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Deconstructing the role of the exposome in youth suicidal ideation: Trauma, neighborhood environment, developmental and gender effects

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ABSTRACT

Environment (E) is pivotal in explaining variability in brain and behavior development, including suicidal ideation (SI) and behavior. It is therefore critical to systematically study relationships among environmental exposures (i.e., exposome) and suicidal phenotypes. Here, we evaluated the role of individual-level adversity and neighborhood environment and their interaction (E x E) in association with youth SI. Sample included youth (N = 7,054, ages 11–21) from the Philadelphia Neurodevelopmental Cohort, which investigated clinical phenotypes in a diverse US community population. We examined cross-sectional associations of environmental exposures with lifetime history of SI (n = 671), focusing on interactions between individual-level exposures to assaultive trauma (n = 917) and neighborhood-level socioeconomic status (SES) quantified using geocoded Census data. Models included potential confounds and overall psychopathology. Results showed that assaultive trauma was strongly associated with SI (OR = 3.3, 95%CI 2.7–4, $p < .001$), while low SES was not ($p = .395$). Both assault and low SES showed stronger association with SI in females, and in early adolescence (all E X gender/age interactions, $p < .05$). In traumatized youths, lower SES was associated with less SI, with no SES effects on SI in non-traumatized youths (Assault X SES interaction, Wald = 8.19, $p = .004$). Associations remained significant controlling for overall psychopathology. No single SES variable emerged above others to explain the moderating effect of SES. These findings may suggest a stress inoculation effect in low SES, where youths from higher SES are more impacted by the deleterious trauma-SI association. Determining which environmental factors contribute to resilience may inform population specific suicide prevention interventions. The cross-sectional study design limits causal inferences.

1. Introduction

1.1. Youth suicidal ideation (SI): risk factors and clinical significance

Suicide, the second leading cause of death in youths and young adults in the United States (National Institute of Mental Health, 2018), is a complex behavior driven by the interaction of predisposing and precipitating factors, which can be analyzed at the population or individual level (Turecki and Brent, 2016). Over the past 20 years, there has been an increase in suicide rates, particularly in adolescents, and most prominently in teens younger than 14 (Ruch et al., 2019). Still, the absolute number of suicide deaths in teens is relatively small. Suicidal ideation (SI) is relatively common and is considered a major risk factor for subsequent suicidal behavior (Reinherz et al., 2006). Hence, studying factors associated with SI is critical and can inform suicide prevention strategies.

Besides family history of suicide, the most established risk factor for teen suicide is a history of early-life trauma (Fazel and Runeson, 2020). Early-life trauma is a well-established risk factor for psychopathology throughout the lifespan, with data suggesting that females are more vulnerable (MacMillan et al., 2001). Mounting evidence indicates that the experience of interpersonal trauma (i.e., assault) is specifically

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associated with suicidal ideation and behavior (Ásgeirsdóttir et al., 2018; Belik et al., 2009; Lebouthillier et al., 2015; Yoo et al., 2018). Interpersonal trauma is strongly associated with adolescent psychopathology (McLaughlin et al., 2013), and with long-lasting risk for SI (Zuromski et al., 2019). Still, not all traumatized youth experience SI, and reasons for this resilience are poorly understood (Barzilay, 2020). Since adolescence is a sensitive period in development and a time in which gender differences in psychopathology emerge (and specifically suicidality) (Miranda-Mendizabal et al., 2019), it is likely that studying relationship among environmental adversities and SI can improve understanding of developmental and gender specific mechanisms underpinning variability in relation to trauma and teen SI (i.e., what makes some individuals develop SI and others resilient).

1.2. Exposome

Social determinants have potential to drive variability in human behavior (Farah, 2017). Recent work suggests that quantifiable contextual factors in county-level environment can reveal associations of exposures with suicide rates (Steelesmith et al., 2019), and specifically with youth suicide (Hoffmann et al., 2020), with potential to inform targeted suicide prevention strategies. Environment can be measured both on (1) an individual level, by querying individuals regarding their personal exposure to adverse events such as trauma; and (2) more distant environment such as neighborhood-level environment, by obtaining geodata from publicly accessible resources like the U.S. Census. Systematic investigation of environmental exposure requires integration of such data. Comprehensive study of environmental exposures is often referred to as the exposome, which relates to the sum of environmental exposures experienced by an individual (Wild, 2005). Exposome has recently been suggested as a major driver of variability in the manifestation of psychiatric phenotypes (Guloksuz et al., 2018), with evidence that individual-level adversity (e.g., trauma exposure) and neighborhood-level adversity (e.g., low socioeconomic status (SES)), can have differential associations with brain and behavior parameters (Gur et al., 2019). Generating data on the exposome's role in driving SI can inform personalized suicide prevention interventions, allowing tailoring of programs to specific populations.

1.3. Philadelphia Neurodevelopmental Cohort as a tool to study exposome-SI associations

The Philadelphia Neurodevelopmental Cohort (PNC) comprises youths with comprehensive clinical phenotyping (Calkins et al., 2015), including SI (Barzilay et al., 2019a), granular data on individual-level trauma (Barzilay et al., 2019b), and neighborhood environment data (Moore et al., 2016). Thus, PNC is a suitable resource to comprehensively study associations among environmental exposures with brain and behavior phenotypes in adolescence, a critical developmental period (Gur et al., 2019). We have previously described the deleterious association of the experience of trauma, especially assault, with adolescent psychopathology in the PNC (Barzilay et al., 2019b). Here we investigate the moderating effect of relationship of neighborhood-level environment on the well-established association between individual-level assaultive trauma exposure (physical or sexual) and SI (primary aim). In addition, we explored gender, age and race effects as both are differentially associated with SI during adolescence (Miranda-Mendizabal et al., 2019; Ruch et al., 2019; Sean et al., 2009). We hypothesized that: (1) different types of environmental adversities (i.e., individual level exposure to assault and neighborhood-level low SES environment) will have different associations with SI; (2) neighborhood environment will moderate the association between individual-level experience of assaultive trauma and SI, and (3) the environment-SI associations will show gender and age specific patterns, with females showing stronger environment-SI link. We further evaluated whether these environmental adversities-SI associations are specific to SI above and beyond overall psychopathology.

2. Methods

2.1. Study population

We analyzed cross-sectional data from the PNC (N = 7,054, ages 11–21, 46% male, 56% Caucasian), a sample recruited between 2009 and 2011 through a collaboration between the Children's Hospital of Philadelphia (CHOP) and the Brain Behavior Laboratory at the University of Pennsylvania. These youths from the greater Philadelphia area were ascertained through the CHOP pediatric health care network. Notably, participants were not recruited from psychiatric clinics, and the sample is not enriched for individuals who seek psychiatric help.

The PNC included children aged 8–21 years (N = 9, 498). For participants aged 8–10, clinical evaluation including probing for suicidal ideation was done using a parent report. For participants 11 and older, clinical evaluation was based on an interview with the youth. In the current analysis, due to low reliability of parent report on SI in children (DeVille et al., 2020), we included all participants who provided self-report (N = 7054) and excluded participants 8–10 years old with parent report of symptoms. All participants aged ≥18 provided written informed consent, and written assent and parental consent were obtained for children aged <18. University of Pennsylvania and CHOP's Institutional Review Boards approved all procedures.

2.2. Measures

2.2.1. Clinical evaluation

Lifetime history of psychopathology symptoms were evaluated by trained and supervised Bachelor's and Master's level assessors who underwent rigorous standardized training and certification using a structured screening interview (Calkins et al., 2015), based on the Kiddie Schedule for Affective Disorders and Schizophrenia (K-SADS) (Kaufman et al., 1997). Lifetime history of SI (yes/no. binary variable) was determined through a direct question about whether the participants ever had thoughts of killing themselves, as described previously (Barzilay et al., 2019a).

2.2.2. Overall psychopathology (p factor)

The overall psychopathology p factor reflects the observation that individuals who score highly on certain psychopathological traits also score highly on others (Caspi et al., 2014). It has been recently shown that this single continuous measure can represent liability to overall psychopathology in youths (Allegrini et al., 2020). To generate the p factor score, we used item-wise (i.e. symptom-level) psychopathology responses (total 110 items) from the clinical interview across all assessed psychopathology domains. An exploratory factor analysis (EFA) extracted four factors of psychopathology dimensions: mood-anxiety, fear (phobias), externalizing symptoms and psychosis spectrum, as previously described (Moore et al., 2019). The items used to calculate factor scores did not include the SI item (dependent variable in the current analysis). This EFA was then used to assign items to factors for a confirmatory factor analysis (CFA). The CFA was estimated using a Bayesian estimator in Mplus, version 7.1. Lastly, a bifactor model estimated overall psychopathology (p factor), representing overall burden of psychopathology while controlling for the presence of specific symptom dimensions.

2.2.3. Measurement of individual-level traumatic stress exposure

As part of the K-SADS based interview, participants were screened for eight traumatic experiences (yes/no items) that fulfill criterion A in post-traumatic-stress-disorder diagnosis (Barzilay et al., 2019b). Participants were queried about assaultive traumatic experiences: been (1) attacked by somebody or badly beaten, (2) forced to do something sexual (including but not limited to rape), and (3) threatened with a

weapon. Participants endorsing at least one of these experiences were deemed to have a history of assaultive trauma (binary variable: at least one assault/no assault). In addition, the interview assessed lifetime history of exposure to non-assaultive stressful events (yes/no items, summed from 0 to 5): (1) a natural disaster, (2) thought they or someone close to them was going to be killed or hurt badly, (3) been in bad accident, (4) seen or heard somebody get killed, hurt badly, or die, or (5) been upset by seeing a dead body or seeing pictures of the dead body of somebody they knew well. Frequencies of trauma exposures are detailed in Supplemental Table 1.

2.2.4. Measurement of neighborhood-level socioeconomic status (SES)

Census neighborhood-level data was used to calculate a SES factor score for each participant as previously described (Moore et al., 2016). Briefly, participants' home addresses were geocoded and linked to the 2010 US Census block-groups, and data from the Census' American Community Survey was used to characterize block-groups ("neighborhoods"). Factor Analysis of the block-group data revealed a clear SES dimension comprising nine variables: median family income, percent of residents in poverty, percent of residents employed, percent of female residents, percent of residents with at least 12 years of education, percent of residents married, median age, population density and percent of vacant lots. The SES factor score weighted each of the SES variables as calculated in the factor analyses and represents a proxy for neighborhood-level SES.

2.3. Data analysis

Univariate comparison between youths with and without SI was done using *t*-test or Chi-square tests, as appropriate. To determine main effects for the association of different environmental exposures and SI we used binary logistic regression models with SI (yes/no) as the dependent variable and assault trauma (as a binary variable) and SES factor-score (as a continuous measure) as the independent variables. Model included age (continuous) and gender, and co-varied for race (Caucasian, African American). We also included exposure to non-assaultive trauma (binary measure, any/none), to allow specificity of findings to the main effect of exposure to assault on SI. Inclusion of non-assault trauma also allowed a comparison of the effect size between assault and non-assault trauma exposure on SI. Separate models co-varied for overall psychopathology through inclusion of the p factor, to allow specificity of main effects to SI, over and above non-SI psychopathology.

To explore age and gender effects, we tested interaction of assault or SES with age and/or gender, we ran a model that included assault/SES by gender, assault/SES by age and gender by age interactions (one model for assault and a separate model for SES).

To address the study question of the moderating effect for neighborhood SES on the relationship between assault and SI, we ran separate regression models to evaluate the interaction of trauma and SES in association with suicide ideation, co-varying for potential confounders mentioned above. Similar exploratory models were run for each Census data variable composing the SES factor score. All interaction terms were multiplicative interactions (i.e., the product of the multiplication of two independent variables). Since exposure to any specific type of trauma often co-occur in individuals (i.e., polyvictimization, where the youth exposed to assault is likely to experience other non-assault trauma) (Finkelhor et al., 2007), we co-varied for the load of exposure to non-assaultive trauma (continuous measure, 0–5), to allow more specificity of findings to the assaultive exposure.

Lastly, we conducted sensitivity analyses to test the effect of using different definitions of assault through substituting the exposure variable "assaultive stress" with "physical assault" or "sexual assault" (two separate models). This model was also run in a gender stratified manner to explore potential gender differences.

For visual presentation of data, SES was categorized to Low SES (lower tertile) or Mid-high SES (top two tertiles), and age was dichotomized as 11–14 or 15 and older.

We used the SPSS 26.0 statistical package for our data analyses.

3. Results

3.1. SI youth characteristics

Youth with lifetime history of SI comprised 9.5% (n = 671) of the study population, were on average a year older (16.8 compared to 15.7 in youth without), were more likely to be female (61% compared to 54% in youth without), and had a similar race distribution and socioeconomic background. Youth with SI reported experiencing more trauma compared to those without SI (70% vs 47% endorsing experience of any trauma, respectively) and specifically more experiences of assault (34% compared to 13%). See Table 1 for descriptive statistics of the sample.

3.2. Association of individual-level exposure to assault with SI

Personal history of assault was robustly associated with SI (Table 2 and Fig. 1A, Odds ratio (OR) = 3.32, 95% confidence interval (CI) 2.73–4.04, $p < .001$, model included age, race, SES and exposure to any non-assaultive traumatic event). This association remained significant when including overall psychopathology (p factor) in the model (OR = 2.04, $p < .001$, Table 2), suggesting that assault-SI association is specific to SI above and beyond the established link between assault and other non-SI psychopathology. History of exposure to non-assaultive trauma was also associated with SI, but to a lesser extent (OR = 1.63 95%CI 1.36–1.95, $p < .001$, Table 2), and was not significantly associated with SI when including the p factor in the model (OR = 0.91, p = .322).

We next conducted exploratory analyses to examine gender and age-related differences in the association of assault and SI. We found that in youth with history of assault, females showed stronger assault-SI association compared to males (Fig. 1B, Assault X Gender interaction, Wald = 9.51, p = .002), and younger participants with a history of assault showed higher increase in SI rate compared to older participants (Fig. 1C, Assault X Age interaction, Wald = 11.64, p = .001). No race effects were observed for these interactions (Assault X Gender X Black Race, $p = .837$; Assault X Age X Black Race, $p = .255$).

3.3. Association of neighborhood-level socioeconomic status (SES) environment with SI

Socioeconomic status was not significantly associated with SI (Table 2 and Fig. 2A, OR = 1.06, p = .395). However, exploratory examination of the SES association with SI revealed distinct gender and age-specific patterns. In lower SES, females showed slightly higher rates of SI, while males showed the opposite trend (Fig. 2B, SES X Gender interaction, Wald = 10.87, p = .001). Lower SES was associated with SI in younger ages (under 14) and not in participants 15 and older (Fig. 2C, SES X Age interaction, Wald = 16.51, $p < .001$). No race effects were observed for these interactions (SES X Gender X Black Race, $p = .228$; SES X Age X Black Race, $p = .68$).

All models that examined age and gender interactions for assault and for SES in association with SI remained significant when including the overall psychopathology p factor in the model (all p's ≤ 0.006, Supplemental Table 2).

3.4. Relationship between individual-level exposure to assault and neighborhood-level SES in association with SI

We next evaluated the moderating effect of the neighborhood environment, as captured by the SES variable, on the robust association between assault and SI, co-varying for gender, age, and race. We found that while in youth with no history of assault there were no differences in SI between Low (bottom tertile) and Mid-high (top two tertiles) SES,

Table 1
Sample characteristics.

	Total sample		Suicidal Ideators		Non SI		Univariate	
	N = 7,054[a]		n = 671		n = 6277		comparison	
	n/mean	%/SD	n/mean	%/SD	n/mean	%/SD	X^2/t	p-value[b]
Age, years	15.77	2.74	16.81	2.56	15.68	2.73	10.27	<.001
Sex, female	3807	54%	410	61%	3360	54%	14.01	<.001
Race, white	3970	56%	365	54%	3549	57%	1.13	0.287
Race, black	2321	33%	233	35%	2052	33%	1.14	0.287
SES z-score	0.01	1	−0.05	1.02	0.013	1	1.58	0.115
Any trauma	3490	50%	469	70%	3015	48%	117.5	<.001
Assaultive trauma[c]	917	13%	228	34%	687	11%	280.8	<.001
Non-assaultive trauma[d]	3307	47%	434	65%	2866	46%	87.7	<.001
Psychopathology p factor[e]	0.19	0.97	1.04	0.75	0.1	0.95	24.95	<.001

Abbreviations: SD = standard deviation of the mean; SI = suicidal ideators; SES = socioeconomic status.
[a] For n = 106 (1.5% of PNC), clinical items including suicidal ideation and trauma items were missing and were therefore excluded from analyses.
[b] Comparing SI to non-SI youths.
[c] Assaultive trauma was considered for participants who endorsed at least one of the following experiences: physical assault (n = 477), having been threatened with a weapon (n = 431) and sexual assault (n = 270).
[d] Non-assaultive trauma was considered for participants who endorsed at least one of the following experiences: natural disaster (n = 283), a bad accident (n = 810), thought that s/he or someone close to him/her could be killed or hurt badly (n = 908), witnessed someone getting killed, badly beaten, or die (n = 1507) or saw a dead body (n = 1908).
[e] Overall psychopathology (p factor) was calculated based item-wise data from the K-SADS[18] clinical interview.

Table 2
Main effects of trauma (assault and non-assault), SES, age and gender in association with suicidal ideation.

	Model a			Model b		
	OR	95%CI	p-value	OR	95%CI	p-value
Assault trauma	3.32	2.73–4.04	<.001	2.04	1.66–2.52	<.001
Non-assault Trauma	1.63	1.36–1.95	<.001	0.91	0.75–1.1	0.322
SES	1.06	.93–1.2	0.395	1.12	0.98–1.28	0.097
Age	1.008	1.01–1.01	<.001	1.01	1.01–1.02	<.001
Gender, female	1.45	1.23–1.72	<.001	1.53	1.28–1.82	<.001

Binary logistic regression models with suicidal ideation as the dependent variable, with exposure to assaultive trauma (physical/sexual, binary variable, any/none) and non-assaultive trauma (binary variable, any/none) as the independent variables.
Model a co-varied for race.
Model b co-varied for race and overall psychopathology (p factor).
Abbreviations: OR = odds ratio; CI = confidence interval; SES = socioeconomic status.

in youth with assaultive trauma there were higher SI rates, and these were even higher in the Mid-high SES group (Fig. 3, Assault X SES interaction, Wald = 8.19, p = .004). This interaction was attenuated but remained significant co-varying for overall psychopathology (Wald = 3.86, p = .049). No race effects were observed for this interactions (Assault X SES X Black Race interactions p = .123, Supplemental Figure 1).

3.5. Association of specific neighborhood-SES variables with youth SI

We then conducted an exploratory analysis to evaluate the role of each of the nine Census data variables that comprise the SES factor score (Moore et al., 2016). We found that there was no single variable that drove the moderation of the Assault X SES interaction with SI. Rather, all nine variables showed the same direction of interaction (Fig. 4), such that higher SES was associated with higher SI rates in youth with history of assaultive stress. Full model statistics including main effects and interaction for each of the 9 individual SES variables can be found in Supplemental Table 3.

3.6. Sensitivity analyses using different definitions of assault

To address the possibility that different assault types (physical/sexual) had differential effects on SI, we substituted the exposure variable "assaultive stress" with "physical assault" or "sexual assault" (two separate models). In addition, to address the potential effect of different distribution of physical and sexual assault between the genders (i.e., males experienced more physical assault and females more sexual assault), we ran the models stratified by gender. Results remained similar to the main analyses as in Fig. 3, with youths from high SES showed higher rates of SI compared to those from lower SES, across the genders

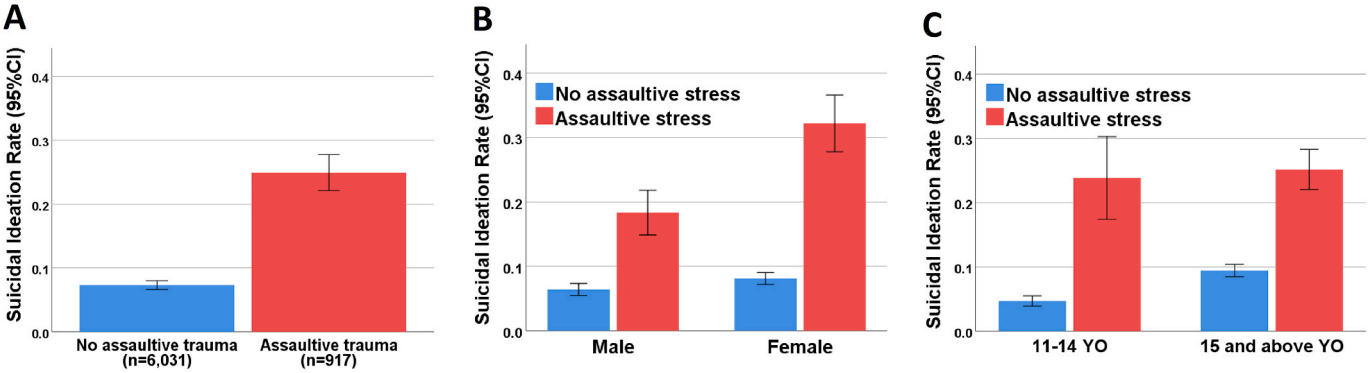

Fig. 1. Individual-level exposure to assaultive stress and youth SI (A), gender (B) and age (C) effects.

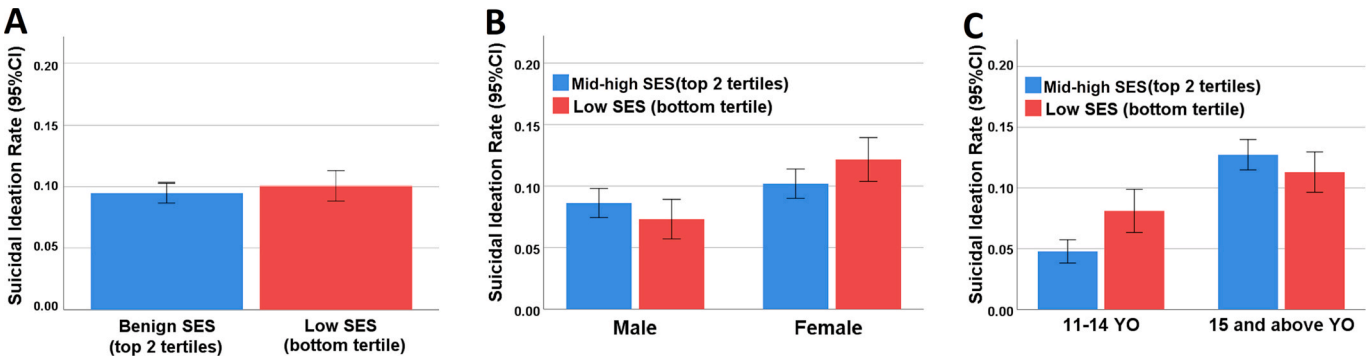

Fig. 2. Neighborhood-level SES and youth SI (A), gender (B) and age (C) effects.

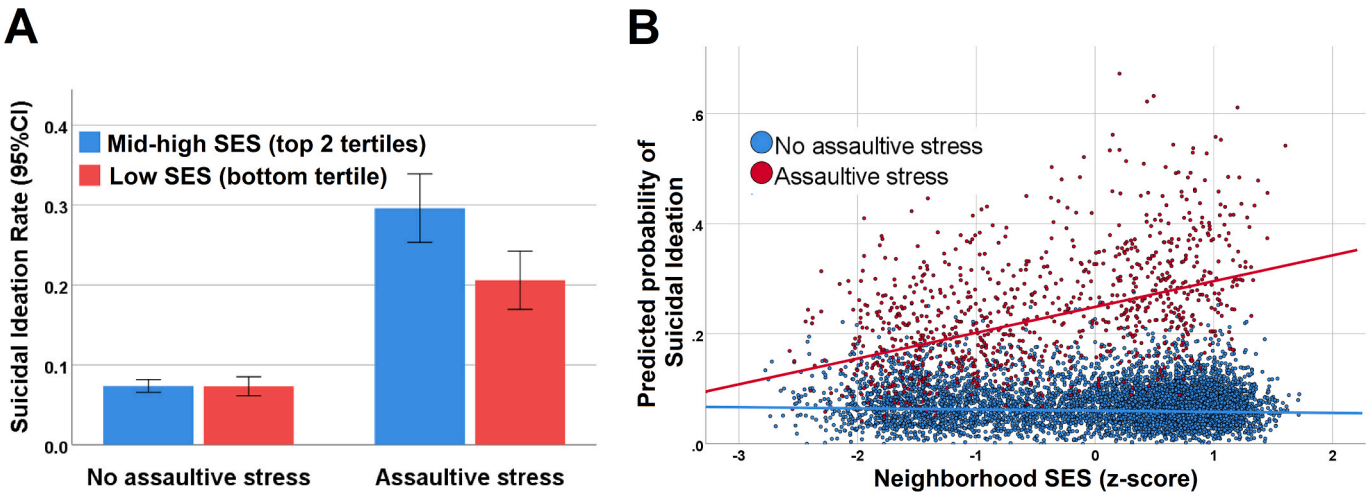

Fig. 3. Individual-level assaultive stress exposure and neighborhood-level SES in association with youth SI.Rates (A) and predicted probabilities (B) of suicidal ideation (SI) among youths with and without a history of assaultive stress across different neighborhood SES levels.
Probabilities were derived from a binary logistic regression model with SI as the dependent variable and assaultive stress (binary variable), neighborhood SES (continuous variable) and their interaction as independent variables. Model co-varied for age, gender, race and non-assault stress exposure.

(Supplemental Table 4).

4. Discussion

4.1. Broad context

Environmental exposures are becoming more widely recognized drivers of variability in human behavior, especially in the development of psychopathology (Guloksuz et al., 2018; Pries et al., 2020). In the current study we show that individual-level trauma and neighborhood-level SES are differentially associated with SI. Stronger association between environmental adversity and SI was observed in younger teens and in females, consistent with the literature of gender specificity of risk factors for suicidal behavior (Miranda-Mendizabal et al., 2019). Furthermore, even when co-varying for these gender and age factors, neighborhood environment moderated the deleterious association of trauma exposure with SI. All environment-SI associations remained significant when controlling for overall psychopathology, suggesting that SI association with individual-level trauma, neighborhood-level SES and age and gender effects, are specific to SI, over and above the association of environmental adversity with other (non-SI) psychopathology. These findings expand the understanding of the role of socioeconomic contextual determinants in suicidal behavior (Hoffmann et al., 2020; Steelesmith et al., 2019). Furthermore, our data dimensionality reduction approach using of a single composite neighborhood SES in the PNC (Moore et al., 2016), allows straightforward interpretation for the important role of neighborhood environment in the development of youth SI. The advantages of using a single SES composite score include statistical efficiency and a simple presentation of results, as using many single measures separately may lead to collinearity and cumbersome or cluttered results, especially when our intention was to reflect a single underlying concept such as neighborhood socioeconomic status (Pickett and Pearl, 2001). Notably, exploratory analyses of 9 specific SES Census variables that comprise our composite SES factor did not result in identification of a single SES variable that seemed to have especially large effect.

4.2. Age effects

Recent suicide epidemiological data highlight the concerning rise in suicides in individuals younger than 14 (Ruch et al., 2019). The age range of our study population spans pre-to post-adolescence, providing an opportunity to explore developmental associations of environmental exposures with SI, within the inherent limitation of a cross-sectional design. We found that in young adolescents (i.e., under 14), the association of environmental adversity is more pronounced (environment by age interaction) in two forms of adverse environmental exposures – individual-level trauma and neighborhood-level low SES. Notably, age interactions showed different patterns for each exposure. For assaultive trauma, we observed a ceiling effect whereby, regardless of age, history of assault was associated with ~25% SI rate. The assault-age interaction was driven by the expected increase in SI throughout adolescence, from

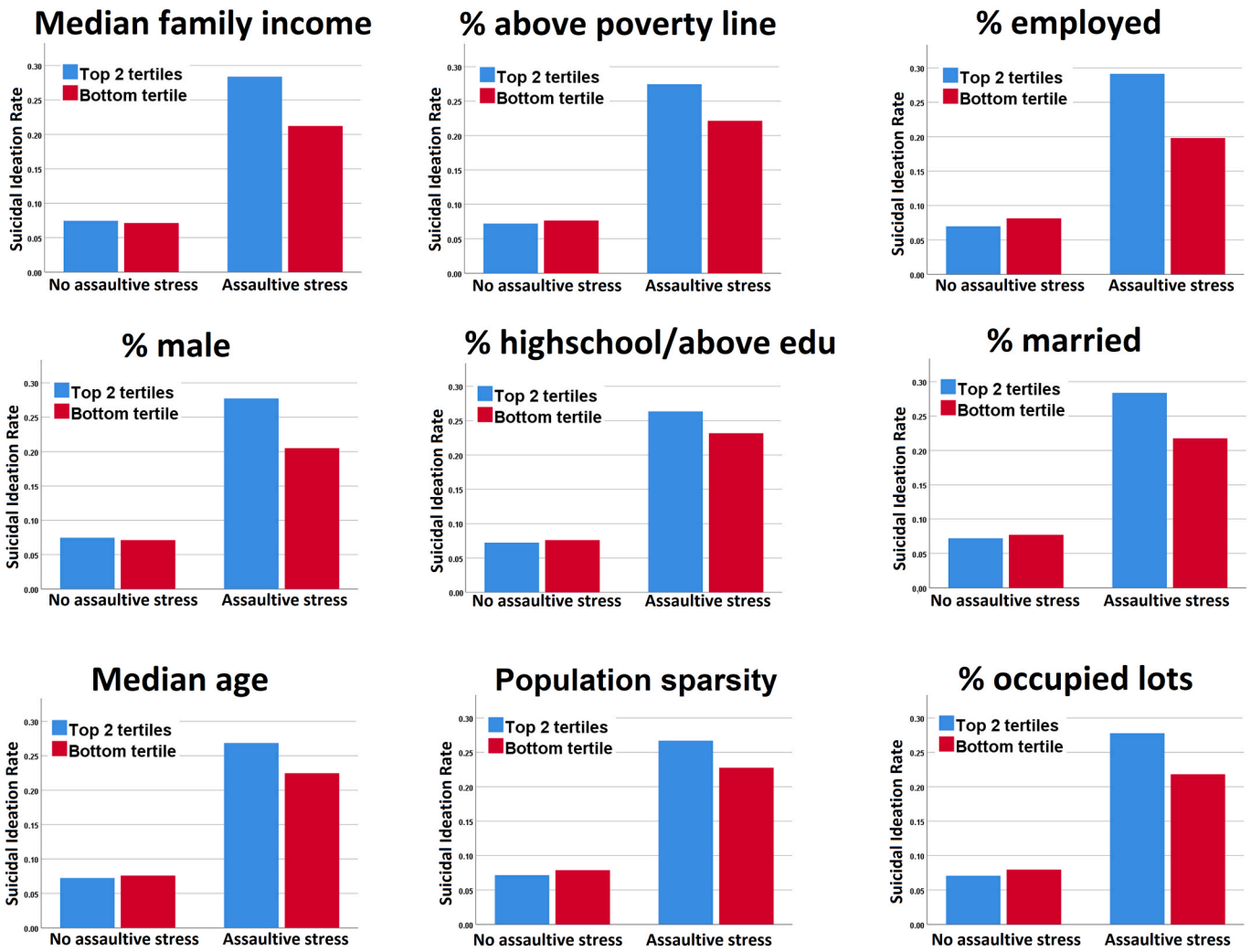

Fig. 4. Visual presentation of the interaction of assaultive stress with specific neighborhood Census variables in association with youth suicidal ideation.

5% in early to 10% in late adolescence in non-traumatized youth. In contrast, age effects for neighborhood SES showed a different pattern, as older adolescents showed no association between SES and SI, while in younger adolescents, low SES was associated with SI. This finding is in line with the notion that from mid adolescence (i.e., ~14 and above), youths rely more on peer support and school based social status, neither of which is captured in the SES variables used in the current analyses (Sweeting and Hunt, 2014). Perhaps in early adolescence (i.e., 11–13), living in a higher SES neighborhood is associated with a latent protective factor, which translates to lower SI rates in young teens, while this factor has no protective effect later in mid-late adolescence. Two potential protective factors that are more influential in younger ages is the school environment and the family environment, which were not assessed in the current analysis, and merit further investigation in cohorts that collect school and family environment data. Notably, school connectedness, associated with higher SES, is a known protective factor for teen mental health (Sampasa-Kanyinga and Hamilton, 2016).

4.3. Stress inoculation

Experience of assaultive stress was robustly associated with SI in our cohort across the entire SES spectrum. Still, the increased odds for endorsing SI was more pronounced in youths from higher SES. When considering evidence suggesting low SES as a risk factor for SI (Dupéré et al., 2009) and for teen suicide (Hoffmann et al., 2020), it is challenging to interpret our findings in the context of the diathesis-stress model of suicidal behavior (Van Heeringen, 2012). According to that framework, one would expect that youths who grow up in low SES would be more sensitive to the second hit of assaultive trauma and thus have more SI. However, it is possible that some environmental exposures in low SES neighborhoods might be associated with a degree of stress inoculation effect, which has been validated in animal studies from rodent to non-human primates (Parker et al., 2004). Notably, two studies have suggested adaptive protective biological mechanisms in youths exposed to family-related related stress, reporting non-linear U-shape effects of childhood adversity on HPA stress reactivity (Hagan et al., 2014) and adaptive augmentation of fronto-subcortical circuits specifically for negative emotional stimuli in children exposed to family-related stress, which was associated with less internalizing symptoms (Herringa et al., 2016). Our findings concur with a study describing lower depressive symptoms in African American youth growing up with high community violence exposure, which was suggested to reflect a desensitization process in which youth "adapt" to repeated exposure by normalizing violence and suppressing emotional distress, such as depressive affect or symptoms (Gaylord-Harden et al., 2016). Notwithstanding, there is growing realization for the deleterious effects of racism and discrimination on mental health, and specifically on suicidal ideation (Goodwill et al., 2019). Indeed, in no way do we suggest that harsh neighborhood environments are positive for developing youths. Rather, our findings emphasize the complexity of environment impact on the onset of teen SI. Thus, this study highlights the need to carefully tease apart deleterious impact of stress from its

"inoculating" effect, which can be informative for better understanding mechanisms of resilience in traumatized youths (Barzilay, 2020).

4.4. Clinical and policy implications

Our findings may have several implications for both clinicians and policy makers. From a clinical perspective, findings may appear counterintuitive in light of evidence for association between low SES and suicidal phenotypes in youth (Dupéré et al., 2009; Hoffmann et al., 2020). Possibly, SES-SI association in youth is more complex, such that in specific developmental period, or in individual life circumstances (like experiencing an assault), SES factors play a moderating role in the association with SI. In clinical settings, our findings highlight the increased risk of SI in youth from higher SES who have experienced significant trauma. From the broader perspective of suicide prevention, the current results underscore the importance of exposome research for informing policy makers on allocating resources to maximize impact of suicide prevention initiatives. For example, personalization of suicide prevention strategies could be tailored to a specific SES (neighborhood-level) population in a specific age group or target specific individuals with a unique composition of individual-level risk exposure.

4.5. Implications for suicide research

This study may also have some implications for suicide research. First, we suggest that the environment is a significant driver of variability and should therefore be rigorously accounted for in research studying suicidal outcomes in youth. Environment is especially important as there is a recognized need in the field to include more diverse populations to allow better generalizability of findings (Cha et al., 2018). Second, our findings might lead to identification of mechanisms that can be targets of interventions aimed at enhancing resilience by improving coping and reducing suicidal ideation in youth experiencing trauma. Future research could aim to identify the modifiable factors associated with lower SES that are driving the stress-inoculation effect and try to enhance them in the context of suicide prevention intervention. Lastly, this study supports the notion that suicide research should aspire to examine environmental exposures comprehensively, integrating individual-level exposures with wider environment exposures, rather than study environmental exposures in isolation without the contextual factors. Analogous to the genomic field moving from candidate genes to polygenic risk scores (Mullins et al., 2019), we suggest that suicide research should embrace the complexity of the exposome. Incorporation of the exposome within an omic approach can play a larger role as increasingly informative datasets are becoming available to study genetic and epigenetic determinants or neuroimaging correlates of suicidal ideation and behavior.

4.6. Limitations

Our findings should be interpreted in light of certain limitations. First, we analyzed cross-sectional data, hence causality cannot be inferred from environmental exposures to SI. In addition, both trauma and SI were evaluated for lifetime occurrence, precluding inferences regarding temporal associations. We suggest that the specific age span of the cohort does allow a developmental perspective, in spite of the cross-sectional design. Future longitudinal studies are warranted to examine causal pathways. Furthermore, the current study was not originally designed to investigate suicidal phenotypes, hence we do not have data on suicide attempts, nor do we have data on chronicity or intensity of SI. For that reason, we are careful to relate our findings specifically to the association of environmental exposures with the lifetime occurrence of SI, and not make claims regarding association with broader suicidal behaviors. Nonetheless, endorsing SI in adolescence is a major risk factor for consequent suicide attempt (Reinherz et al., 2006; Turecki and Brent, 2016), hence we argue that the SI phenotype in PNC is of high clinical interest. Another limitation is that we did not have a subjective measure of trauma effect on the individual, and no data regarding perceived severity of trauma, and no measure of discrimination that could be a major stressor related to suicidal phenotypes (Goodwill et al., 2019). Youths from different SES background can experience trauma differently; for example, traumatic experience for someone from a higher SES neighborhood will not necessarily be perceived as traumatic for a lower SES counterpart. We believe that the traumatic experience considered as exposure in the current analysis—specifically, physical/sexual assault or been threatened with a weapon—would be perceived as an objective traumatic event in all SES levels. Furthermore, we rigorously controlled for non-assault trauma exposures in all statistical models.

5. Conclusions

To conclude, we report a moderation effect of neighborhood-level environment on the association between individual-level experience of assault and youth SI. Results suggest that clinicians should be aware of contextual factors in youth at risk for SI and highlight the role and complexity of environmental exposures driving variability in adolescent SI. Future studies should incorporate environmental exposures in studying exposome effects on youth suicidal phenotypes, including contexts that have major influence on youth suicidal ideation and behavior and were not assessed in the current study, like the home and school environment. Longitudinal studies are especially warranted to clarify causal mechanisms and identify modifiable environmental exposures.

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Role of the funding source

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Declaration of competing interest

RB serves on the scientific board and reports stock ownership in 'Taliaz Health', with no conflict of interest relevant to this work. MAO receives royalties from Research Foundation for Mental Hygiene for the commercial use of the C-SSRS. She owns shares in Mantra, Inc. Her family owns shares in Bristol Myers Squibb. All other authors declare no potential conflict of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ynstr.2021.100314.

Credit Author Statement

RB conceptualized the study questions, hypotheses and design, conducted the analyses and wrote the first draft of the manuscript.

TMM supervised the analyses and contributed to methodology of statistical approach.

MEC collected the data and substantially contributed to the writing of the original draft.

LM curated the data and performed literature review and

substantially helped to formulate the study questions and hypotheses, and helped write the original draft.

JDJ, RCB, VW, TDB and MAO provided content expertise and substantial input when designing the analyses and helped write the final version of the manuscript through multiple reviews and editing of the original draft.

RCG and REG collected the data, provided funding for the project, supervised the analyses and substantially contributed to the writing of the manuscript from the original draft to its final version.

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