, -0.12], $t(4660)$ = -15.31, $p < 0.001$), suggesting that performance slightly decreased over the course of the task. Somewhat surprisingly, controlling for block number, participants performed better on more difficult blocks (b = 0.21, 95% CI [0.11, 0.31], $t(4660)$ = 4.06, $p < 0.001$). When interpreted in terms of total coins won, however, both of these effects were small (an estimated 0.14 fewer coins won per increase in block

number and an estimated difference of 0.21 coins won in difficult versus easy blocks). Using a multilevel logistic regression, we analyzed whether, controlling for block number and block difficulty, within-block trial number predicted trial-level binary coin outcomes (i.e., coin won or not won). As expected, participants were more likely to win a coin on later trials within a block, after controlling for block number and block difficulty (OR = 1.02, 95% CI [1.01, 1.04], $z(75940) = 2.97$, $p = 0.003$). This pattern suggests that participants were effectively learning the reward probabilities for the block-specific hiding spots, and were more likely to make optimal choices as the trials progressed within each block.

Trial-level choice behavior as a function of expected value, reward uncertainty, and stimulus novelty. We next designed a model to analyze how differences in expected value, reward uncertainty, and stimulus novelty between the right and left choice options predicted trial-level choice behavior in the task. We used a multilevel logistic regression to model the probability that a participant chose the left option on a given trial, with trial-level differences in expected value, reward uncertainty, and stimulus novelty between the left and right choice options included as fixed and random effects in the model. The outcome was a binary variable indicating whether or not the participant chose the left option on a given trial. As expected, participants were more likely to choose the option with a higher expected value (OR = 3.00, 95% CI [2.08, 3.19], $z(75940) = 34.90$, $p < 0.001$). The effects of reward uncertainty and stimulus novelty also supported our hypotheses: Participants were less likely to choose the option with greater reward uncertainty (OR = 0.76, 95% CI [0.73, 0.79], $z(75940) = -15.00$, $p < 0.001$), and more likely to choose the option with higher stimulus novelty (OR = 1.26, 95% CI [1.24, 1.29], $z(75940) = 22.30$, $p < 0.001$). A summary of choice behavior at different levels of expected value, uncertainty, and novelty is provided in *Figure 11* (plotted as proportions for visualization purposes).

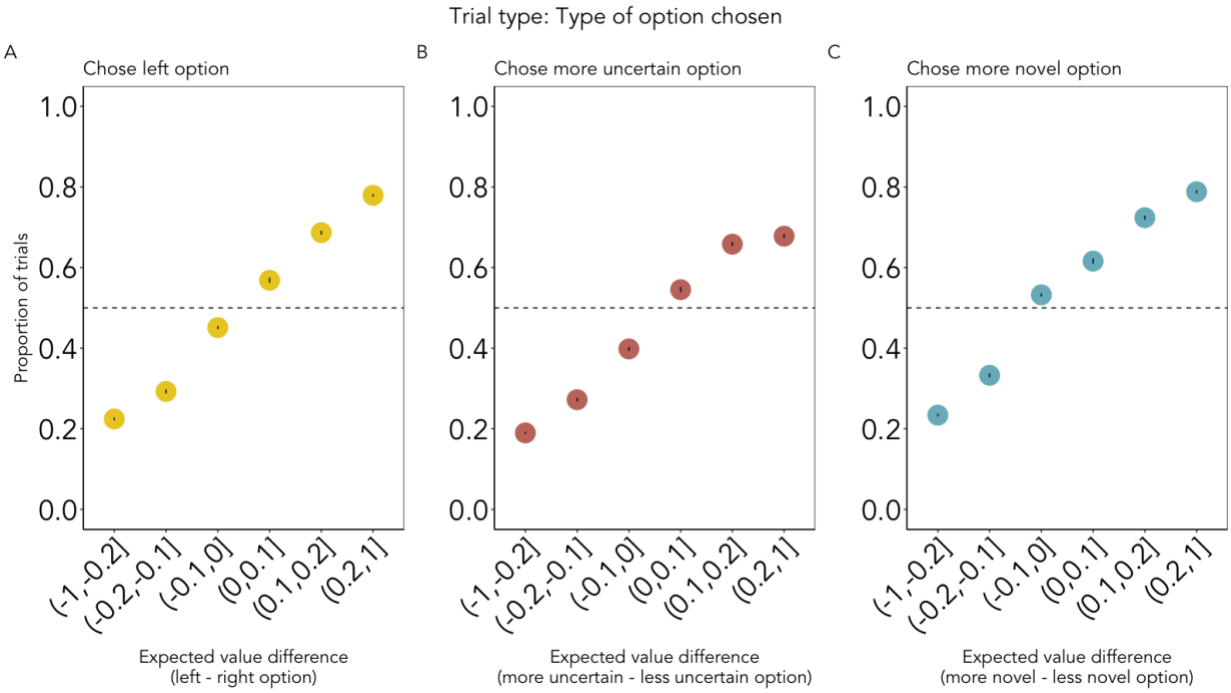


Figure 11. Summary of choice behavior. Proportion of trials in which participants chose the (A) left option, (B) more uncertain option, and (C) more novel option at different levels of the expected value difference between the (A) left vs. right option, (B) more uncertain vs. less uncertain option, and (C) more novel vs. less novel option.

ELA and task behavior.

ELA and task performance. We used a linear regression to test whether ELA was associated with overall task performance, indicated by total coins won in the task. As expected, ELA was negatively associated with overall performance, with individuals with higher CTQ scores obtaining fewer total coins on average in the task (b = -0.87, 95% CI [-1.43, -0.31], $t(516) = 3.05$, p = 0.002). This association remained after controlling for which sample (Sona or Prolific) participants were in (b = -0.97, 95% CI [-1.53, -0.41], $t(515) = -3.38$, $p < 0.001$).

ELA and overall task behavior. We next tested whether ELA related to broad patterns of behavior throughout the task. In three separate Spearman rank correlations, we examined whether ELA related to the overall proportion of trials in which individuals choose the more valuable, more

uncertain, or more novel option. In line with the task performance results, higher CTQ scores were negatively correlated with the proportion of trials in which participants chose the more valuable option, although this did not reach significance ($r_s(516) = -0.08$, 95% CI [-0.16, 0.01], $p = 0.08$). Higher CTQ scores were positively correlated with the proportion of trials in which participants chose the more uncertain option, though this effect was trending ($r_s(516) = 0.09$, 95% CI [-0.0001, 0.17], $p = 0.05$). We did not observe a significant correlation between CTQ scores and the proportion of trials in which participants chose the more novel option ($r_s(516) = -0.009$, 95% CI [-0.10, 0.08], $p = 0.84$). Because these were separate correlations examining average behavior across the task, they did not capture how reward, novelty, and uncertainty shaped decisions at the trial level or account for their shared variance. We next conducted trial-level analyses that accounted for shared variance across these features in order to more accurately model how these features differentially shaped exploratory decision-making on each trial.

Trial-level interactive effects between ELA history and expected value, reward uncertainty, and stimulus novelty on choice. We next examined whether the trial-level effects of expected value, reward uncertainty, and stimulus novelty varied as a function of ELA history. This model included differences in expected value, reward uncertainty, and stimulus novelty between the left and right choice option as fixed and random effects. Interactions between CTQ and differences in expected value, reward uncertainty, and stimulus novelty were included as three interactive terms (*Figure 12*). The effect of expected value on choice behavior did not significantly interact with CTQ scores (OR = 0.97, 95% CI [0.91, 1.03], $z(75940) = -1.14$, $p = 0.255$). Although the effects of stimulus novelty appeared to vary based on ELA history, such that individuals with higher CTQ scores were more novelty-seeking, this interaction did not reach statistical significance (OR = 1.02, 95% CI [0.998, 1.04], $z(75940) = 1.77$, $p = 0.08$). We observed a significant interaction between CTQ

scores and reward uncertainty, suggesting that individuals with higher CTQ scores were less avoidant of stimuli with higher reward uncertainty than those with lower CTQ scores (OR = 1.04, 95% CI [1.002, 1.08], $z(75940) = 2.06$, $p = 0.04$; *Figure 13*).

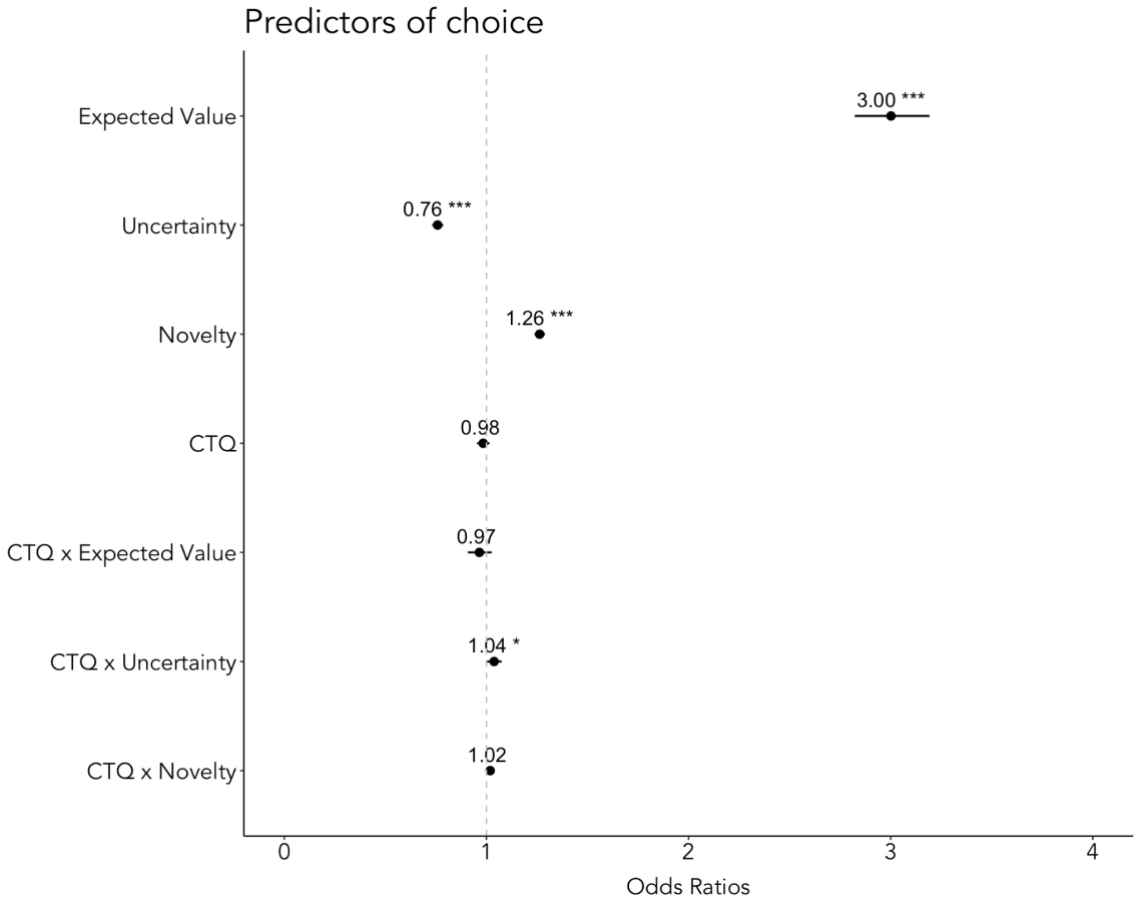


Figure 12. Conditional effects of expected value, uncertainty, novelty, and ELA history (CTQ scores), and interactions between CTQ scores and expected value, reward uncertainty, and stimulus novelty in predicting trial-level choice behaviors. Odds ratios for each effect are plotted.

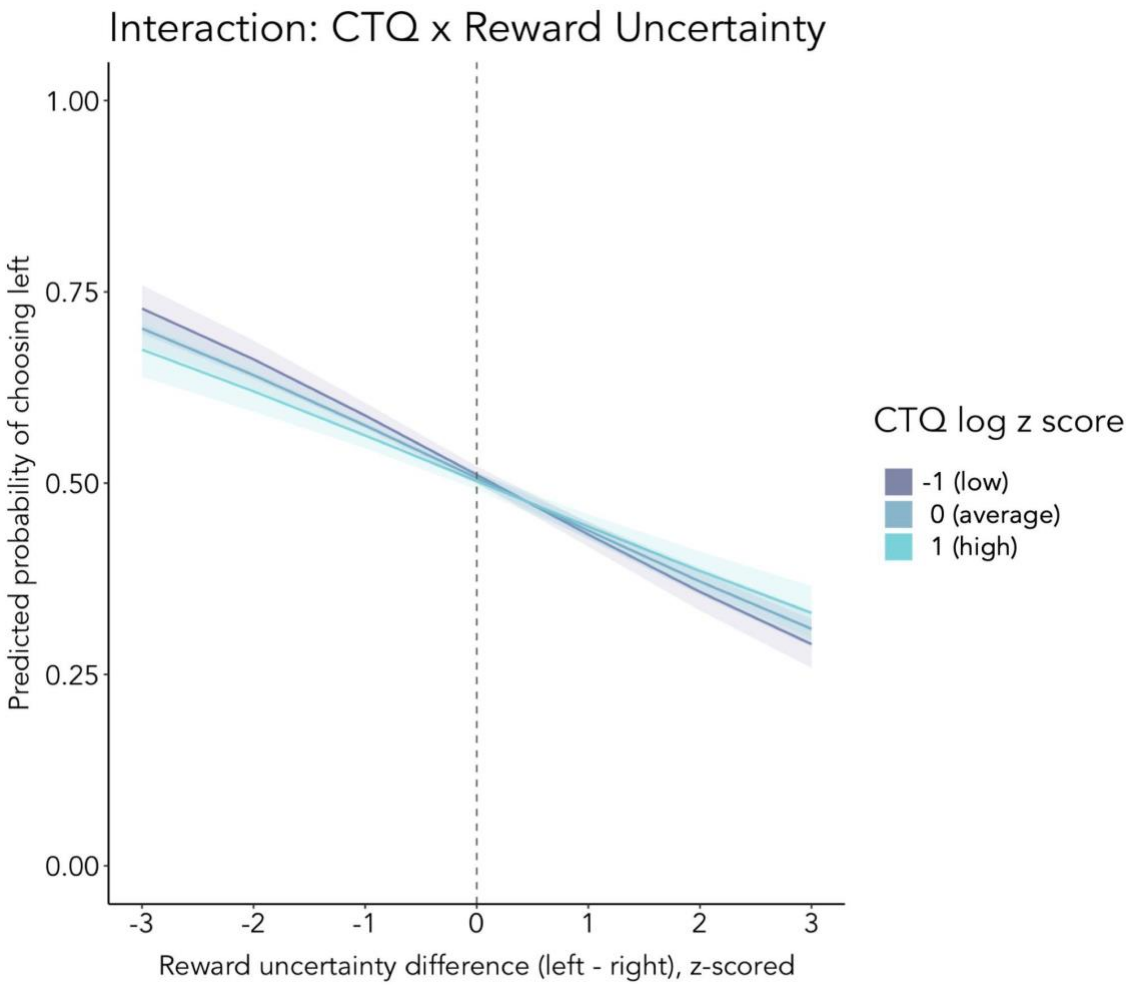


Figure 13. Model predicted effect of reward uncertainty on choice behavior based on ELA history. Model predicted effect of reward uncertainty (z-scored difference in reward uncertainty between the two choice options) on choice behavior based on ELA history (CTQ scores) after accounting for other coefficients in the model. Estimated from multilevel logistic regression. Plotted at CTQ log z scores of -1, 0, and 1 (corresponding to relatively low, average, and high ELA history) for visualization.

The observed interaction between CTQ scores and reward uncertainty raised the question of whether individuals with higher CTQ scores actually preferred more uncertain options (i.e., were uncertainty-seeking), whether they were simply less averse to uncertainty than individuals with low CTQ scores (but still averse to uncertainty overall), or whether their choices were unaffected by reward uncertainty. To better understand the observed pattern of results, we conducted an additional analysis in which we fit the original model with fixed effects of expected

value, reward uncertainty, and stimulus novelty (without interactive terms) separately for high and low CTQ groups. For this analysis, we divided participants into categorical groups corresponding to high (N = 252) or low ELA (N = 266), based on median-split CTQ total scores. Results from the model fit to the high ELA group demonstrated that participants were more likely to choose the left option as its expected value relative to the right option increased (OR = 2.95, 95% CI [2.71, 3.21], $z(36831) = 24.71$, $p < 0.001$), an effect that also seen in the low ELA group model (OR = 3.06, 95% CI [2.80, 3.34], $z(39081) = 24.68$, $p < 0.001$). Additionally, the high ELA group model demonstrated that participants were more likely to choose options as their relative novelty increased (OR = 1.29, 95% CI [1.25, 1.33], $z(36831) = 16.41$, $p < 0.001$), a pattern also observed in the low ELA group (OR = 1.24, 95% CI [1.21, 1.27], $z(39081) = 15.17$, $p < 0.001$). Lastly, the results from the high ELA group model verified that high ELA individuals were also averse to uncertainty (i.e., were less likely to choose options as their relative uncertainty increased; OR = 0.77, 95% CI [0.74, 0.81], $z(36831) = -10.48$, $p < 0.001$), similar to the pattern observed in the low ELA group (OR = 0.75, 95% CI [0.71, 0.79], $z(39081) = -10.8$, $p < 0.001$). In tandem with the interactive model, these patterns suggest that high and low ELA groups are both more likely to choose options with higher expected value and higher novelty, and less likely to choose options with higher uncertainty, but demonstrate small differences in the extent to which uncertainty shapes their behavior (*Figure 13*).

Trial-level interactive effects between ELA history and expected value, reward uncertainty, and stimulus novelty on reaction time. We next analyzed how expected value, reward uncertainty, and stimulus novelty of the chosen option interacted with ELA in predicting log-transformed reaction times. Results from this linear mixed-effects model demonstrated that participants responded faster when selecting options with higher value (b = -0.02, 95% CI [-0.02, -0.01],

t(537.54) = -6.14, *p* < 0.001), and more slowly when selecting options with greater uncertainty (*b* = 0.05, 95% CI [0.04, 0.05], *t*(644.60) = 18.05, *p* < 0.001) and novelty (*b* = 0.05, 95% CI [0.05, 0.06], *t*(614.82) = 22.99, *p* < 0.001). CTQ scores did not significantly interact with the expected value (*b* = 0.0001, 95% CI [-0.005, 0.006], *t*(536.26) = 0.03, *p* = 0.976) or novelty (*b* = 0.003, 95% CI [-0.001, 0.007], *t*(615.13) = 1.39, *p* = 0.164) of the chosen option in predicting reaction time. In contrast, CTQ scores significantly interacted with the uncertainty of the chosen option (*b* = -0.006, 95% CI [-0.01, -0.001], *t*(642.13) = -2.46, *p* = 0.01), such that the slowing effect of uncertainty on reaction time was attenuated in individuals with higher CTQ scores (*Figure 14*).

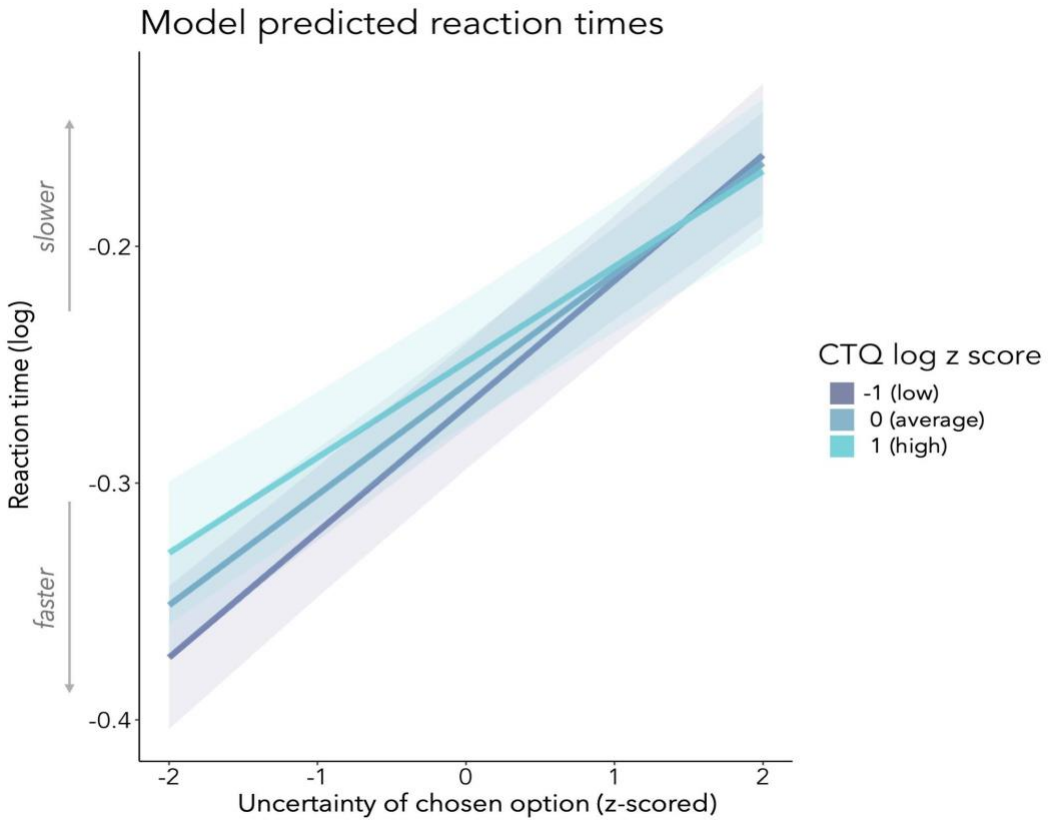


Figure 14. Interaction between ELA and reward uncertainty on reaction time. Model predicted log-transformed reaction times based on the uncertainty of chosen option (z-scored) at different levels of ELA (CTQ log z scores) after accounting for other coefficients in the model. Estimated from multilevel linear regression.

ELA and task behavior based on adversity type.

Trial-level interactive effects between ELA history and expected value, reward uncertainty, and stimulus novelty on choice by adversity type (abuse or neglect). We next tested whether the interactive effects between ELA and expected value, uncertainty, and novelty on choice behavior differed depending on the type of adversity considered (abuse or neglect). In two models, rather than modeling the effects of cumulative ELA exposure (CTQ total scores) we examined the CTQ subscales for abuse and neglect separately. We analyzed how abuse history interacted with expected value, uncertainty, and novelty in predicting choice in a model that controlled for experiences of neglect. In a separate model, we analyzed how neglect history interacted with expected value, uncertainty, and novelty in predicting choice while controlling for experiences of abuse. Results from these two models indicate differences in the way in which abuse and neglect interact with uncertainty to shape decisions. After controlling for experiences of neglect, abuse subscale scores did not significantly interact with expected value (OR = 0.95, 95% CI [0.89, 1.01], $z(75921) = -1.71$, $p = 0.09$) or novelty (OR = 1.02 , 95% CI [0.997, 1.04], $z(75921) = 1.64$, $p = 0.10$) in predicting trial-level choice. In line with the cumulative ELA model, abuse subscale scores significantly interacted with reward uncertainty, such that aversion to reward uncertainty was attenuated in individuals who experienced higher levels of abuse (OR = 1.05, 95% CI [1.01, 1.08], $z(75921) = 2.50$, $p = 0.01$). Conversely, after controlling for experiences of abuse, neglect subscale scores did not interact with expected value (OR = 0.99, 95% CI [0.93, 1.05], $z(75921) = -0.29$, $p = 0.77$), novelty (OR = 1.02, 95% CI [0.998, 1.04], $z(75921) = 1.77$, $p = 0.08$), or uncertainty (OR = 1.02, 95% CI [0.99, 1.06], $z(75921) = 1.19$, $p = 0.24$) in predicting choice behavior. This pattern of results suggests that the previously observed effect, in which aversion to reward uncertainty was

attenuated in individuals who experienced higher cumulative ELA (total CTQ scores), may stem primarily from experiences of abuse.

Trial-level interactive effects between childhood unpredictability and expected value, reward uncertainty, and stimulus novelty on choice. In addition to exploring the separable effects of cumulative ELA, abuse, and neglect (all measured by the CTQ) on choice behavior, we also examined whether unpredictability in the caregiving environment during childhood (measured by the QUIC) interacted with expected value, reward uncertainty, and stimulus novelty in shaping exploratory decision-making (*Figure 15*). Caregiving unpredictability did not significantly interact with expected value (OR = 0.995, 95% CI [0.94 , 1.06], $z(75922) = -0.15$, $p = 0.89$) or uncertainty (OR = 1.03, 95% CI [0.99, 1.07], $z(75922) = 1.55$, $p = 0.12$) in predicting choice behavior. However, we did observe a significant association between caregiving unpredictability and novelty, such that individuals with greater unpredictability in their caregiving environments during childhood were more novelty-seeking in their choice behavior (OR = 1.03, 95% CI [1.01, 1.06], $z(75922) = 3.22$, $p = 0.001$; *Figure 16*).

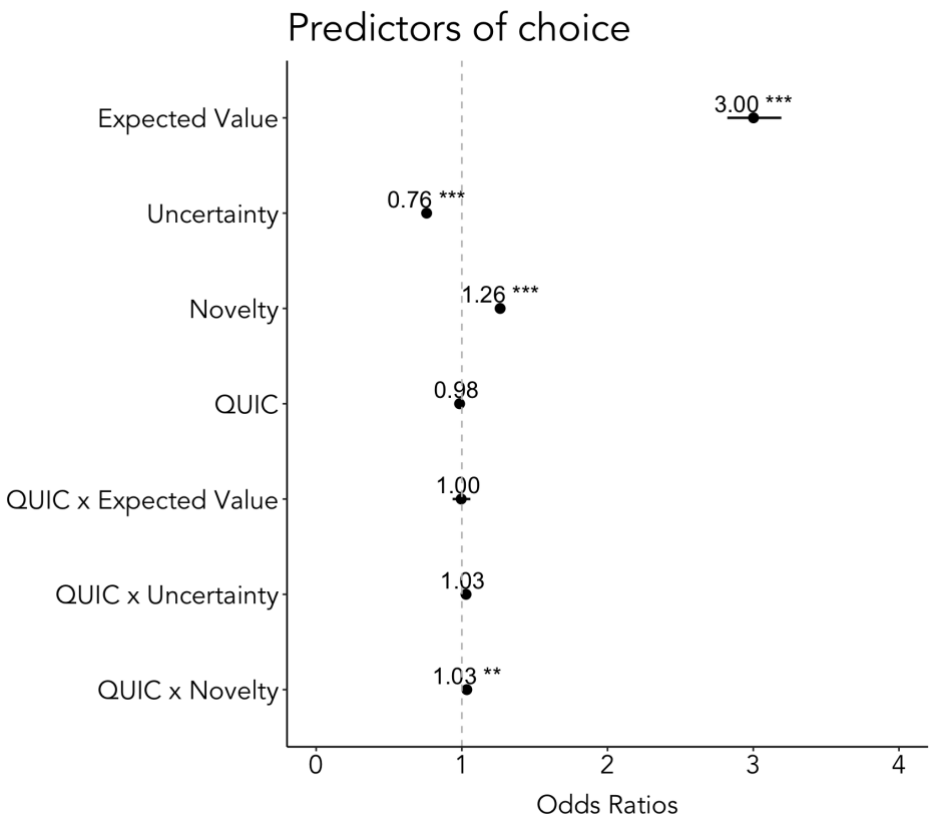


Figure 15. Conditional effects of expected value, uncertainty, novelty, and unpredictability in the caregiving environment (QUIC scores), and interactions between QUIC scores and expected value, reward uncertainty, and stimulus novelty in predicting trial-level choice behaviors. Odds ratios for each effect are plotted.

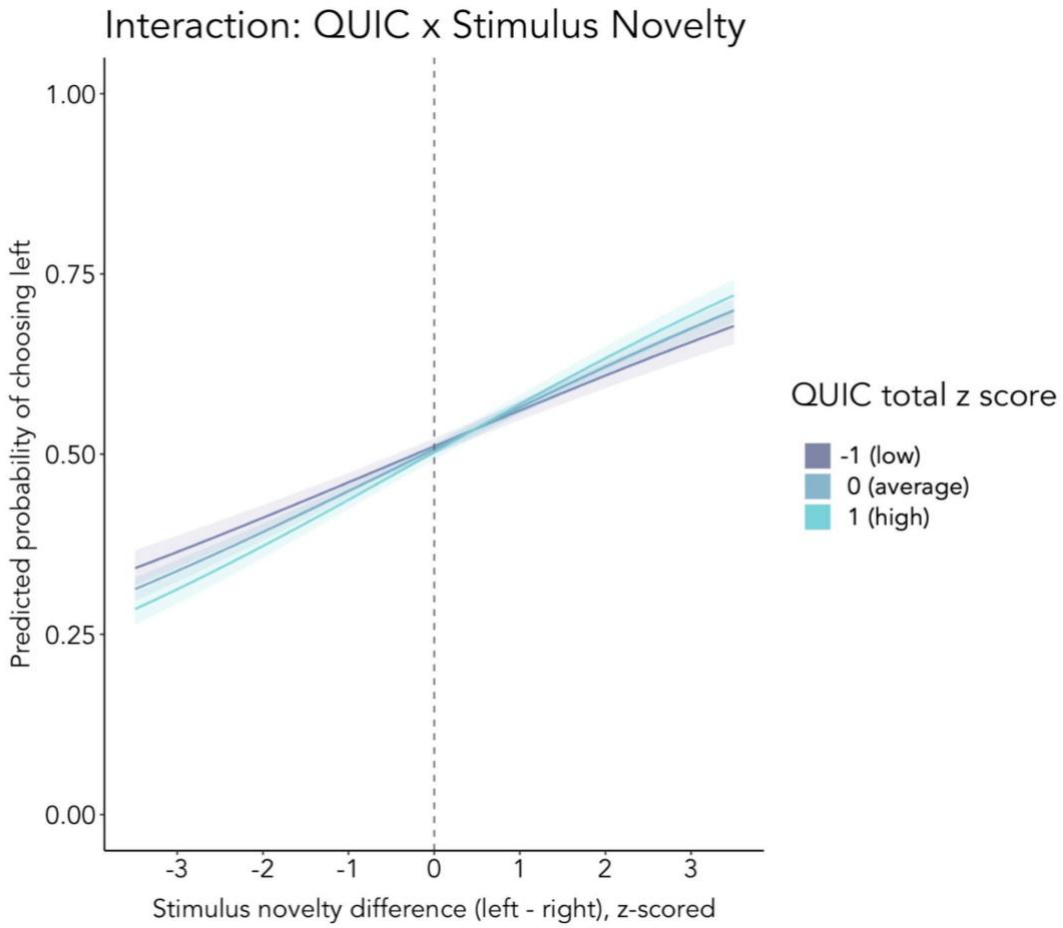


Figure 16. Model predicted effect of stimulus novelty (z-scored difference in stimulus novelty between the two choice options) on choice behavior based on unpredictability in the caregiving environment (QUIC scores) after accounting for other coefficients in the model. Estimated from multilevel logistic regression. Plotted at QUIC total z scores of -1, 0, and 1 (corresponding to relatively low, medium, and high childhood unpredictability) for visualization.

Discussion.

Exploratory behaviors are thought to promote wellbeing by facilitating learning about the environment and promoting interactions with novel, rewarding experiences (Heller et al., 2020; Krebs et al., 2009; Saragosa-Harris et al., 2022). In explore-exploit paradigms, participants choose between exploiting a familiar option with a known reward probability or exploring an unfamiliar, potentially better option. These paradigms provide a useful framework for measuring how

individuals adaptively update their exploratory behavior in response to environmental uncertainties (Cohen et al., 2007). Studies utilizing these paradigms have linked alterations in exploratory decision-making processes to early life adversity (Humphreys, Lee, et al., 2015; Lloyd et al., 2022; Loman et al., 2014; Y. Xu et al., 2023) and to psychopathology risk (Addicott et al., 2017). Recent work suggests that sensitivity to uncertainty and sensitivity to novelty have distinct effects on exploratory decision-making which may, in part, explain individual differences in exploration (Cockburn et al., 2022; Nussenbaum et al., 2023). In this study, we set out to understand how these two motivators of exploratory behavior differ based on early life experiences. We found that reward uncertainty, but not expected value or stimulus novelty, significantly interacted with cumulative ELA scores (combined experiences of abuse and neglect) to predict trial-level choice behavior. Individuals with a history of greater cumulative ELA were less averse to reward uncertainty, an effect that appeared to stem primarily from experiences of childhood abuse. In contrast, higher levels of unpredictability in the caregiving environment predicted greater novelty-seeking tendencies in the task.

Cumulative ELA is associated with lowered avoidance of uncertain stimuli.

Adaptive exploration requires a balance between the motivation to avoid uncertainty and the desire to experience novel, potentially more rewarding experiences. However, in many explore-exploit paradigms, stimuli that are novel are also inherently uncertain, making it difficult to determine the extent to which the novelty versus uncertainty of choice options guide behavior. Here, we used a task adapted from Cockburn et al. (2022) and Nussenbaum, Martin et al. (2023) designed to distinguish the unique effects of expected value, stimulus novelty, and reward uncertainty on trial-by-trial choices. We did not observe significant differences in the effects of

expected value or novelty on trial-level choices based on cumulative ELA history (Childhood Trauma Questionnaire, or CTQ, total scores). However, in contrast to our hypothesis, we found that individuals who reported experiencing greater levels of cumulative ELA were seemingly less averse to reward uncertainty in the task (i.e., avoided stimuli with relatively higher reward uncertainty to a lesser extent). That is, although individuals with high and low ELA scores both avoided stimuli with high reward uncertainty on average, these effects were dampened in individuals with higher cumulative ELA scores. These patterns were also reflected in reaction time analyses, which revealed that the slowing effect of reward uncertainty on reaction time was attenuated in individuals with higher cumulative ELA scores. Together, these suggest that avoidance of uncertainty in the task was present, but dampened, in individuals with higher cumulative ELA scores. Given that in questionnaire data, higher cumulative ELA was associated with greater self-reported intolerance of uncertainty, these findings are puzzling at first glance. Here, we offer two potential interpretations of this pattern of results: these results could reflect "younger" decision-making processes in individuals exposed to higher degrees of ELA, or they could stem from differences in trait anxiety.

The task used in the present study was originally designed by Nussenbaum, Martin et al. (2023) to assess age-related differences in the effects of novelty and uncertainty on exploration. In an examination of participants ages 8 to 27 years old, they found that younger participants evidenced similar novelty-seeking biases but less aversion to reward uncertainty than older participants. Similar to the patterns observed in individuals with a history of high ELA, the slowing effect of reward uncertainty on reaction time was weakened in younger participants. Additionally, like individuals with high ELA scores, younger participants demonstrated decreased overall performance on the task, obtaining fewer coins. Thus, when considering behavior in the face of

uncertainty and overall performance, adults in our sample who experienced higher levels of ELA behave similarly to children and adolescents from the prior study. These parallel patterns could indicate that childhood trauma disrupts the normative developmental process in which exploratory behaviors decrease with age (Gopnik, 2020). It is also possible that individuals with higher ELA experiences experience adult levels of uncertainty aversion but have difficulty translating this into goal-aligned behavior. Given the development of goal-directed behavior (Raab & Hartley, 2018), this could also indicate "younger" decision-making. This account, in which individuals with greater ELA history demonstrate seemingly "younger" choice patterns, would counter a recent theoretical perspective arguing that early adversity accelerates the developmental shift from exploration to exploitation (Frankenhuis & Gopnik, 2023). Given the restricted age range of our sample, we were not able to interrogate developmental trajectories or their relation to ELA in the current study. Future work in developmental samples with a wider age range and range of ELA experiences is needed to determine how these developmental processes vary based on ELA history. Our results suggest that blunted aversion to uncertainty in the task following ELA may stem specifically from experiences of childhood abuse. Thus, future work that specifically investigates how abuse alters these developmental trajectories of uncertainty aversion and exploration is needed.

Another possibility is that more frequent sampling of uncertain stimuli stems from heightened anxiety in individuals who experienced childhood adversity. In the current study, individuals with greater childhood trauma self-reported higher intolerance of uncertainty. Based on these patterns, it would be reasonable to hypothesize that individuals with higher ELA scores would demonstrate heightened avoidance of uncertain stimuli in the task. However, we found that individuals with greater ELA scores were seemingly less avoidant of uncertainty in the task.

Similarly counterintuitive patterns have been observed in studies examining exploratory behaviors in anxious individuals. Although anxiety has consistently been associated with higher intolerance of uncertainty (Gentes & Ruscio, 2011; Norr et al., 2013; Osmanağaoğlu et al., 2018) — a pattern also observed in our self-report data — some studies find that anxious individuals demonstrate a heightened tendency to select uncertain stimuli in exploration tasks. In these scenarios, highly anxious individuals appear to sample more uncertain stimuli as a means to reduce their relative uncertainty (i.e., evidence heightened "directed exploration") (Aberg et al., 2021; Chou et al., 2024). These effects are aligned with patterns observed outside of the laboratory: Anxious individuals exhibit maladaptive attempts to reduce uncertainty, such as checking and reassurance seeking (Kobori & Salkovskis, 2013; Schut et al., 2001). Given the association between ELA and anxiety in our sample, it is thus possible that the lowered avoidance of uncertain stimuli in the task is indicative of an anxious phenotype in individuals with high ELA scores. More generally, these patterns could reflect a motivation to sample highly uncertain stimuli in order to better learn their reward contingencies and reduce their uncertainty. Uncertainty-reducing biases could indicate an adaptive response to early caregiving environments. Information-seeking behavior, particularly when it reduces uncertainty regarding potential threat or danger, could be an effective way to protect an individual from harm. That these patterns appear specific to experiences of abuse suggests that these uncertainty-reducing behaviors may be particularly important in highly threatening environments. Future work would benefit from examining how the valence of the uncertain outcome shapes uncertainty-reducing tendencies. While we examined the effects of an uncertain reward, it is possible that uncertainty-reducing behaviors following ELA, and abuse in particular, would be especially heightened in the face of an uncertain threat.

Greater unpredictability in the caregiving environment is associated with heightened novelty-seeking.

Converging evidence from animal models and humans suggests that unpredictable caregiving is a unique dimension of caregiving adversity that shapes brain development and risk for psychopathology (Glynn & Baram, 2019). Thus, in addition to the cumulative effects of abuse and neglect, we examined how unpredictability of the early caregiving environment shaped the effects of expected value, reward uncertainty, and stimulus novelty on exploratory decision-making. Prior research suggests that early caregiving unpredictability alters the development of reward circuitry (Glynn & Baram, 2019) and is associated with heightened anhedonia in adulthood (Spadoni et al., 2022). Based on these patterns, we expected that individuals who experienced greater unpredictability in their early caregiving environments (i.e., higher total QUIC scores) would demonstrate lower sensitivity to expected value and lower novelty-seeking behaviors in the task. Contrary to our hypothesis, we did not observe an interaction between childhood unpredictability and sensitivity to expected value in the task. This may be because the main effects of expected value were so large that any subtle differences as a function of ELA were difficult to detect.

Also in contrast to our hypothesis, we found that individuals who experienced greater childhood unpredictability appeared to have heightened novelty-seeking behaviors in the task. That is, the extent to which stimulus novelty motivated choice was increased in individuals who self-reported greater childhood unpredictability. Though unexpected, studies of addiction and substance use suggest that blunted reward sensitivity can lead to heightened novelty-seeking and sensation-seeking behaviors (Blum et al., 2000). To the extent that caregiving unpredictability leads to dampened reward sensitivity, the observed results could suggest a similar pattern.

However, this account is complicated in light of the questionnaire results, wherein individuals who experienced greater unpredictability self-reported lower (but only slightly so) novelty-seeking tendencies. Future research is thus needed to understand how unpredictable caregiving shapes novelty-seeking behaviors into adulthood. We also note that a similar interactive effect was observed when examining the interaction between CTQ scores and task novelty-seeking, with higher CTQ scores predicting slightly greater novelty-seeking in the task, but this did not reach significance. This suggests that the novelty-seeking effect might be highest when modeling the effects of caregiving unpredictability, but is likely not specific to this type of adversity.

Conclusion.

The transition from adolescence to adulthood is a formative stage of development in which exploratory behaviors are thought to increase and support healthy development as individuals gain autonomy (Saragosa-Harris et al., 2022; Spear, 2000). The current study examined how experiences of abuse, neglect, and caregiving unpredictability shape exploratory decision-making during this developmental stage. We found that ELA is associated with differences in responses to uncertainty and novelty, and that these effects may differ based on the type of adversity experienced. In contrast to prior work linking ELA to decreased exploration (Humphreys, Lee, et al., 2015; Lloyd et al., 2022; Y. Xu et al., 2023), the lowered aversion to uncertainty and heightened novelty-seeking observed in the current study suggest heightened exploration in individuals with a history of caregiving adversity. Future work is needed to better understand the contexts in which ELA promotes versus undermines exploratory behaviors. Together, these findings suggest that early caregiving adversity shapes learning and decision-making processes, which may have lasting effects on mental health into adulthood.

General Discussion.

Early life adversity (ELA) is estimated to affect over 60% of American youth (Merrick et al., 2018). Individuals who have experienced ELA are at heightened risk for a number of mental health challenges, including mood, anxiety, behavior, and substance use disorders (Kessler et al., 2010). Heightened risk for psychopathology following ELA may stem, in part, from altered development of threat-responsive neural circuitry (Callaghan & Tottenham, 2016; McLaughlin & Sheridan, 2016). ELA is hypothesized to increase vigilance for potential threat by sensitizing neural threat-detection mechanisms (McLaughlin & Lambert, 2017; Nusslock & Miller, 2016; Silvers et al., 2017), potentially resulting in overestimations of threat in ambiguous or uncertain situations (Lange et al., 2019). Notably, intolerance of ambiguity and uncertainty is a common feature among a number of internalizing disorders (Hirsch et al., 2016; McEvoy & Mahoney, 2011). However, few studies have examined how exposure to ELA relates to neural representations of ambiguity or how this putative intolerance of uncertainty shapes decision-making following caregiving adversity.

In this dissertation, we integrated self-report, neuroimaging, and behavioral data from individuals with ranging experiences of ELA to comprehensively examine how ELA relates to neurobehavioral responses to ambiguity and uncertainty. In Study 1 and Study 2, we leveraged representational similarity analysis to examine neural multivariate representations of ambiguity and threat. In Study 1, we found that ELA is associated with reduced neural differentiation between ambiguous and threatening stimuli within affective neural circuitry. These patterns may indicate low thresholds for threat detection, an adaptive response that serves to protect an individual living in a high-threat environment from further harm. However, these patterns were not evident in Study 2 when comparing previously institutionalized (PI) youth to a control group. In Study 3, we found

that ELA was associated with less avoidance of uncertainty in an explore-exploit task and that greater childhood unpredictability was associated with heightened novelty-seeking behaviors in the task. Across three studies, this research provides insight into how ELA shapes neural and behavioral functioning in the face of the unknown and how these processes relate to mental health. In this discussion, I contextualize these findings in the broader literature and offer suggestions for future research.

Does early life adversity shape neural or behavioral responses to ambiguity or uncertainty?

This dissertation evaluated responses to ambiguity and uncertainty following different forms of early life adversity. Though ambiguity and uncertainty are similar, there are subtle differences in these two concepts. Here, we define ambiguity as "here and now" situations characterized by vagueness or equivocality, whereas we define uncertainty as future-oriented scenarios involving unpredictability or obscurity (Grenier et al., 2005).[1] Results from Study 1 and Study 3 suggest that ELA is associated with differences in responses to both ambiguity and uncertainty.

Results from Study 1 suggest that cumulative experiences of abuse and neglect are associated with less differentiation between representations of ambiguity and threat within threat-sensitive neural circuitry. Lowered differentiation between ambiguity and threat may indicate hypersensitivity to potential threat following childhood adversity. This suggests that individuals who experienced higher cumulative ELA evidence lower tolerance for ambiguity (specifically, a tendency to respond to ambiguity as threatening) at the neural level. Hypersensitive threat

[1]Note that alternative definitions of ambiguity and uncertainty exist. For instance, some distinguish between uncertainty, in which the probabilities of a given outcome are known (e.g., a gamble with 25% chance of winning), and ambiguity, in which the probability structure is not known (Kahn & Sarin, 1988).

detection mechanisms are likely adaptive in adverse environments, protecting an individual by enabling rapid detection of threat. In line with these neuroimaging findings, analyses of questionnaire data from Study 3 revealed that higher cumulative ELA is associated with lower self-reported tolerance of ambiguity and lower self-reported tolerance of uncertainty. Together, results from the neuroimaging and self-report data suggest that initial negative neural representations of ambiguity are reflected in everyday attitudes about ambiguity and uncertainty.

The extent to which these initial negative responses to ambiguity translate into behavioral aversion to ambiguity, however, is unclear. In Study 1 we found that, as hypothesized, individuals with higher cumulative ELA exhibited a greater tendency to evaluate ambiguous expressions negatively (i.e., heightened negativity biases). However, this effect was only evident after controlling for global functioning scores and was trending after excluding one participant's low-accuracy blocks in a sensitivity analysis. Moreover, representational similarity between ambiguous and threatening images did not predict negativity biases. Differences between the fMRI and post-scan tasks may, in part, explain why associations with ELA were more robustly observed in the fMRI data than behavioral data. The fMRI task probed rapid, uninstructed neural responses to ambiguous images in the absence of any explicit evaluations of the stimuli. In contrast, the post-scan task prompted participants to make judgments about the facial expressions by rating whether the expression was positive or negative. Prior work suggests that positive evaluations of ambiguity require top-down regulatory mechanisms (Neta et al., 2022; Neta & Tong, 2016). In line with this idea, longer trial-level reaction times predicted more positive ratings of ambiguous stimuli. Thus, although the neuroimaging results suggest greater intolerance for ambiguity following ELA, the behavioral findings indicate that initially negative responses to ambiguity may be attenuated at the decision-making stage, potentially due to regulatory mechanisms. Understanding the extent to

which these regulatory processes differ as a function of ELA is an important avenue for future work.

While the Study 1 behavioral task measured valence judgments about ambiguous stimuli, the behavioral task in Study 3 was designed to measure participants' propensity to interact with uncertain stimuli in the context of an exploration task. Results from analyses of self-report and behavioral data in Study 3 are somewhat contradictory: Participants who experienced greater cumulative ELA self-reported greater intolerance of uncertainty, but exhibited less avoidance of uncertainty in the exploration task. It is possible that heightened sampling of uncertain stimuli reflects directed exploration, in which individuals select uncertain stimuli in reward tasks in order to learn from their outcomes and reduce their uncertainty (Cockburn et al., 2022). Information-seeking actions that decrease uncertainty may be prioritized by individuals who find uncertainty more aversive. In line with this reasoning, similar patterns have been demonstrated in individuals with anxiety (Aberg et al., 2021). Interestingly, prior work has found that ELA is associated with less strategic information seeking in the context of exploration (Y. Xu et al., 2023). In our task, we found that ELA was associated with fewer coins won overall. It is therefore possible that a tendency to oversample more uncertain options — potentially stemming from a motivation to reduce their uncertainty — lowered task performance, lending support to the idea that ELA may lead to less strategic information-seeking behaviors.

Future neuroimaging work may shed light onto the mechanisms linking ELA to uncertainty biases in the context of exploratory decision-making. Cockburn et al. (2022) found that individuals tracked the prospective value of information offered by uncertain stimuli in an explore-exploit task, and that this was reflected in ventromedial prefrontal cortex (vmPFC) functional activity. Aberg et al. (2021) found that anxious individuals, who were more likely to select uncertain stimuli

in order to reduce their uncertainty, exhibited heightened coupling between outcome uncertainty and activity within the anterior insula. Notably, in our Study 1 results, participants who experienced higher ELA demonstrated greater representational overlap between ambiguity and threat within both of these neural regions. Future work examining functional activity within the anterior insula and vmPFC during exploratory decision-making might clarify how ELA shapes representations of uncertainty and how this affects exploratory behaviors.

In summary, analyses of neuroimaging, behavioral, and self-report data from Study 1 and Study 3 suggest that heightened cumulative ELA (specifically, combined experiences of abuse and neglect) is generally associated with differences in neural and behavioral responses to ambiguity and uncertainty, but the ways in which these differences are expressed may depend on context.

Do responses to ambiguity and uncertainty differ depending on the type of adversity experienced?

A notable strength of this dissertation is the incorporation of multiple measures of caregiving adversity. Study 1 and Study 3 both examined the effects of cumulative ELA via total scores on the Childhood Trauma Questionnaire, which combines reports of emotional abuse, physical abuse, sexual abuse, physical neglect, and emotional neglect into a broad measure of adversity exposure (Bernstein et al., 2003). Given the large sample size of Study 3, we were also able to interrogate the unique effects of abuse and neglect separately in that sample using the same questionnaire. Within this sample, we additionally examined the effects of unpredictability in the caregiving environment across five domains (parental involvement, parental predictability, parental environment, physical environment, and safety and security). While Study 1 and Study 3 employed continuous, retrospective measures of ELA in community samples, Study 2 focused on the lasting effects of a specific and severe form of ELA, previous institutionalization in orphanage care. By interrogating the distinct effects of abuse, neglect, caregiving unpredictability, and

institutionalization, this dissertation offers novel insights into how distinct forms of caregiving adversity uniquely shape responses to ambiguity and uncertainty.

Results from Study 1 suggest that cumulative experiences of abuse and neglect are associated with lowered differentiation between representations of ambiguity and threat at the neural level. However, in Study 2 we did not observe significant group differences between previously institutionalized (PI) youth and control youth in representational similarity between ambiguous and threatening images. Although there are many methodological differences in the tasks used in Study 1 and Study 2 that could explain this discrepancy in results (see *Study 2 Discussion*), it is also possible that the disparity in results stem from the different forms of adversity assessed in the two studies (cumulative experiences of abuse and neglect versus previous orphanage care). Institutionalization in orphanage care is a rare and extreme form of adversity. With this in mind, it is not surprising that the neural responses evident in a community sample of individuals with varying experiences of cumulative ELA differ from those observed in PI youth. It is possible that this specific form of ELA is not associated with differences in ambiguity tolerance. That said, given that the task used in Study 2 was not originally designed to assess valence biases or ambiguity tolerance, future research specifically examining the propensity to respond to ambiguity as threatening in PI youth is merited.

Given the large sample size of Study 3, we were able to more comprehensively examine how different forms of adversity shaped behavioral responses to uncertainty and novelty. We found that higher cumulative experiences of abuse and neglect predicted less avoidance of uncertainty in the exploration task. When abuse and neglect were considered separately, this effect appeared specific to experiences of abuse. This pattern of results offers empirical support for the threat-deprivation framework, which posits that caregiving experiences characterized by threat

(e.g., abuse) and deprivation (e.g., neglect) have distinct effects on neurodevelopment (McLaughlin et al., 2014). In particular, abuse is thought to alter development of threat-sensitive neural circuitry (McLaughlin et al., 2014), including regions sensitive to uncertainty (Hein & Monk, 2017). Together, this could suggest that this form of adversity in particular is associated with differences in processing uncertainty. In contrast, we found that a different dimension of adversity, unpredictability of the caregiving environment, predicted greater novelty-seeking behaviors in the task. However, a similar, though not statistically significant, effect was observed when modeling the cumulative effects of abuse and neglect. Thus, it is difficult to determine whether altered novelty-seeking behaviors were specific to one dimension of adversity. Together, the behavioral modeling results from Study 3 suggest some degree of specificity in how different forms of adversity shape behavior, and in particular responses to uncertainty.

Do responses to ambiguity and uncertainty depend on the age or chronicity of caregiving adversity?

One question that this dissertation is unable to answer is the degree to which associations between ELA and ambiguity processing differ depending on the age at which an individual experiences caregiving adversity. It is also unclear whether adverse experiences that are more chronic have larger effects on ambiguity or uncertainty tolerance. The Childhood Trauma Questionnaire, the primary measure used to index ELA in Study 1 and Study 3, assesses experiences of abuse and neglect before the age of fourteen. We did not assess the specific age at which a given adversity was experienced or how long the adversity lasted. We know from prior work that timing of adversity exposure is an important factor to consider when evaluating the effects of ELA on neurodevelopment (Cohodes et al., 2021; Gee & Casey, 2015). Given the development of frontolimbic circuitry across childhood and adolescence, the consequences of

adversity likely differ depending on the developmental stage in which they occur, especially if they coincide with sensitive periods of development (Cohodes et al., 2021; Gee & Casey, 2015). Given that PI youth in Study 2 were adopted before the age of two, this study offers a more focused examination of how ELA experienced during a discrete stage of life shapes later outcomes. That said, it is important to acknowledge the heterogeneity in ages of adoption in our sample. Given the rapid brain development that occurs during the first two years of life (Huang et al., 2015), differences in adoption timing, even during this relatively narrow window of time, has lasting implications for developmental outcomes (Gunnar et al., 2000; Rutter, 1998; Tottenham et al., 2010). Although we did not have sufficient statistical power to evaluate the effects of age of adoption on ambiguity processing, this is an important area for future research.

Clinical considerations.

In this dissertation, we provide evidence that ELA is associated with differences in processing of ambiguity and uncertainty. Neuroimaging results from Study 1 suggest that these patterns may stem from hypersensitivity to potential threat. In an environment characterized by a high prevalence of threat, it is rational to infer threat when presented with an ambiguous scenario (Dunsmoor & Paz, 2015). For individuals raised in threatening environments, such as those who experienced maltreatment, having a low threshold for threat detection is likely adaptive, protecting an individual by enabling rapid detection of threat. However, in safer contexts, these biases for assuming threat may become maladaptive. For instance, intolerance of uncertainty has been shown to mediate the relationship between childhood maltreatment and obsessive-compulsive personality traits (Gray et al., 2024) and nonsuicidal self injury (Ghaderi et al., 2020). Moreover, theoretical work posits that impaired pattern separation following ELA leads to overgeneralization of fear and can increase risk for anxiety, depressive and psychotic symptoms, and general psychopathology

(Lecei & van Winkel, 2020). Results from Study 1 suggest that people who experienced ELA show reduced differentiation between ambiguous and negative stimuli within threat-sensitive neural circuitry. An important avenue for future research will be to examine how difficulties distinguishing between ambiguous and negative stimuli at the neural level shape memory processes and risk for alexithymia and depression. In addition to potential mental health consequences, neural hypersensitivity to potential threat is thought to promote chronic low-grade inflammation, linking ELA to risk for physical health challenges (Nusslock & Miller, 2016). These findings underscore the importance of clinical interventions designed to treat threat generalization and intolerance of uncertainty following caregiving adversity.

Prior clinical intervention work in samples not recruited based on ELA demonstrates the promise of interventions that target intolerance of uncertainty. For example, following one cognitive behavioral intervention designed to reduce intolerance of uncertainty, in which therapists helped patients correct erroneous beliefs about worry, practice problem orientation, and practice cognitive exposure, 77% of participants no longer met criteria for generalized anxiety disorder (Ladouceur et al., 2000). This suggests that responses to uncertainty may be malleable and that interventions focused on addressing uncertainty biases can benefit mental health. In Study 1, we found that taking longer to evaluate ambiguous images — presumably reflecting a top-down regulatory mechanism (Neta et al., 2022; Neta & Tong, 2016) — was associated with better global functioning. However, this effect was dampened in individuals who experienced greater adversity. Future work is needed to determine whether interventions that target responses to uncertainty and ambiguity need to be tailored based on adversity history. Interventions may be most effective during the transition to adulthood, a pivotal period in which risk for psychopathology is heightened (Solmi et al., 2022), particularly for those who have experienced caregiving adversity (van der

Vegt et al., 2009), and responses to ambiguity are believed to have an increased effect on mental health (Bardi et al., 2009; Silvers & Peris, 2023). Prevention and intervention efforts focused on behavior in the face of ambiguity and uncertainty have the potential to promote wellbeing in populations with a history of caregiving adversity.

Appendix: Supplementary Materials.

Supplemental Text.

Study 3.

Methods.

Computational modeling.

In addition to the logistic regression described (see *Study 3 Methods*), we fit participant data with three different reinforcement learning models previously formalized in Cockburn et al. (2022) and Nussenbaum, Martin et al. (2023). In these models, the probability of choosing a given option is expressed as a choice probability that takes into account the subjective utility of the option ($V(s_i)$) and a softmax function with an inverse temperature parameter, βsm, which serves as a weight for how much the subjective utility ($V(s_i)$) guided choices. Higher values of βsm reflect greater sensitivity to value while lower values of βsm indicate greater choice stochasticity. The probability of c_t, the choice they made on trial t is modeled as:

$$p(c_t = 1) = \frac{1}{1 + e^{\beta sm * (V(s_{right}) - V(s_{left}))}}$$

This same formula was used for all models tested (baseline, novelty initialization, familiarity gate). The calculation of the subjective utility ($V(s_i)$) — specifically, in how uncertainty or novelty of the choice options affected $V(s_i)$) — differed depending on the model. After fitting participant data with each model, we then tested which model best characterized participant choices.

Baseline model: Expected value only. In a baseline model, the subjective utility (*V*) of each option (s_i) is predicted by its expected value (*Q*). In line with Cockburn et al. (2022) and Nussenbaum (2022), we modeled participant learning as that of a 'forgetful Bayesian learner'. In this formalization, the expected value (*Q*) of each choice option is calculated as the mean of a beta distribution Beta [α,β], where α and β capture recency-weighted history of wins and losses respectively for a given option (see equation below). The uncertainty of each choice option (U) is defined as the variance of that same distribution, but this value was not included in the baseline model. That is, V(s_i) = *Q*(s_i) in a baseline model that does not account for uncertainty or novelty biases. A learning rate free parameter (η) reflects recency weighting, with higher values reflecting greater weight placed on more recent outcomes.

$$\alpha_i = 1 + \sum_{t=0}^{T-1} \eta^{T-t} \times O_t^w$$

$$\beta_i = 1 + \sum_{t=0}^{T-1} \eta^{T-t} \times O_t^L$$

$$T = current\ trial$$

$$O_t^W = binary\ indicator\ (1\ or\ 0)\ of\ whether\ the\ observed\ outcome\ on\ trial\ t\ was\ a\ win$$

$$O_t^L = binary\ indicator\ (1\ or\ 0)\ of\ whether\ the\ observed\ outcome\ on\ trial\ t\ was\ a\ loss$$

$$\eta = learning\ rate\ free\ parameter, where\ greater\ values\ indicate\ greater\ weight\ on\ more\ recent\ outcomes$$

Novelty initialization model. In this model, we added a novelty bias (free parameter N) to the baseline model by inflating either α or β for each option on its first appearance in the task. This parameter either inflates α (optimistic initialization, indicative of novelty-seeking) or β (pessimistic initialization, indicative of novelty aversion). This model also included an uncertainty bias, where each option's utility is the sum of its expected value (Q) and a weighted uncertainty value (rather than simply its expected value). A free parameter w_U weights the uncertainty value (U) for each option. As described previously, U is equal to the variance of beta distribution Beta [α,β] as previously defined. A negative w_U would represent uncertainty aversion (i.e., decreasing expected value by the uncertainty value) whereas a positive w_U would represent uncertainty seeking (i.e., increasing expected value by the uncertainty value). In this model, $V(s_i) = Q_N(s_i) + w_U U(s_i)$, where Q_N represents the optimistically initialized expected value and $w_U U(s_i)$ represents the stimulus uncertainty weighted by the uncertainty bias.

Familiarity gate model. While the novelty initialization model includes separable novelty and uncertainty biases, the familiarity gate model captures the possibility that novelty and uncertainty interact to affect the subjective utility of choice options. This model included a "familiarity gate", wherein uncertainty affected subjective utility more for less novel (more familiar) options. In doing so, this model reflects the hypothesis that aversion to uncertainty may be buffered in the presence of novelty. In this model, option familiarity (F) was defined as F = 1 – option novelty, where novelty was novelty was calculated as the variance of a beta distribution Beta [α,β], with α = 1 + the number of times the participant had previously seen the given option and β = 1 (in line with model-free analyses). The stimulus uncertainty ($U(s_i)$) was then multiplied by the uncertainty bias (w_U) and the option familiarity (F_i), such that $V(s_i) = Q(s_i) + F_i * w_U * U(s_i)$.

We used a random-effects Bayesian model selection procedure using the Computational Behavioral Modeling (CBM) toolkit (Piray et al., 2019) to determine which of the three models fit the data best. We then tested whether the parameters from the best-fitting model differed as a function of ELA scores.

Results.

Computational modeling of trial-level choices.

We used a random-effects Bayesian model selection procedure with simultaneous hierarchical parameter estimation to determine which of the three computational models (baseline expected value, novelty initialization, or familiarity gate; see *Study 3 Methods* for description) fit the data best. We assessed protected exceedance probabilities (PXPs), which indicate the likelihood that a particular model in a comparison set is the best-fitting model across participants, accounting for variations in model frequencies that could occur by chance. In line with Cockburn et al. (2022) and Nussenbaum et al. (2023), the familiarity gate model was the best-fitting model across participants (*Supplemental Figure 14*). This model accounts for interactions between novelty and uncertainty, such that aversion to uncertainty is lower for more novel options. We then used Spearman rank correlations to test whether participants' estimated parameters from this best-fitting model (using the first-level, nonhierarchical model fits) differed as a function of ELA history (total CTQ scores). CTQ scores were not significantly associated with the extent to which decisions were value-driven (softmax inverse temperature parameter βsm; $r_s(516) = -0.03$, 95% CI [-0.11, 0.06], $p = 0.51$). Contrary to our hypotheses, CTQ scores were not significantly associated with uncertainty biases (parameter w_U; $r_s(516) = -0.03$, 95% CI [-0.11, 0.06], $p = 0.52$). CTQ scores were significantly associated with the extent to which more recent outcomes guided

decisions (the learning rate parameter η), such that individuals with higher CTQ scores placed greater weight on more recent outcomes ($r_s(516) = 0.10$, 95% CI [0.01, 0.18], $p = 0.03$; *Supplemental Figure 15*).

Supplemental Tables.

Study 1.

	Negativity bias (percent of ambiguous faces interpreted negatively; z-scored)					
Predictors	*Estimates*	*95% CI*	*t*	*DF*	*standard error*	*p*
Intercept	-0.03	-0.35 – 0.28	-0.21	38.00	0.16	0.834
ELA (log CTQ score, z-scored)	0.20	-0.12 – 0.52	1.25	38.00	0.16	0.220
Observations	40					
R^2 / R^2 adjusted	0.039 / 0.014					

Supplemental Table 1. Relationship between ELA and negativity biases (the number of ambiguous faces interpreted negatively).

	Negativity bias (percent of ambiguous faces interpreted negatively; z-scored)					
Predictors	*Estimates*	*95% CI*	*t*	*DF*	*standard error*	*p*
Intercept	-0.042	-0.381 – 0.297	-0.249	36.000	0.167	0.805
Global functioning impairment (HoNOS z-score)	-0.117	-0.460 – 0.227	-0.688	36.000	0.169	0.496
Observations	38					
R^2 / R^2 adjusted	0.013 / -0.014					

Supplemental Table 2. Relationship between global functioning and negativity biases (the number of ambiguous faces interpreted negatively).

	Global functioning impairment (HoNOS z-score)					
Predictors	*Estimates*	*95% CI*	*t*	*DF*	*standard error*	*p*
Intercept	-0.10	-0.40 – 0.20	-0.68	33.00	0.15	0.501
ELA (log CTQ score, z-scored)	0.39	0.09 – 0.69	2.64	33.00	0.15	**0.013**
Negativity bias (percent of ambiguous faces interpreted negatively; z-scored)	-0.23	-0.58 – 0.12	-1.32	33.00	0.17	0.196
ELA x negativity bias	0.10	-0.20 – 0.41	0.69	33.00	0.15	0.496
Observations	37					
R^2 / R^2 adjusted	0.220 / 0.150					

Supplemental Table 3. Interaction between ELA and negativity biases in predicting global functioning.

	Negativity bias (percent of ambiguous faces interpreted negatively; z-scored)					
Predictors	*Estimates*	*95% CI*	*t*	*DF*	*standard error*	*p*
Intercept	-0.00	-0.32 – 0.32	-0.00	39.00	0.16	1.000
Average reaction time: ambiguous images (z-scored)	-0.10	-0.42 – 0.22	-0.63	39.00	0.16	0.529
Observations	41					
R^2 / R^2 adjusted	0.010 / -0.015					

Supplemental Table 4. Relationship between average reaction time to ambiguous images and negativity biases (the number of ambiguous faces interpreted negatively).

	Nonthreatening/ambiguous		Threatening/ambiguous		Threatening/nonthreatening	
Region	**Left**[1]	**Right**[1]	**Left**[1]	**Right**[1]	**Left**[1]	**Right**[1]
Amygdala	0.40 (0.08)	0.40 (0.09)	0.38 (0.11)	0.39 (0.10)	0.35 (0.10)	0.36 (0.09)
Accumbens	0.37 (0.07)	0.36 (0.08)	0.36 (0.09)	0.36 (0.09)	0.35 (0.07)	0.35 (0.08)
Anterior Insula	0.39 (0.10)	0.38 (0.10)	0.37 (0.12)	0.38 (0.11)	0.36 (0.10)	0.36 (0.09)
vmPFC	0.35 (0.09)	0.36 (0.10)	0.36 (0.10)	0.37 (0.11)	0.37 (0.08)	0.36 (0.09)
V1	0.65 (0.19)	0.64 (0.19)	0.64 (0.19)	0.63 (0.19)	0.64 (0.21)	0.63 (0.20)
[1] Mean (SD)						

Supplemental Table 5. Average and standard deviation of representational similarity by region and hemisphere.

	Ambiguous/nonthreatening overlap (Fisher z score): Right amygdala					
Predictors	*Estimates*	*95% CI*	*t*	*DF*	*standard error*	*p*
Intercept	0.40	0.37 – 0.42	31.29	38.00	0.01	**<0.001**
ELA (log CTQ score, z-scored)	0.03	0.01 – 0.06	2.56	38.00	0.01	**0.014**
Observations	40					
R^2 / R^2 adjusted	0.148 / 0.125					

	Ambiguous/nonthreatening overlap (Fisher z score): Left amygdala					
Predictors	*Estimates*	*95% CI*	*t*	*DF*	*standard error*	*p*
Intercept	0.40	0.37 – 0.42	30.12	38.00	0.01	**<0.001**
ELA (log CTQ score, z-scored)	0.01	-0.02 – 0.03	0.59	38.00	0.01	0.559
Observations	40					
R^2 / R^2 adjusted	0.009 / -0.017					

	Ambiguous/nonthreatening overlap (Fisher z score): Right nucleus accumbens					
Predictors	*Estimates*	*95% CI*	*t*	*DF*	*standard error*	*p*
Intercept	0.36	0.33 – 0.38	30.84	38.00	0.01	**<0.001**
ELA (log CTQ score, z-scored)	0.01	-0.02 – 0.03	0.44	38.00	0.01	0.662
Observations	40					
R^2 / R^2 adjusted	0.005 / -0.021					

	Ambiguous/nonthreatening overlap (Fisher z score): Left nucleus accumbens					
Predictors	*Estimates*	*95% CI*	*t*	*DF*	*standard error*	*p*
Intercept	0.37	0.34 – 0.39	32.98	38.00	0.01	**<0.001**
ELA (log CTQ score, z-scored)	-0.01	-0.03 – 0.01	-0.96	38.00	0.01	0.342
Observations	40					
R^2 / R^2 adjusted	0.024 / -0.002					

	Ambiguous/nonthreatening overlap (Fisher z score): Right anterior insula					
Predictors	*Estimates*	*95% CI*	*t*	*DF*	*standard error*	*p*
Intercept	0.38	0.35 – 0.41	25.69	38.00	0.01	**<0.001**
ELA (log CTQ score, z-scored)	0.03	-0.00 – 0.06	1.96	38.00	0.01	0.057
Observations	40					
R^2 / R^2 adjusted	0.092 / 0.068					

	Ambiguous/nonthreatening overlap (Fisher z score): Left anterior insula					
Predictors	*Estimates*	*95% CI*	*t*	*DF*	*standard error*	*p*
Intercept	0.38	0.35 – 0.41	25.46	38.00	0.02	**<0.001**
ELA (log CTQ score, z-scored)	0.02	-0.01 – 0.05	1.16	38.00	0.02	0.253
Observations	40					
R^2 / R^2 adjusted	0.034 / 0.009					

	Ambiguous/nonthreatening overlap (Fisher z score): Right vmPFC					
Predictors	*Estimates*	*95% CI*	*t*	*DF*	*standard error*	*p*
Intercept	0.36	0.33 – 0.39	22.71	38.00	0.02	**<0.001**
ELA (log CTQ score, z-scored)	0.01	-0.02 – 0.04	0.49	38.00	0.02	0.628
Observations	40					
R^2 / R^2 adjusted	0.006 / -0.020					

	Ambiguous/nonthreatening overlap (Fisher z score): Left vmPFC					
Predictors	*Estimates*	*95% CI*	*t*	*DF*	*standard error*	*p*
Intercept	0.35	0.32 – 0.38	23.57	38.00	0.01	**<0.001**
ELA (log CTQ score, z-scored)	0.01	-0.02 – 0.05	0.96	38.00	0.02	0.343
Observations	40					
R^2 / R^2 adjusted	0.024 / -0.002					

	Ambiguous/nonthreatening overlap (Fisher z score): Right V1					
Predictors	*Estimates*	*95% CI*	*t*	*DF*	*standard error*	*p*
Intercept	0.63	0.57 – 0.69	21.18	38.00	0.03	**<0.001**
ELA (log CTQ score, z-scored)	-0.03	-0.09 – 0.03	-0.99	38.00	0.03	0.327
Observations	40					
R^2 / R^2 adjusted	0.025 / -0.000					

	Ambiguous/nonthreatening overlap (Fisher z score) Left V1					
Predictors	*Estimates*	*95% CI*	*t*	*DF*	*standard error*	*p*
Intercept	0.636	0.576 – 0.696	21.503	38.000	0.030	**<0.001**
ELA (log CTQ score, z-scored)	-0.033	-0.094 – 0.028	-1.103	38.000	0.030	0.277
Observations	40					
R^2 / R^2 adjusted	0.031 / 0.006					

Supplemental Table 6. ELA and ambiguous/nonthreatening overlap.

Region	Standardized beta estimate	t value	uncorrected p value	FDR corrected q value
right amygdala	0.033	2.56	0.014	0.14
left amygdala	0.008	0.59	0.559	0.66
right nucleus accumbens	0.005	0.44	0.662	0.66
left nucleus accumbens	-0.011	-0.96	0.342	0.49
right anterior insula	0.029	1.96	0.057	0.29
left anterior insula	0.018	1.16	0.253	0.49
right vmPFC	0.008	0.49	0.628	0.66
left vmPFC	0.015	0.96	0.343	0.49
right V1	-0.030	-0.99	0.327	0.49
left V1	-0.033	-1.10	0.277	0.49

Supplemental Table 7. ELA and ambiguous/nonthreatening overlap, with false discovery rate corrected q-values.

	Threatening/nonthreatening overlap (Fisher z score): Right amygdala					
Predictors	*Estimates*	*95% CI*	*t*	*DF*	*standard error*	*p*
Intercept	0.36	0.33 – 0.39	26.12	38.00	0.01	**<0.001**
ELA (log CTQ score, z-scored)	0.03	-0.00 – 0.06	1.97	38.00	0.01	0.056
Observations	40					
R^2 / R^2 adjusted	0.093 / 0.069					

	Threatening/nonthreatening overlap (Fisher z score): Left amygdala					
Predictors	*Estimates*	*95% CI*	*t*	*DF*	*standard error*	*p*
Intercept	0.35	0.32 – 0.38	21.63	38.00	0.02	**<0.001**
ELA (log CTQ score, z-scored)	0.02	-0.01 – 0.05	1.19	38.00	0.02	0.243
Observations	40					
R^2 / R^2 adjusted	0.036 / 0.010					

	Threatening/nonthreatening overlap (Fisher z score): Right nucleus accumbens					
Predictors	*Estimates*	*95% CI*	*t*	*DF*	*standard error*	*p*
Intercept	0.35	0.32 – 0.38	26.40	38.00	0.01	**<0.001**
ELA (log CTQ score, z-scored)	0.00	-0.02 – 0.03	0.17	38.00	0.01	0.866
Observations	40					
R^2 / R^2 adjusted	0.001 / -0.026					

	Threatening/nonthreatening overlap (Fisher z score): Left nucleus accumbens					
Predictors	*Estimates*	*95% CI*	*t*	*DF*	*standard error*	*p*
Intercept	0.35	0.33 – 0.37	31.55	38.00	0.01	**<0.001**
ELA (log CTQ score, z-scored)	0.00	-0.02 – 0.03	0.42	38.00	0.01	0.674
Observations	40					
R^2 / R^2 adjusted	0.005 / -0.021					

	Threatening/nonthreatening overlap (Fisher z score): Right anterior insula					
Predictors	*Estimates*	*95% CI*	*t*	*DF*	*standard error*	*p*
Intercept	0.360	0.332 – 0.387	26.332	38.000	0.014	**<0.001**
ELA (log CTQ score, z-scored)	0.031	0.003 – 0.059	2.229	38.000	0.014	**0.032**
Observations	40					
R^2 / R^2 adjusted	0.116 / 0.092					

	Threatening/nonthreatening overlap (Fisher z score): Left anterior insula					
Predictors	*Estimates*	*95% CI*	*t*	*DF*	*standard error*	*p*
Intercept	0.36	0.33 – 0.39	24.14	38.00	0.01	**<0.001**
ELA (log CTQ score, z-scored)	0.03	-0.00 – 0.06	1.89	38.00	0.02	0.066
Observations	40					
R^2 / R^2 adjusted	0.086 / 0.062					

	Threatening/nonthreatening overlap (Fisher z score): Right vmPFC					
Predictors	*Estimates*	*95% CI*	*t*	*DF*	*standard error*	*p*
Intercept	0.36	0.34 – 0.39	25.69	38.00	0.01	**<0.001**
ELA (log CTQ score, z-scored)	0.00	-0.03 – 0.03	0.23	38.00	0.01	0.820
Observations	40					
R^2 / R^2 adjusted	0.001 / -0.025					

	Threatening/nonthreatening overlap (Fisher z score): Left vmPFC					
Predictors	*Estimates*	*95% CI*	*t*	*DF*	*standard error*	*p*
Intercept	0.37	0.34 – 0.40	27.42	38.00	0.01	**<0.001**
ELA (log CTQ score, z-scored)	0.01	-0.02 – 0.03	0.40	38.00	0.01	0.688
Observations	40					
R^2 / R^2 adjusted	0.004 / -0.022					

	Threatening/nonthreatening overlap (Fisher z score): Right V1					
Predictors	*Estimates*	*95% CI*	*t*	*DF*	*standard error*	*p*
Intercept	0.62	0.56 – 0.69	19.54	38.00	0.03	**<0.001**
ELA (log CTQ score, z-scored)	-0.01	-0.08 – 0.05	-0.39	38.00	0.03	0.700
Observations	40					
R^2 / R^2 adjusted	0.004 / -0.022					

	Threatening/nonthreatening overlap (Fisher z score): Left V1					
Predictors	*Estimates*	*95% CI*	*t*	*DF*	*standard error*	*p*
Intercept	0.631	0.565 – 0.697	19.329	38.000	0.033	**<0.001**
ELA (log CTQ score, z-scored)	-0.017	-0.084 – 0.050	-0.503	38.000	0.033	0.618
Observations	40					
R^2 / R^2 adjusted	0.007 / -0.020					

Supplemental Table 8. ELA and threatening/nonthreatening overlap.

Region	Standardized beta estimate	t value	uncorrected p value	FDR corrected q value
right amygdala	0.027	1.97	0.056	0.22
left amygdala	0.020	1.19	0.243	0.61
right nucleus accumbens	0.002	0.17	0.866	0.87
left nucleus accumbens	0.005	0.42	0.674	0.87
right anterior insula	0.031	2.23	0.032	0.22
left anterior insula	0.028	1.89	0.066	0.22
right vmPFC	0.003	0.23	0.820	0.87
left vmPFC	0.006	0.41	0.688	0.87
right V1	-0.013	-0.39	0.700	0.87
left V1	-0.017	-0.50	0.618	0.87

Supplemental Table 9. ELA and threatening/nonthreatening overlap, with false discovery rate corrected q-values.

	Ambiguous/threatening overlap (Fisher z score): Right amygdala					
Predictors	*Estimates*	*95% CI*	*t*	*DF*	*standard error*	*p*
Intercept	0.389	0.353 – 0.424	22.237	36.000	0.017	**<0.001**
Global functioning impairment (HoNOS z-score)	-0.001	-0.037 – 0.035	-0.040	36.000	0.018	0.968
Observations	38					
R^2 / R^2 adjusted	0.000 / -0.028					

	Ambiguous/threatening overlap (Fisher z score): Left amygdala					
Predictors	*Estimates*	*95% CI*	*t*	*DF*	*standard error*	*p*
Intercept	0.37	0.34 – 0.41	20.67	36.00	0.02	**<0.001**
Global functioning impairment (HoNOS z-score)	0.01	-0.03 – 0.04	0.28	36.00	0.02	0.781
Observations	38					
R^2 / R^2 adjusted	0.002 / -0.026					

	Ambiguous/threatening overlap (Fisher z score): Right nucleus accumbens					
Predictors	*Estimates*	*95% CI*	*t*	*DF*	*standard error*	*p*
Intercept	0.36	0.33 – 0.39	24.17	36.00	0.01	**<0.001**
Global functioning impairment (HoNOS z-score)	0.01	-0.02 – 0.04	0.54	36.00	0.01	0.595
Observations	38					
R^2 / R^2 adjusted	0.008 / -0.020					

	Ambiguous/threatening overlap (Fisher z score): Left nucleus accumbens					
Predictors	*Estimates*	*95% CI*	*t*	*DF*	*standard error*	*p*
Intercept	0.37	0.34 – 0.40	24.17	36.00	0.02	**<0.001**
Global functioning impairment (HoNOS z-score)	-0.01	-0.04 – 0.02	-0.42	36.00	0.02	0.675
Observations	38					
R^2 / R^2 adjusted	0.005 / -0.023					

	Ambiguous/threatening overlap (Fisher z score): Right anterior insula					
Predictors	*Estimates*	*95% CI*	*t*	*DF*	*standard error*	*p*
Intercept	0.3776	0.3411 – 0.4140	21.0082	36.0000	0.0180	**<0.001**
Global functioning impairment (HoNOS z-score)	-0.0001	-0.0370 – 0.0369	-0.0031	36.0000	0.0182	0.998
Observations	38					
R^2 / R^2 adjusted	0.000 / -0.028					

	Ambiguous/threatening overlap (Fisher z score): Left anterior insula					
Predictors	*Estimates*	*95% CI*	*t*	*DF*	*standard error*	*p*
Intercept	0.37	0.33 – 0.41	18.67	36.00	0.02	**<0.001**
Global functioning impairment (HoNOS z-score)	0.01	-0.03 – 0.05	0.36	36.00	0.02	0.722
Observations	38					
R^2 / R^2 adjusted	0.004 / -0.024					

	Ambiguous/threatening overlap (Fisher z score): Right vmPFC					
Predictors	*Estimates*	*95% CI*	*t*	*DF*	*standard error*	*p*
Intercept	0.37	0.33 – 0.40	20.85	36.00	0.02	**<0.001**
Global functioning impairment (HoNOS z-score)	0.03	-0.01 – 0.07	1.71	36.00	0.02	0.095
Observations	38					
R^2 / R^2 adjusted	0.075 / 0.050					

	Ambiguous/threatening overlap (Fisher z score): Left vmPFC					
Predictors	*Estimates*	*95% CI*	*t*	*DF*	*standard error*	*p*
Intercept	0.36	0.33 – 0.40	21.29	36.00	0.02	**<0.001**
Global functioning impairment (HoNOS z-score)	0.02	-0.02 – 0.05	0.89	36.00	0.02	0.382
Observations	38					
R^2 / R^2 adjusted	0.021 / -0.006					

	Ambiguous/threatening overlap (Fisher z score): Right V1					
Predictors	*Estimates*	*95% CI*	*t*	*DF*	*standard error*	*p*
Intercept	0.63	0.57 – 0.69	20.84	36.00	0.03	**<0.001**
Global functioning impairment (HoNOS z-score)	-0.01	-0.08 – 0.05	-0.48	36.00	0.03	0.631
Observations	38					
R^2 / R^2 adjusted	0.006 / -0.021					

	Ambiguous/threatening overlap (Fisher z score): Left V1					
Predictors	*Estimates*	*95% CI*	*t*	*DF*	*standard error*	*p*
Intercept	0.64	0.58 – 0.71	19.89	36.00	0.03	**<0.001**
Global functioning impairment (HoNOS z-score)	-0.03	-0.09 – 0.04	-0.82	36.00	0.03	0.417
Observations	38					
R^2 / R^2 adjusted	0.018 / -0.009					

Supplemental Table 10. Relationship between ambiguous/threatening overlap and global functioning.

	Negativity bias (percent of ambiguous faces interpreted negatively; z-scored)					
Predictors	*Estimates*	*95% CI*	*t*	*DF*	*standard error*	*p*
Intercept	0.22	-1.03 – 1.48	0.36	39.00	0.62	0.723
Ambiguous/threatening overlap (Fisher z score): Right amygdala	-0.57	-3.71 – 2.56	-0.37	39.00	1.55	0.714
Observations	41					
R^2 / R^2 adjusted	0.003 / -0.022					

	Negativity bias (percent of ambiguous faces interpreted negatively; z-scored)					
Predictors	*Estimates*	*95% CI*	*t*	*DF*	*standard error*	*p*
Intercept	0.09	-1.10 – 1.27	0.15	39.00	0.59	0.880
Ambiguous/threatening overlap (Fisher z score): Left amygdala	-0.24	-3.27 – 2.80	-0.16	39.00	1.50	0.875
Observations	41					
R^2 / R^2 adjusted	0.001 / -0.025					

	Negativity bias (percent of ambiguous faces interpreted negatively; z-scored)					
Predictors	*Estimates*	*95% CI*	*t*	*DF*	*standard error*	*p*
Intercept	0.31	-1.05 – 1.68	0.46	39.00	0.68	0.646
Ambiguous/threatening overlap (Fisher z score): Right nucleus accumbens	-0.87	-4.57 – 2.82	-0.48	39.00	1.83	0.636
Observations	41					
R^2 / R^2 adjusted	0.006 / -0.020					

	Negativity bias (percent of ambiguous faces interpreted negatively; z-scored)					
Predictors	*Estimates*	*95% CI*	*t*	*DF*	*standard error*	*p*
Intercept	-0.72	-2.07 – 0.62	-1.09	39.00	0.67	0.284
Ambiguous/threatening overlap (Fisher z score): Left nucleus accumbens	1.98	-1.61 – 5.57	1.12	39.00	1.77	0.271
Observations	41					
R^2 / R^2 adjusted	0.031 / 0.006					

	Negativity bias (percent of ambiguous faces interpreted negatively; z-scored)					
Predictors	*Estimates*	*95% CI*	*t*	*DF*	*standard error*	*p*
Intercept	-0.07	-1.27 – 1.14	-0.12	39.00	0.60	0.907
Ambiguous/threatening overlap (Fisher z score): Right anterior insula	0.18	-2.89 – 3.26	0.12	39.00	1.52	0.904
Observations	41					
R^2 / R^2 adjusted	0.000 / -0.025					

	Negativity bias (percent of ambiguous faces interpreted negatively; z-scored)					
Predictors	*Estimates*	*95% CI*	*t*	*DF*	*standard error*	*p*
Intercept	0.39	-0.67 – 1.44	0.74	39.00	0.52	0.462
Ambiguous/threatening overlap (Fisher z score): Left anterior insula	-1.05	-3.76 – 1.67	-0.78	39.00	1.34	0.440
Observations	41					
R^2 / R^2 adjusted	0.015 / -0.010					

	Negativity bias (percent of ambiguous faces interpreted negatively; z-scored)					
Predictors	*Estimates*	*95% CI*	*t*	*DF*	*standard error*	*p*
Intercept	0.14	-0.99 – 1.26	0.25	39.00	0.56	0.807
Ambiguous/threatening overlap (Fisher z score): Right vmPFC	-0.37	-3.31 – 2.57	-0.26	39.00	1.45	0.799
Observations	41					
R^2 / R^2 adjusted	0.002 / -0.024					

	Negativity bias (percent of ambiguous faces interpreted negatively; z-scored)					
Predictors	*Estimates*	*95% CI*	*t*	*DF*	*standard error*	*p*
Intercept	-0.17	-1.38 – 1.03	-0.29	39.00	0.59	0.770
Ambiguous/threatening overlap (Fisher z score): Left vmPFC	0.48	-2.71 – 3.68	0.31	39.00	1.58	0.762
Observations	41					
R^2 / R^2 adjusted	0.002 / -0.023					

	Negativity bias (percent of ambiguous faces interpreted negatively; z-scored)					
Predictors	*Estimates*	*95% CI*	*t*	*DF*	*standard error*	*p*
Intercept	0.25	-0.88 – 1.37	0.44	39.00	0.55	0.660
Ambiguous/threatening overlap (Fisher z score): Right V1	-0.39	-2.11 – 1.32	-0.46	39.00	0.85	0.646
Observations	41					
R^2 / R^2 adjusted	0.005 / -0.020					

	Negativity bias (percent of ambiguous faces interpreted negatively; z-scored)					
Predictors	*Estimates*	*95% CI*	*t*	*DF*	*standard error*	*p*
Intercept	0.18	-0.94 – 1.30	0.33	39.00	0.55	0.746
Ambiguous/threatening overlap (Fisher z score): Left V1	-0.28	-1.97 – 1.40	-0.34	39.00	0.83	0.735
Observations	41					
R^2 / R^2 adjusted	0.003 / -0.023					

Supplemental Table 11. Relationship between ambiguous/threatening overlap and negativity biases (number of ambiguous faces interpreted negatively).

Study 2.

Amygdala.

Parameter	Coefficient	SE	95% CI	t(75)	p
(Intercept)	1.00	0.06	(0.88, 1.13)	15.87	< .001
ELA group (PI)	-0.02	0.02	(-0.06, 0.01)	-1.31	0.194
Number of voxels in amygdala	-1.62e-03	7.15e-04	(-3.04e-03, -1.96e-04)	-2.27	0.026
Age (z-scored)	0.01	8.12e-03	(-1.35e-03, 0.03)	1.83	0.072

Nucleus accumbens.

Parameter	Coefficient	SE	95% CI	t(75)	p
(Intercept)	0.84	0.05	(0.75, 0.93)	18.52	< .001
ELA group (PI)	6.36e-03	0.01	(-0.02, 0.03)	0.45	0.654
Number of voxels in nucleus accumbens	4.93e-04	1.04e-03	(-1.57e-03, 2.56e-03)	0.48	0.636
Age (z-scored)	8.59e-04	6.93e-03	(-0.01, 0.01)	0.12	0.902

Anterior insula.

Parameter	Coefficient	SE	95% CI	t(75)	p
(Intercept)	0.76	0.06	(0.64, 0.88)	12.41	< .001
ELA group (PI)	0.01	0.01	(-0.01, 0.04)	0.98	0.329
Number of voxels in anterior insula	3.14e-04	2.25e-04	(-1.33e-04, 7.61e-04)	1.40	0.166
Age (z-scored)	4.16e-03	7.04e-03	(-9.87e-03, 0.02)	0.59	0.557

vmPFC.

Parameter	Coefficient	SE	95% CI	t(74)	p
(Intercept)	0.88	0.04	(0.81, 0.95)	24.96	< .001
ELA group (PI)	-5.56e-03	0.01	(-0.03, 0.02)	-0.43	0.669
Number of voxels in vmPFC	-2.36e-04	3.05e-04	(-8.43e-04, 3.71e-04)	-0.78	0.440
Age (z-scored)	0.01	6.46e-03	(-2.66e-03, 0.02)	1.58	0.118

V1.

Parameter	Coefficient	SE	95% CI	t(74)	p
(Intercept)	0.83	0.05	(0.73, 0.93)	16.43	< .001
ELA group (PI)	0.03	0.02	(-8.42e-03, 0.06)	1.49	0.139
Number of voxels in V1	2.61e-04	2.07e-04	(-1.52e-04, 6.74e-04)	1.26	0.213
Age (z-scored)	-6.35e-03	7.94e-03	(-0.02, 9.48e-03)	-0.80	0.427

Supplemental Table 12. Relationship between ELA group (PI or control) and representational overlap between threatening and ambiguous images, controlling for linear age.

Amygdala.

Parameter	Coefficient	SE	95% CI	t(76)	p
(Intercept)	0.75	0.06	(0.64, 0.87)	13.27	< .001
ELA group (PI)	0.01	0.02	(-0.02, 0.05)	0.92	0.363
number voxels happy run amy bilateral Thr50	9.80e-04	6.50e-04	(-3.14e-04, 2.27e-03)	1.51	0.136
Age (z-scored)	-4.03e-03	7.70e-03	(-0.02, 0.01)	-0.52	0.602

Nucleus accumbens.

Parameter	Coefficient	SE	95% CI	t(76)	p
(Intercept)	0.81	0.05	(0.72, 0.91)	17.04	< .001
ELA group (PI)	4.63e-03	0.01	(-0.02, 0.03)	0.31	0.756
Number of voxels in nucleus accumbens	6.50e-04	1.13e-03	(-1.59e-03, 2.89e-03)	0.58	0.565
Age (z-scored)	-0.01	7.30e-03	(-0.03, 2.94e-04)	-1.95	0.055

Anterior insula.

Parameter	Coefficient	SE	95% CI	t(76)	p
(Intercept)	0.77	0.06	(0.64, 0.90)	11.84	< .001
ELA group (PI)	-7.15e-03	0.02	(-0.04, 0.03)	-0.44	0.661
Number of voxels in anterior insula	2.72e-04	2.38e-04	(-2.01e-04, 7.46e-04)	1.15	0.255
Age (z-scored)	-7.50e-04	7.97e-03	(-0.02, 0.02)	-0.09	0.925

vmPFC.

Parameter	Coefficient	SE	95% CI	t(76)	p
(Intercept)	0.82	0.05	(0.73, 0.91)	17.98	< .001
ELA group (PI)	7.77e-03	0.02	(-0.03, 0.04)	0.47	0.639
Number of voxels in vmPFC	1.41e-04	4.00e-04	(-6.55e-04, 9.38e-04)	0.35	0.725
Age (z-scored)	-2.26e-03	8.08e-03	(-0.02, 0.01)	-0.28	0.780

V1.

Parameter	Coefficient	SE	95% CI	t(75)	p
(Intercept)	0.81	0.05	(0.71, 0.91)	15.95	< .001
ELA group (PI)	0.02	0.02	(-0.02, 0.05)	0.86	0.394
Number of voxels in V1	2.57e-04	2.11e-04	(-1.63e-04, 6.76e-04)	1.22	0.227
Age (z-scored)	-0.02	8.29e-03	(-0.03, -1.01e-03)	-2.11	0.038

Supplemental Table 13. Relationship between ELA group (PI or control) and representational overlap between nonthreatening and ambiguous images, controlling for linear age.

Parameter	Coefficient	SE	95% CI	t(73)	p
(Intercept)	-3.68	1.95	(-7.56, 0.21)	-1.89	0.063
Fear/neutral overlap	3.92	2.24	(-0.54, 8.38)	1.75	0.084
ELA group (PI)	0.28	2.73	(-5.16, 5.72)	0.10	0.918
Age group (child)	0.17	0.24	(-0.30, 0.65)	0.73	0.467
ELA group x fear/neutral overlap	0.15	3.17	(-6.17, 6.48)	0.05	0.962

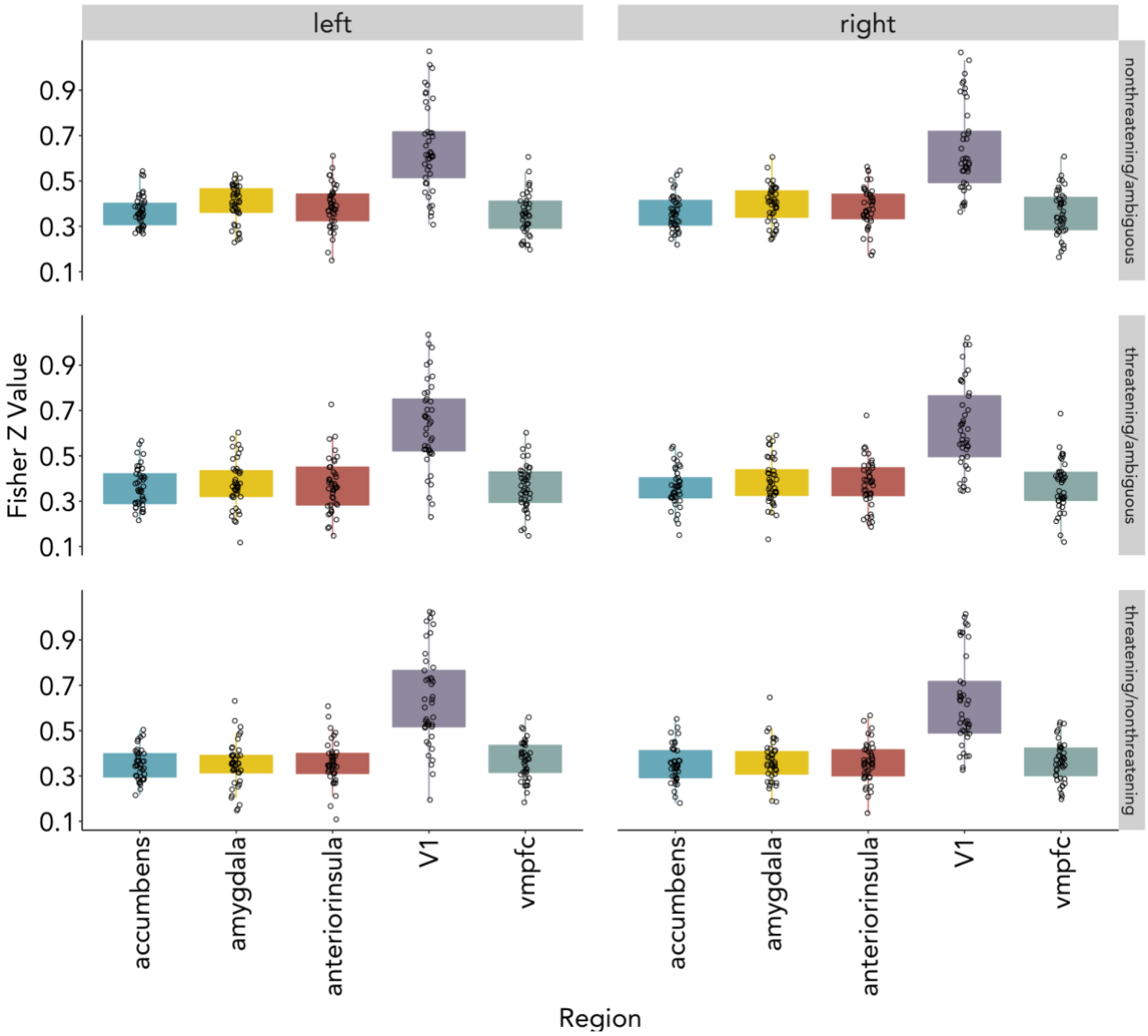
Supplemental Table 14. Interaction: ELA group (PI or control) and representational overlap between threatening and ambiguous images within the amygdala in predicting anxiety.

Parameter	Coefficient	SE	95% CI	t(74)	p
(Intercept)	1.45	1.88	(-2.31, 5.20)	0.77	0.445
Happy/neutral overlap	-1.97	2.22	(-6.40, 2.45)	-0.89	0.377
ELA group (PI)	2.31	3.01	(-3.69, 8.31)	0.77	0.445
Age group (child)	0.10	0.24	(-0.38, 0.59)	0.42	0.673
ELA group x happy/neutral overlap	-2.32	3.56	(-9.41, 4.76)	-0.65	0.516

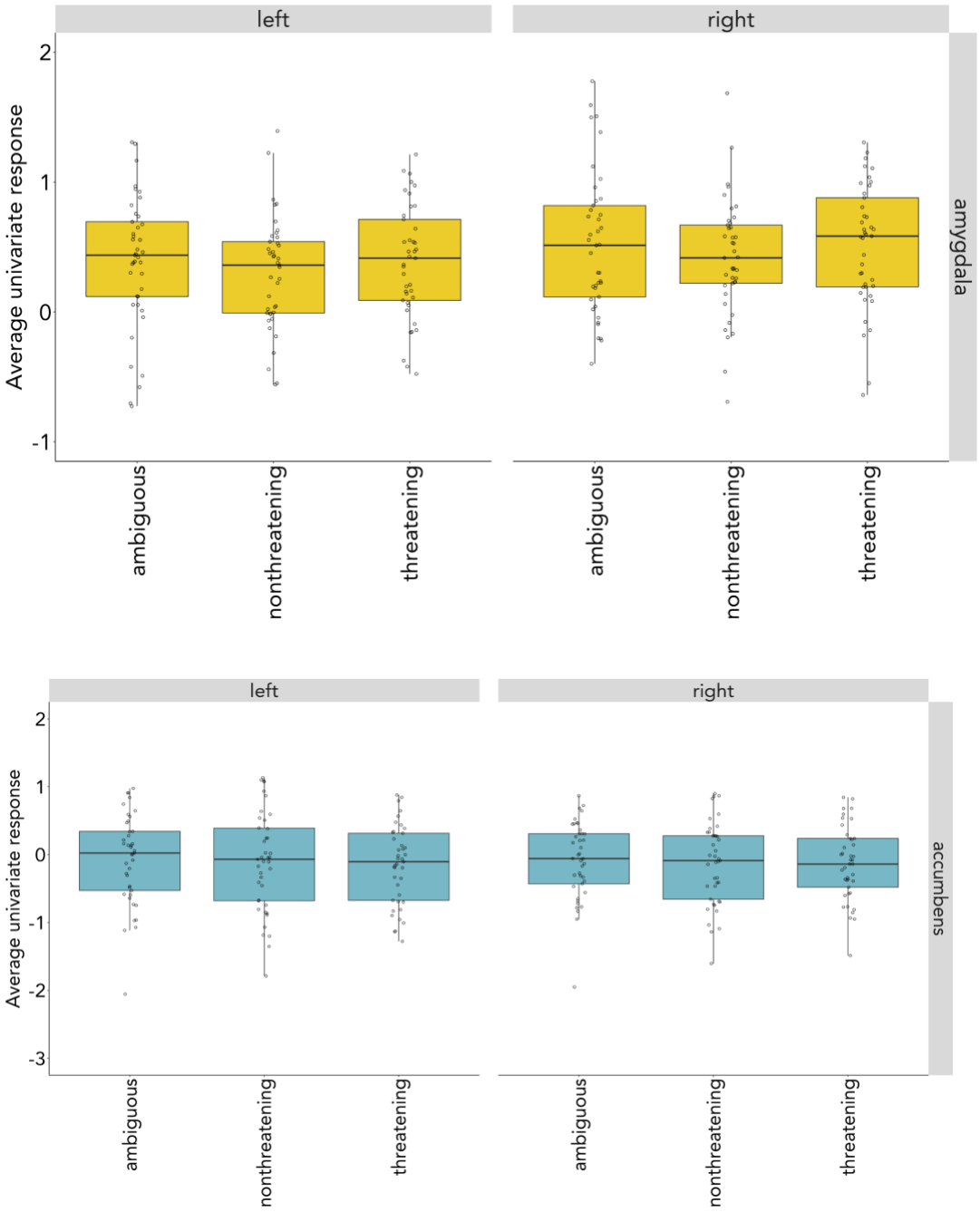
Supplemental Table 15. Interaction: ELA group (PI or control) and representational overlap between nonthreatening and ambiguous images within the amygdala in predicting anxiety.

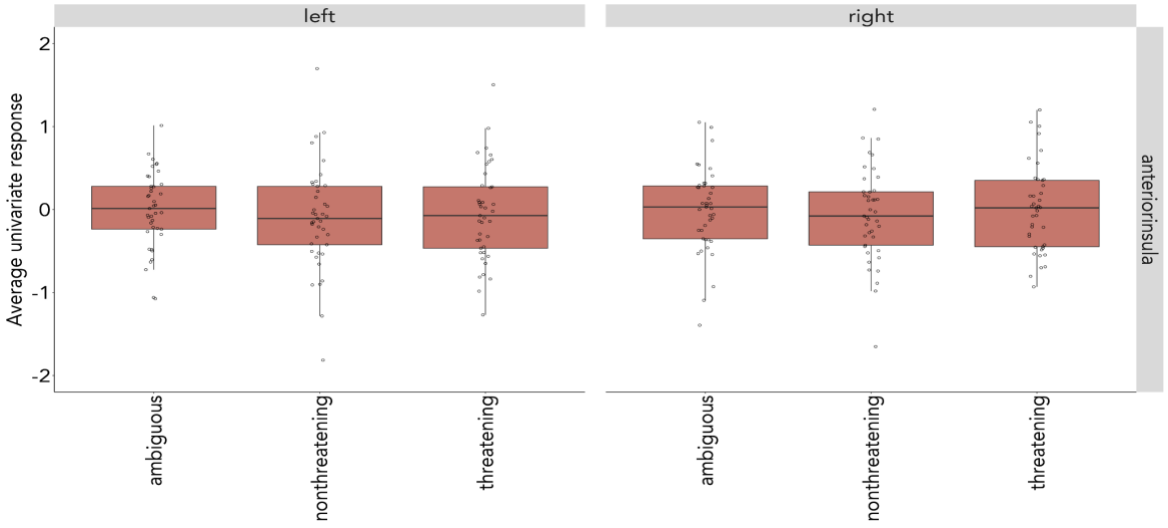
Supplemental Figures.

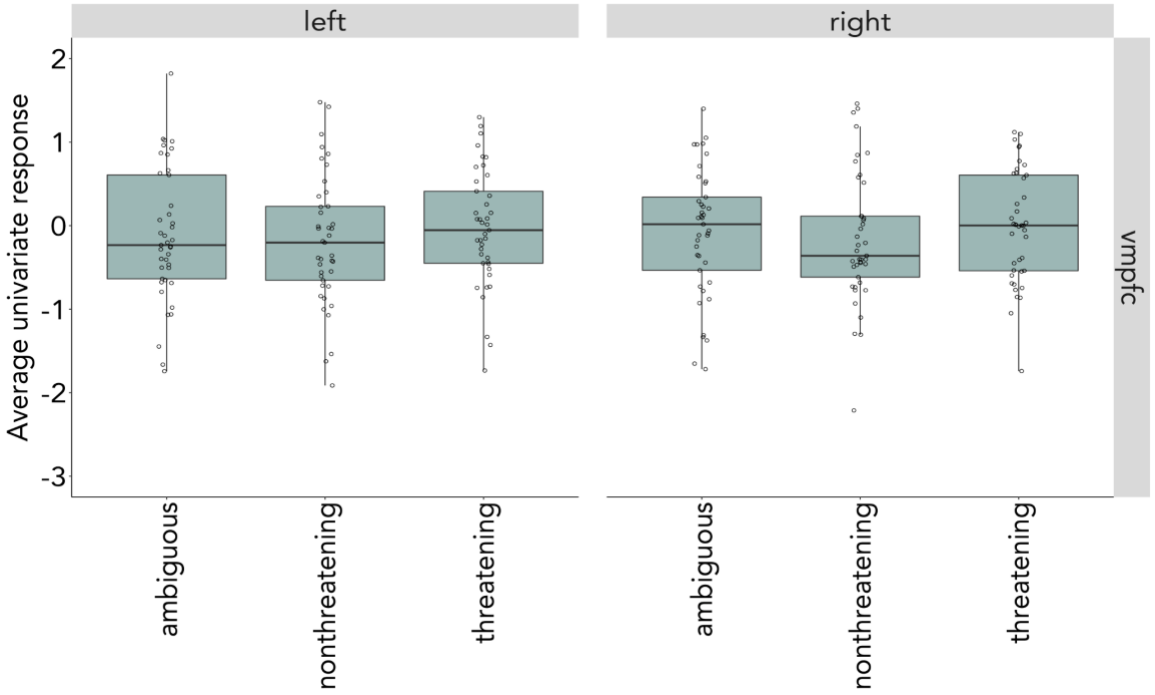
Study 1.

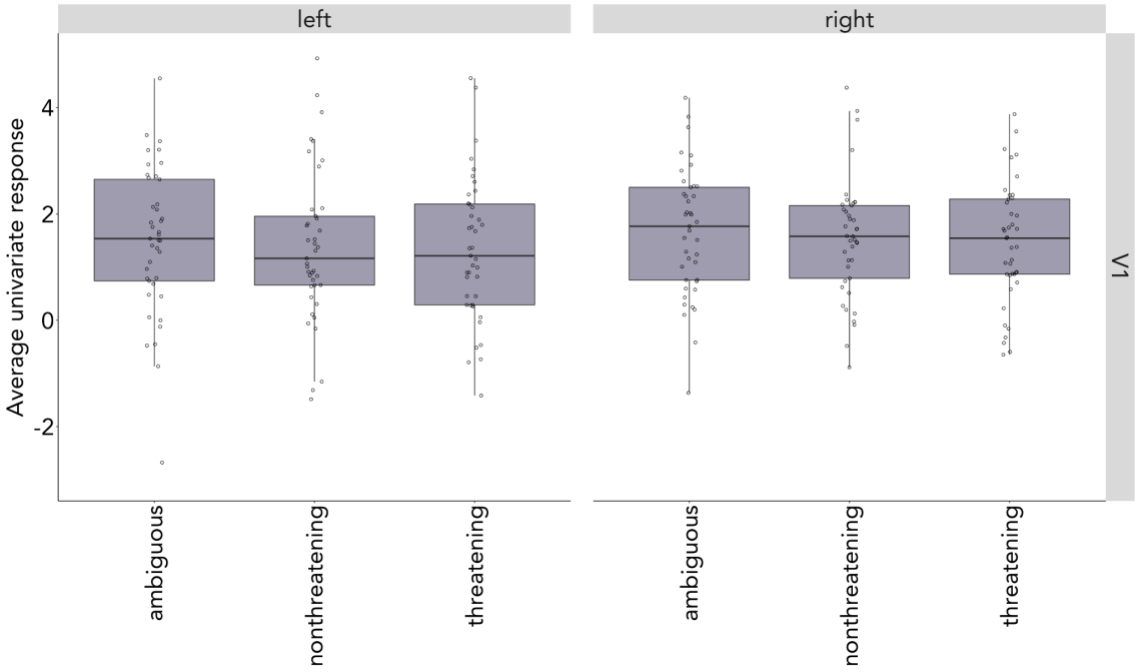


Supplemental Figure 1. Fisher z-transformed correlation values from RSA by condition pair within each region of interest.

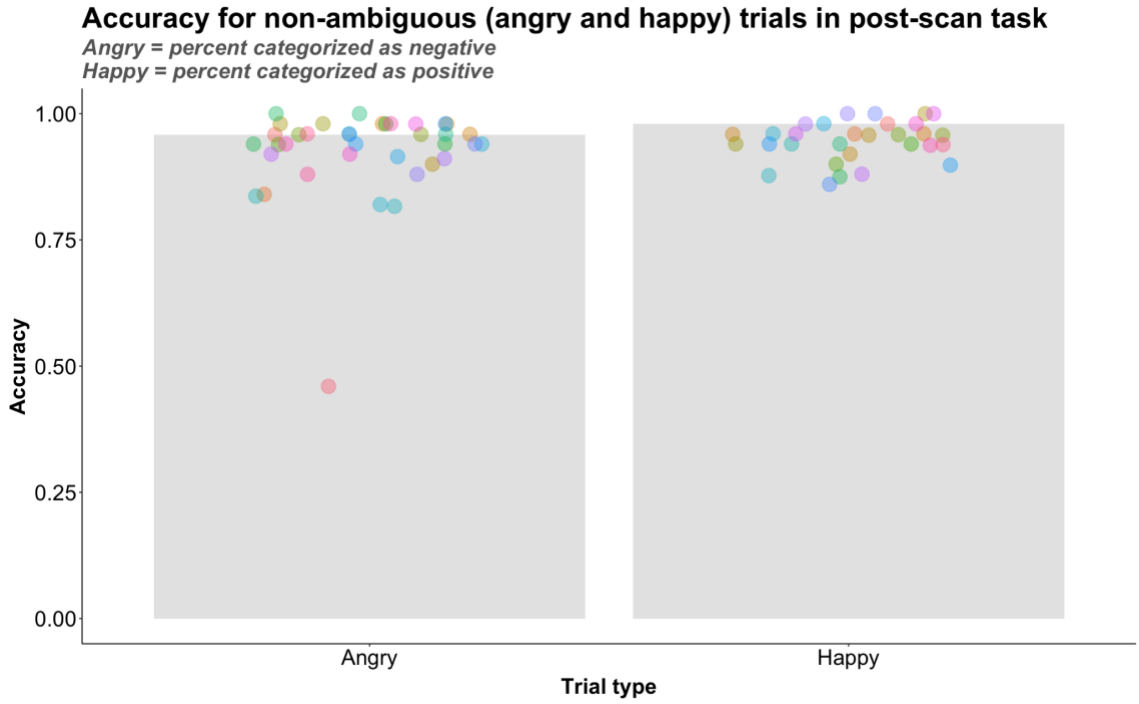

left
right
amygdala
accumbens
Average univariate response
2
1
0
-1
-2
-3
ambiguous
nonthreatening
threatening


left
right
anteriorinsula
Average univariate response
2
1
0
-1
-2
ambiguous
nonthreatening
threatening


left
right
vmpfc
Average univariate response
2
1
0
-1
-2
-3
ambiguous
nonthreatening
threatening



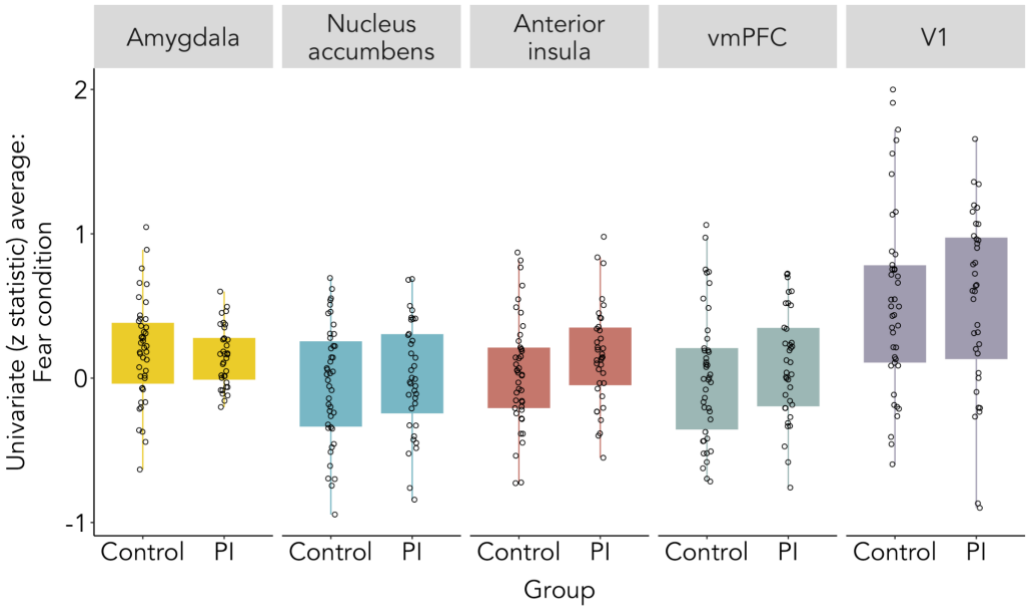
Supplemental Figure 2. Average univariate values (z statistics) by condition within each region.



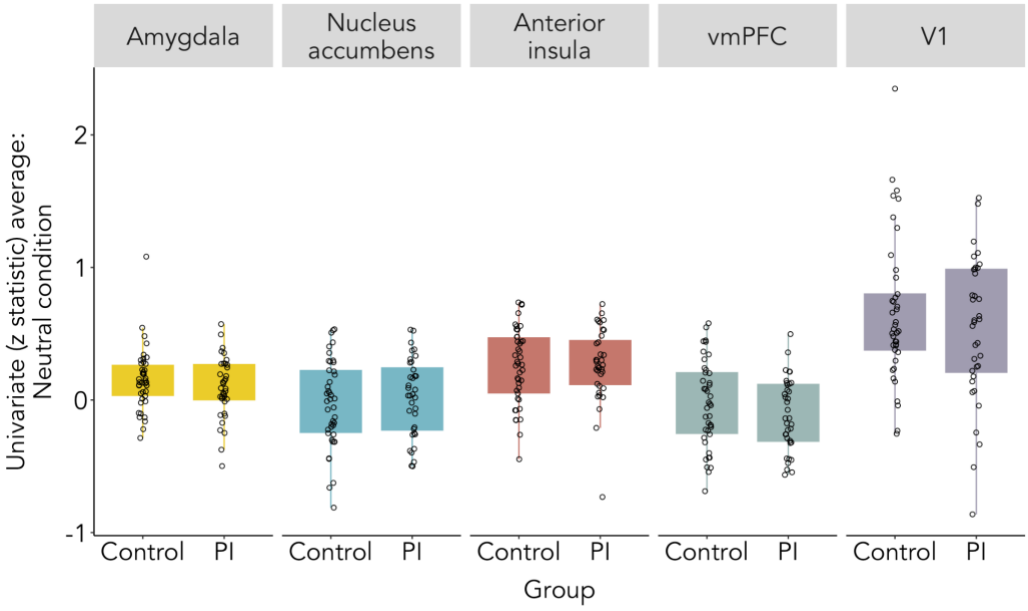
Supplemental Figure 3. Accuracy for threatening (angry) and nonthreatening (happy) trials in the post-scan task.

Study 2.

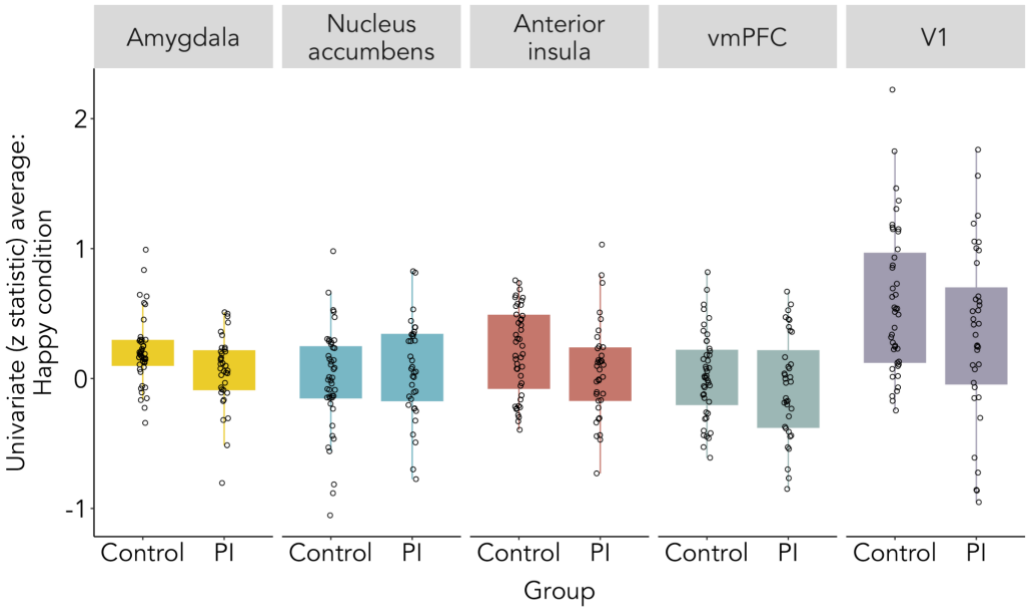
(A)


Amygdala
Nucleus accumbens
Anterior insula
vmPFC
V1
Univariate (z statistic) average: Fear condition
2
1
0
-1
Control
PI
Group

(B)

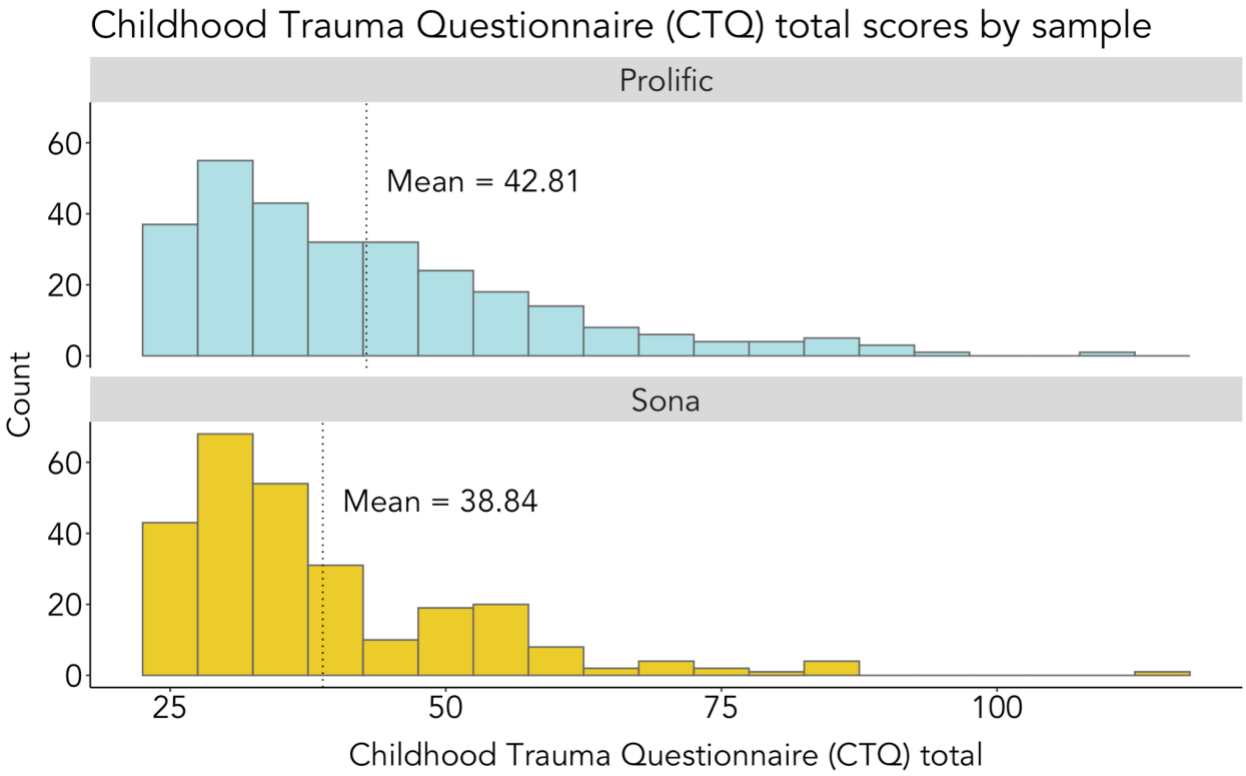

Amygdala
Nucleus accumbens
Anterior insula
vmPFC
V1
Univariate (z statistic) average: Neutral condition
2
1
0
-1
Control
PI
Group

(C)

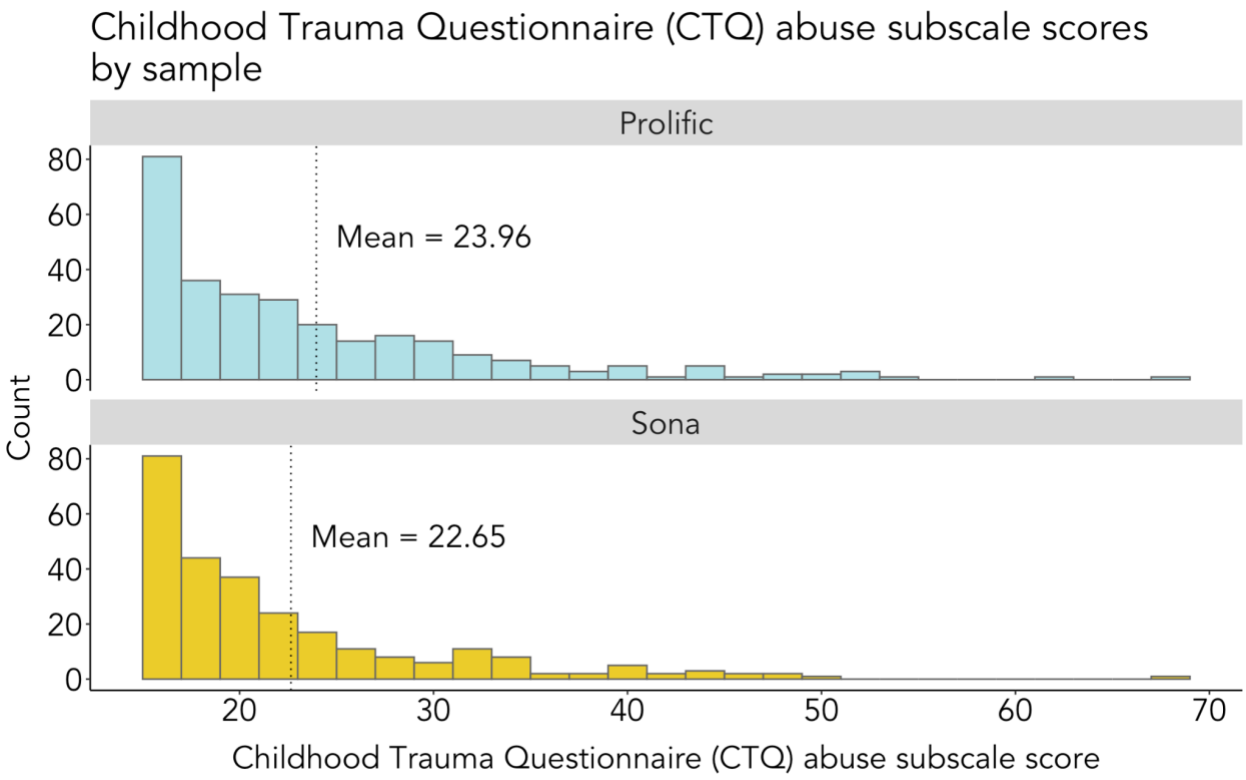


Supplemental Figure 4. Average univariate values (z statistics) for the (A) fearful, (B) neutral, and (C) happy conditions within each region.

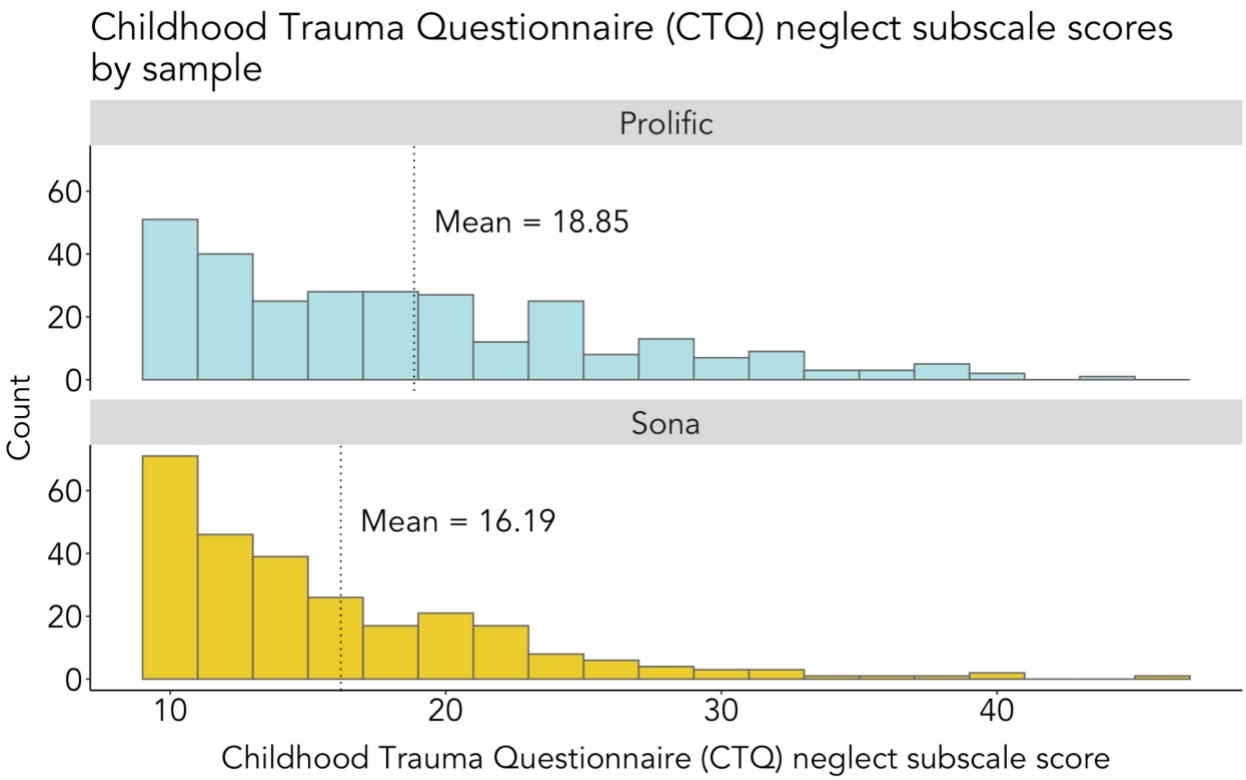
Study 3.



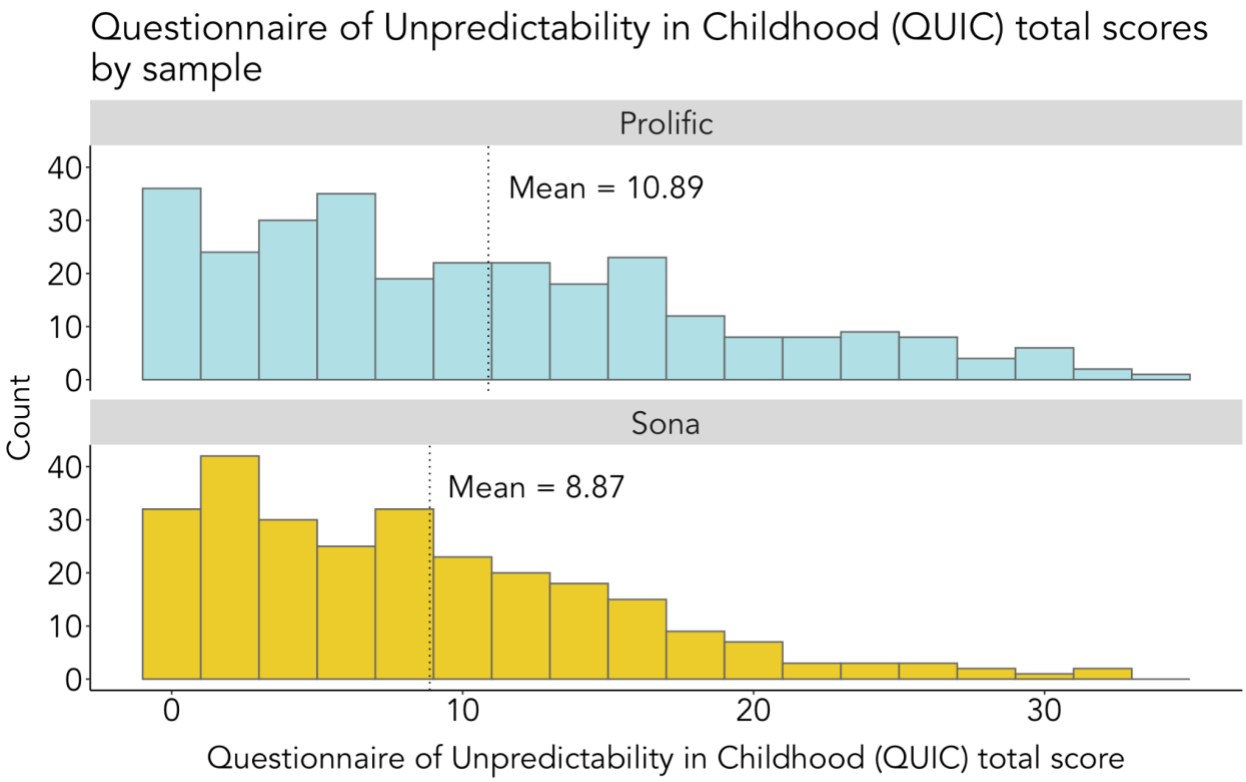
Supplemental Figure 5. Distribution and mean of Childhood Trauma Questionnaire (CTQ) total scores by sample. Higher scores indicate greater cumulative experiences of childhood trauma, including abuse and neglect.



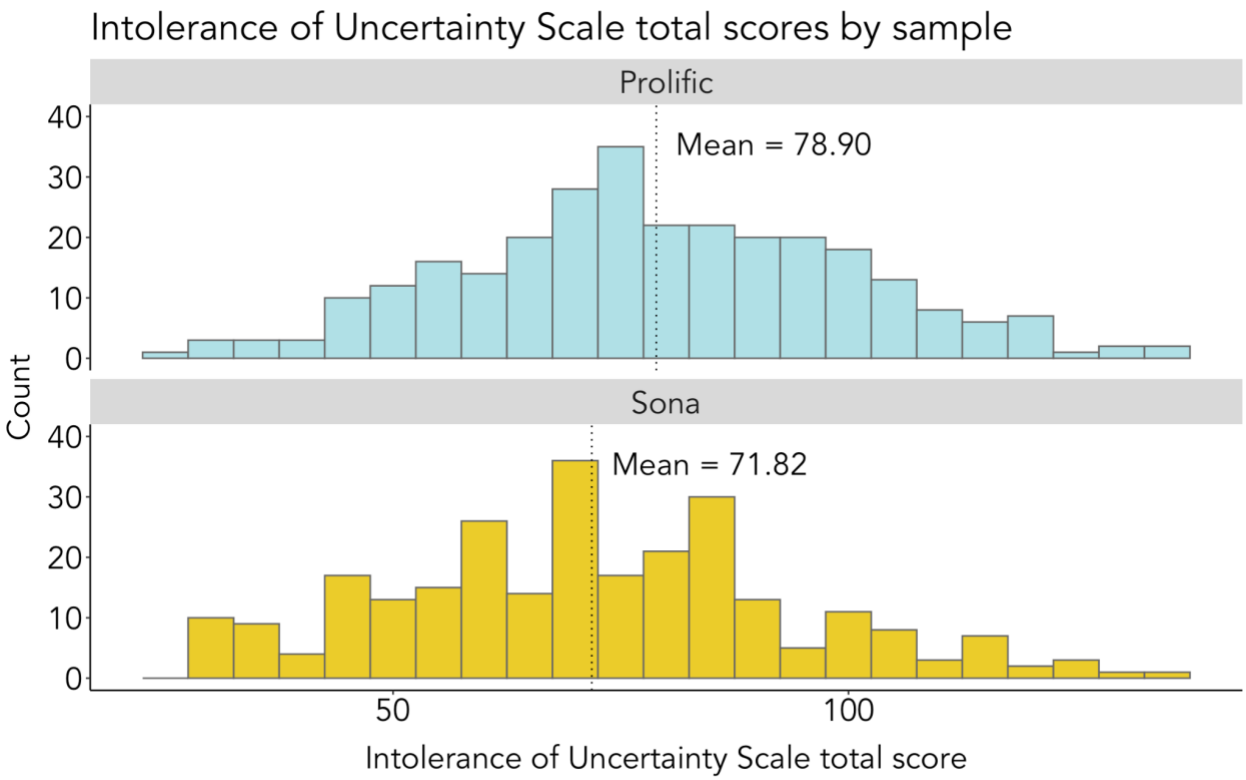
Supplemental Figure 6. Distribution and mean of Childhood Trauma Questionnaire (CTQ) abuse subscale scores (sum of emotional abuse, physical abuse, and sexual abuse) by sample.



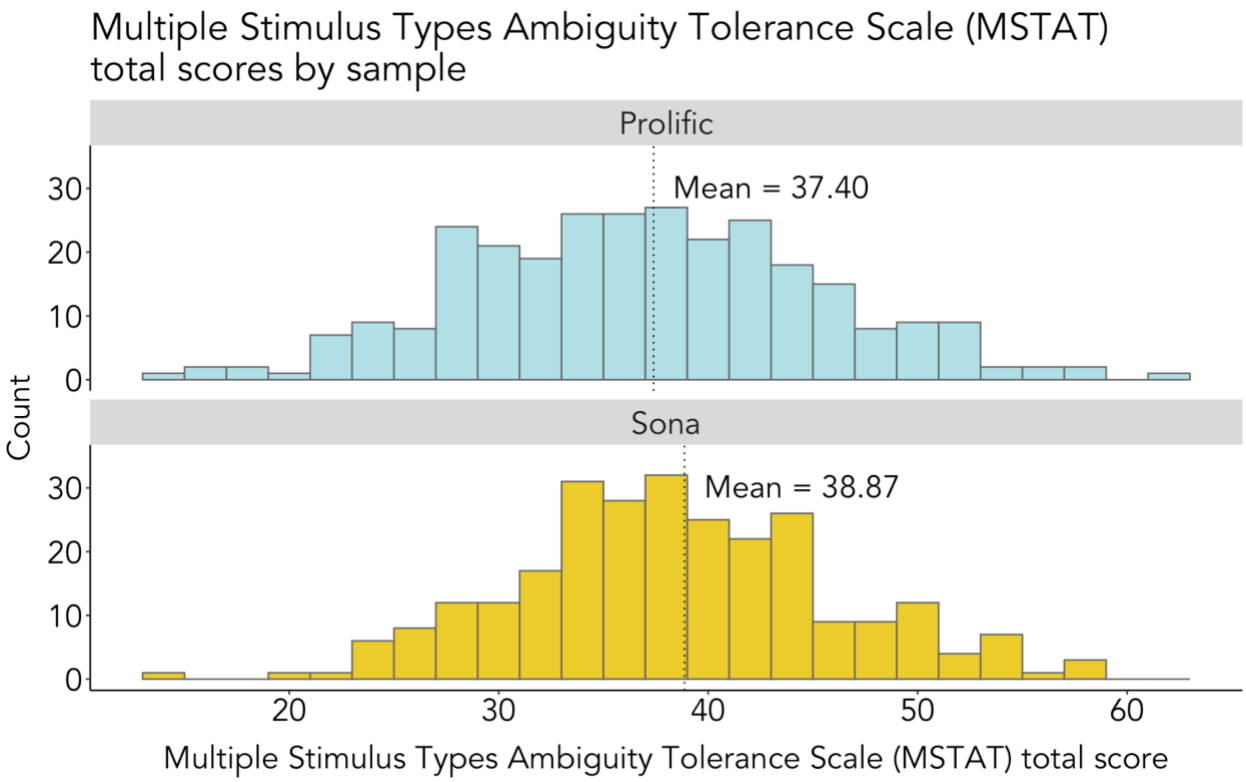
Supplemental Figure 7. Distribution and mean of Childhood Trauma Questionnaire (CTQ) neglect subscale scores (sum of emotional neglect and physical neglect) by sample.



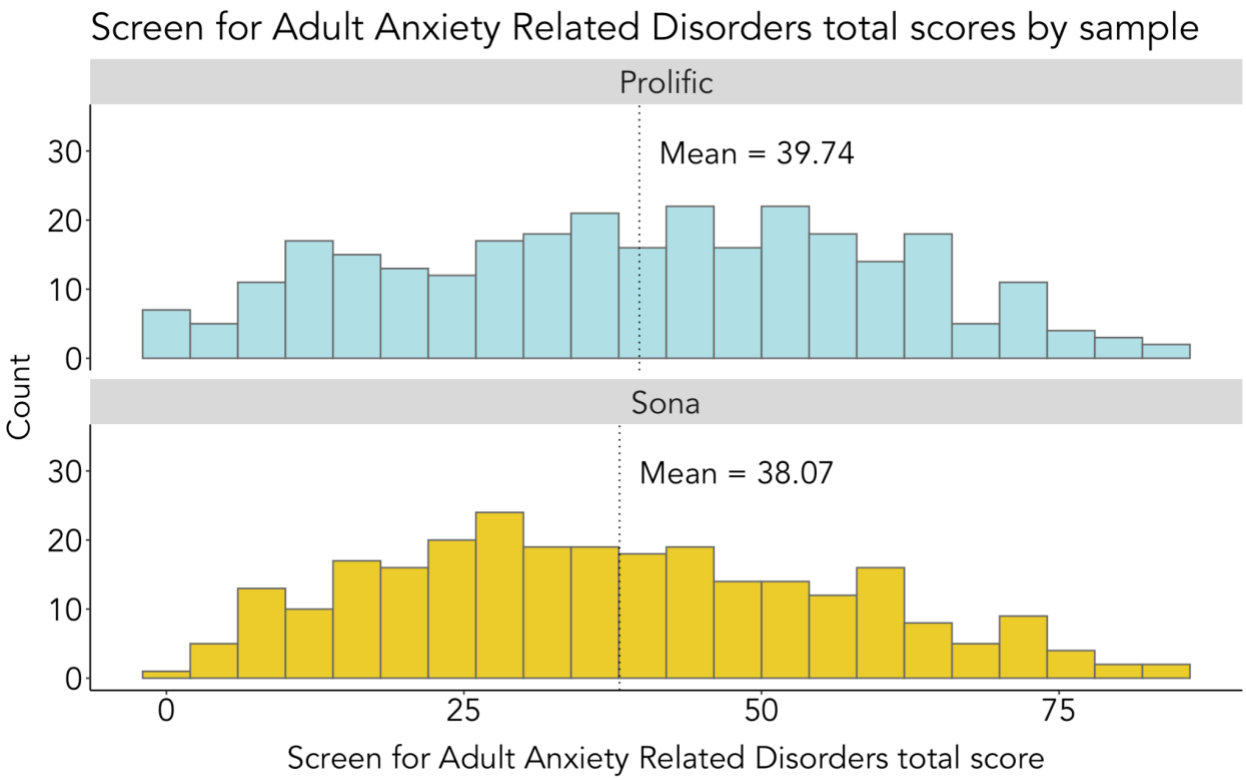
Supplemental Figure 8. Distribution and mean of Questionnaire of Unpredictability in Childhood (QUIC) scores by sample. Higher scores indicate greater exposure to unpredictability in the caregiving environment during childhood.



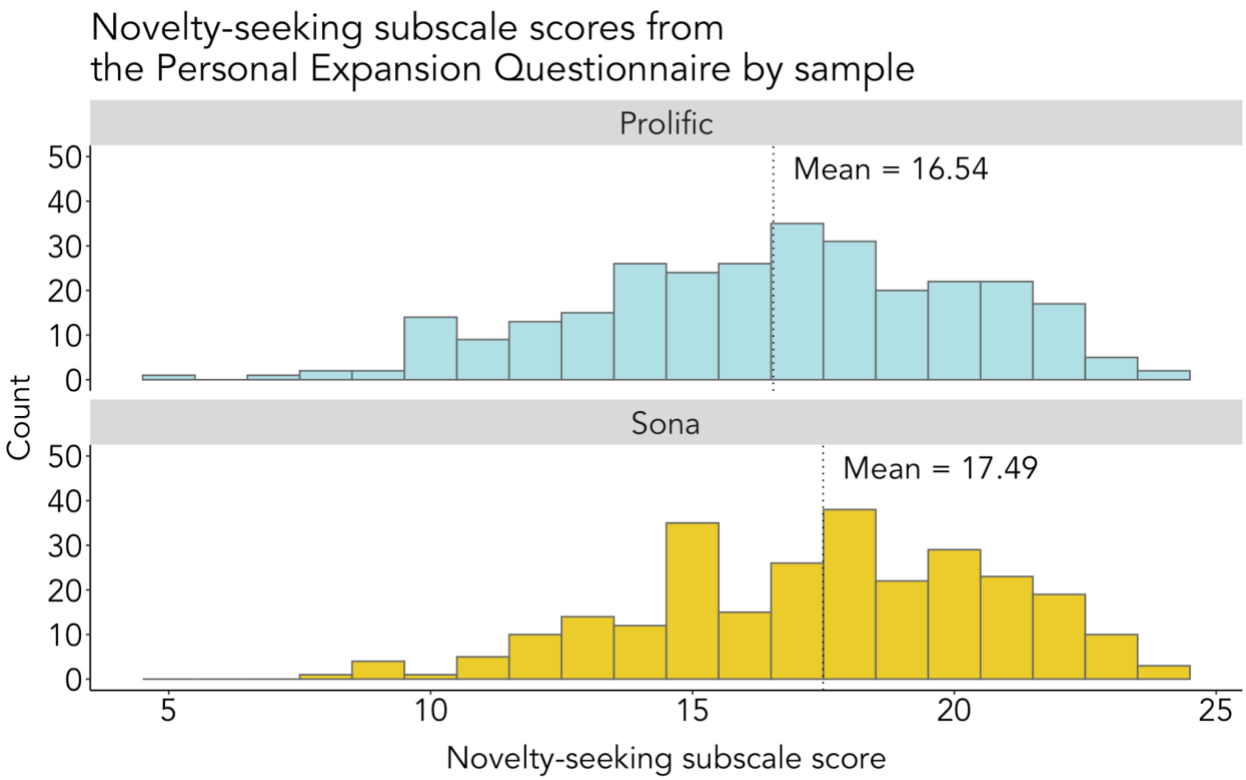
Supplemental Figure 9. Distribution and mean of Intolerance of Uncertainty Scale scores by sample. Higher scores indicate greater intolerance (i.e., lower tolerance) for uncertainty.



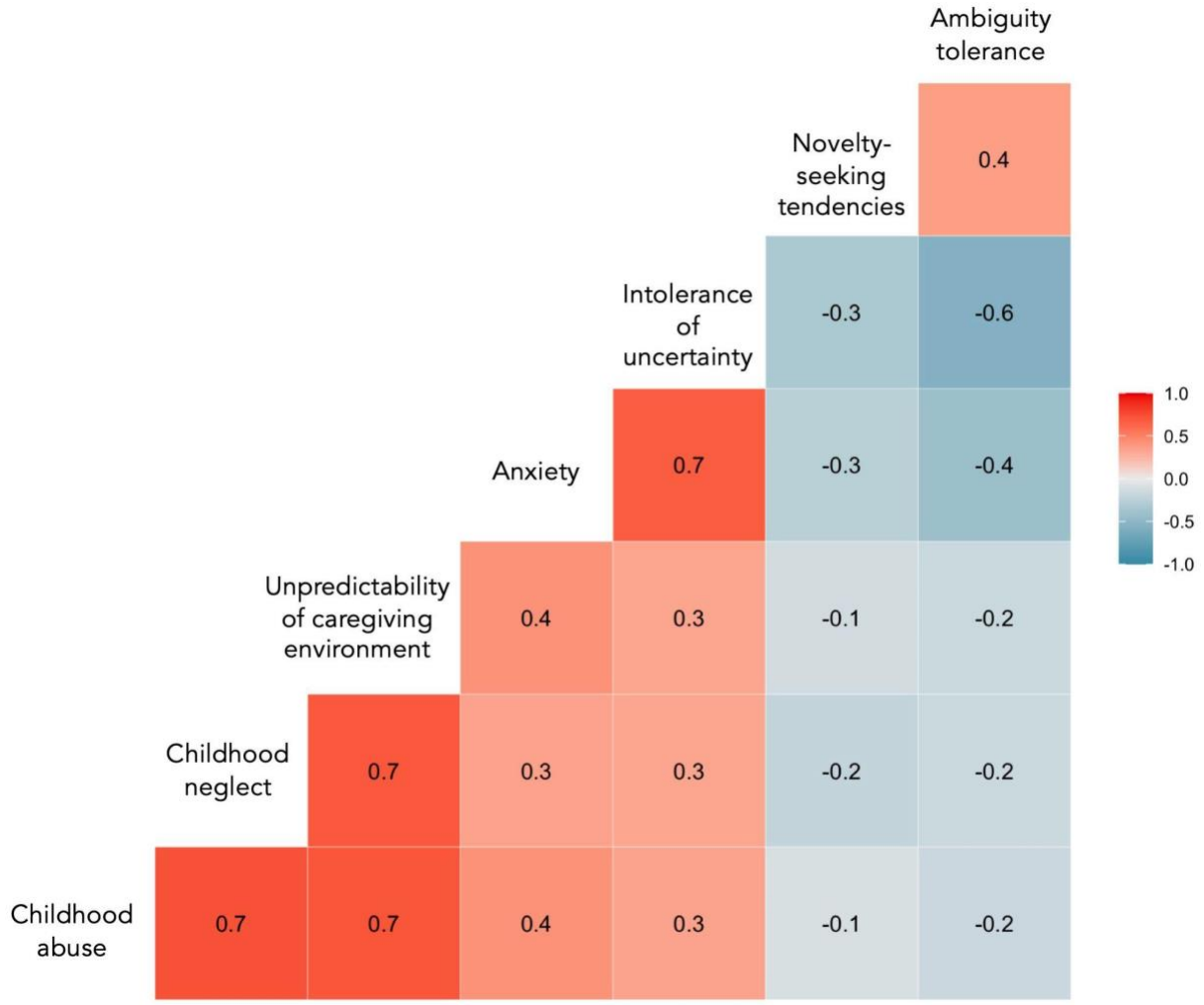
Supplemental Figure 10. Distribution and mean of Multiple Stimulus Types Ambiguity Tolerance Scale-II (MSTAT) scores by sample. Higher scores indicate greater tolerance for ambiguity.



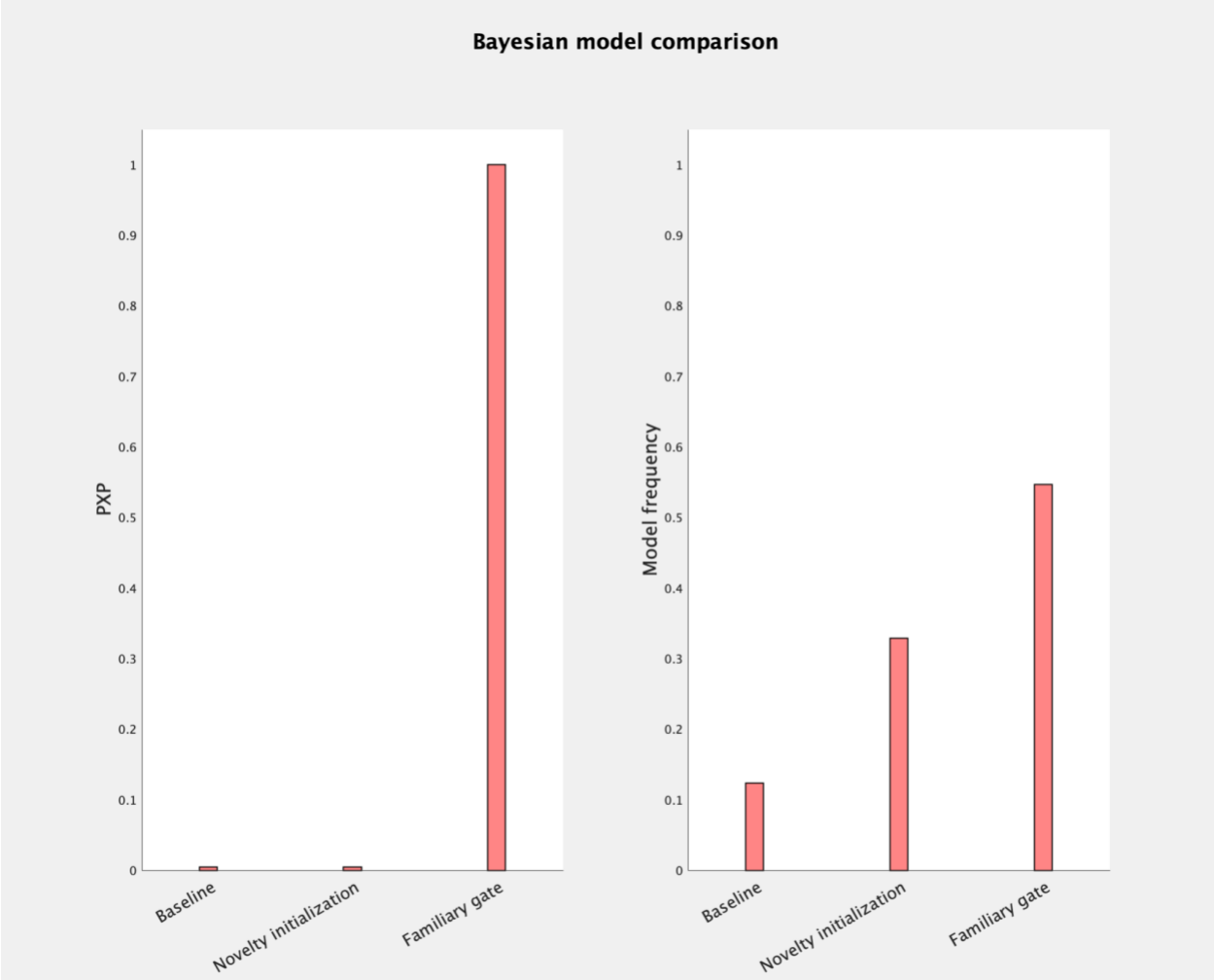
Supplemental Figure 11. Distribution and mean of anxiety scores from the Screen for Adult Anxiety Related Disorders questionnaire by sample. Higher scores indicate greater anxiety symptomatology.



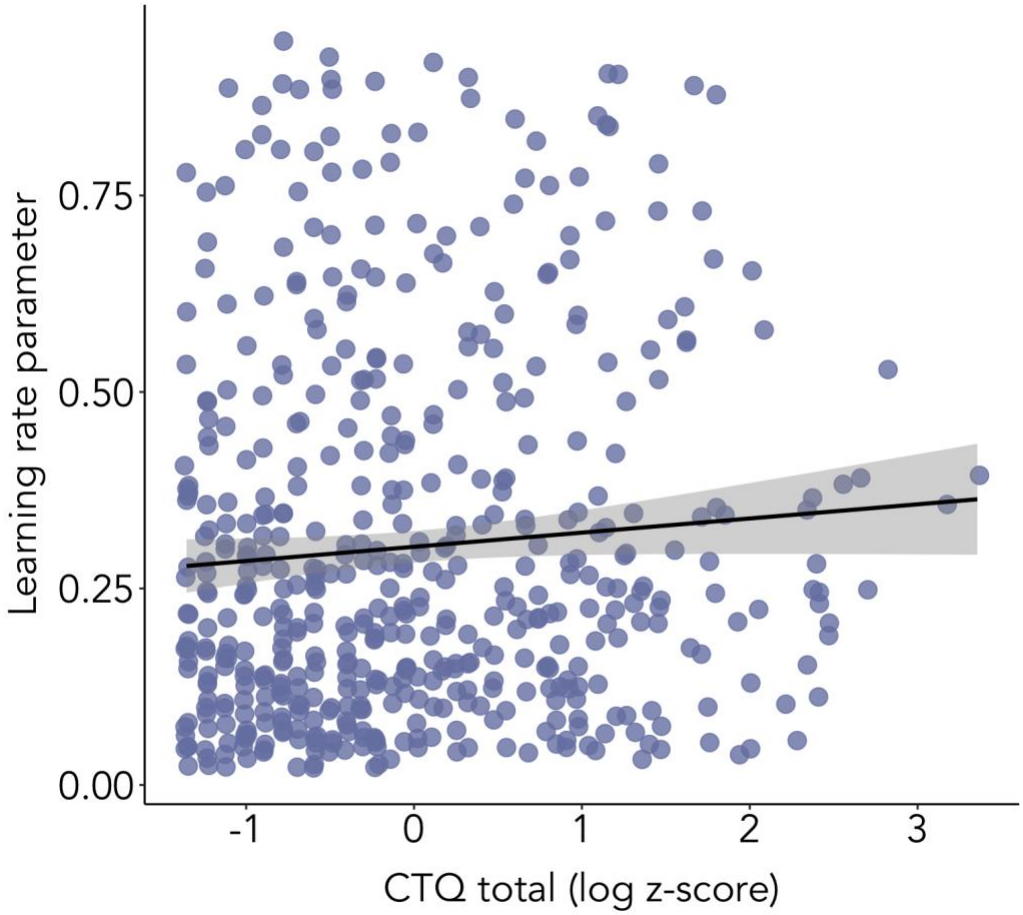
Supplemental Figure 12. Distribution and mean of self-reported novelty-seeking tendencies, measured by the novelty subscale from the Personal Expansion Questionnaire, by sample. Greater scores indicate more novelty-seeking tendencies.



Supplemental Figure 13. Correlation matrix summarizing Spearman rank correlations (rho values) among all questionnaires, with the abuse and neglect subscales from the Childhood Trauma Questionnaire separated. Color indicates direction of association and shading indicates strength of association. All associations are significant ($p < 0.05$).



Supplemental Figure 14. Bayesian model comparison for the three computational models tested.



Supplemental Figure 15. CTQ scores were significantly associated with learning rate free parameter η, such that individuals with higher CTQ scores placed greater weight on more recent outcomes.

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