Quasi-Experimental Analysis Reveals Neuro-Genetic Susceptibility to Neighborhood Socioeconomic Adversity in Children's Psychotic-Like Experiences

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Author Contributions: J.J.P. and J.C. designed research; J.J.P. and M.C. performed research; J.J.P., M.C., E.L., B.-G.K., G.K., Y.Y.J. analyzed data; and J.J.P., M.C., and J.C. wrote the paper.

Competing Interest Statement: Authors have no competing interests.

Keywords: Intertemporal reward valuation, Psychotic-like experiences, Causal machine learning, Childhood socioeconomic environment, Heterogeneous effects

Abstract

Socioeconomic deprivation is linked to psychiatric vulnerability in children, yet the sources of individual variability remain unclear. Using an instrumental-variable random-forest framework (IV Forest) in a longitudinal cohort of 2,135 children, we estimate the association between neighborhood socioeconomic deprivation and delay discounting and psychotic-like experiences (PLEs) using variation in neighborhood adversity induced by state source-of-income anti-discrimination laws. Under standard IV assumptions, higher neighborhood adversity relates to steeper delay discounting and higher PLEs on average, and these associations vary systematically across children. These findings support the behavioral poverty trap framework, which is a self-reinforcing cycle where poverty-induced psychological distress relates to decisions that may perpetuate economic hardship. Moving beyond average relationships, an integrated IV Forest model that combines delay discounting, prefrontal-limbic morphometry, reward-task activation, and polygenic scores delineates marked significant heterogeneity in associations between neighborhood adversity and PLEs across children. Children most vulnerable to neighborhood adversity showed a paradoxical pattern: higher genetic predisposition for cognitive achievement (GPS for cognitive performance, IQ, and educational attainment) combined with specific limbic alterations (reduced volumes, heightened reward-related activation). These findings challenge diathesis-stress models and support differential susceptibility theory. By identifying who is most vulnerable to neighborhood disadvantage and why, our results inform precision-medicine approaches to preventing childhood psychopathology and breaking cycles of socioeconomic disadvantage.

Introduction

A child's environment is a powerful predictor of their lifelong health and economic outcomes. Adverse childhood environments, such as low family income, malnutrition, physical or sexual abuse, and unsafe neighborhoods, are linked to an heightened risk of various mental or physical health issues, including psychosis (1-3), impoverished cognitive ability (1-3), anxiety, bipolar disorder, self-harm, depression (4-6), substance abuse, and obesity (2, 3, 7). Furthermore, these environments are associated with negative social outcomes, such as poor academic performance (8, 9), low income, unemployment (10, 11), higher rates of imprisonment, and increased likelihood of teen pregnancy (12, 13). Additionally, exposure to these adverse conditions in childhood is associated with a propensity for engaging in risky behaviors, including criminal activity (13, 14), excessive consumption of calorie-dense foods (15), substance use (16, 17), deficient self-control (18), and disrupted reward processing (19).

One prominent framework, the “behavioral poverty trap,” posits that exposure to socioeconomic deprivation alters reward valuation, promoting impulsive decision-making that can lead to a range of suboptimal behavior and outcomes (20, 21). Individuals with steeper discounting of future rewards (i.e., value present rewards much higher than future rewards) are more likely to save less, invest less in their education, engage in criminal activities, exhibit lower academic performance, and accumulate less economic wealth (20, 22-24). Such impairments in intertemporal valuation are not only associated with financial and social disadvantages but are also linked to psychiatric disorders, including psychosis, attention deficit/hyperactivity disorder (ADHD), and addiction (25, 26).

In this paper, we focused on psychotic-like experiences (PLEs) as a key psychiatric

outcome. Around 17% of 9-12 years old children report PLEs (27), individuals with PLEs at age 11 had greater risk of developing psychosis in adulthood (28, 29). Prior studies revealed that PLEs are correlated to heightened vulnerability to other psychopathologies (30) including suicidal behavior (1), mood, anxiety, and substance disorders (31-33) and exhibit the strongest association with environmental risk factors in comparison to other internalizing/externalizing symptoms during adolescence (2).

The link between deprivation and PLEs is likely moderated by core neurodevelopmental processes, and we propose that delay discounting provides a critical window into these mechanisms (31, 34, 35). Delay discounting, which is evidenced by the extent to which individuals' discount future rewards, pertains to their intertemporal decision-making and impulsive behavior. This measure of intertemporal choice is not merely a behavioral quirk but a quantifiable index of reward valuation governed by prefrontal-limbic circuits (25, 26). Children who experienced social adversities show steeper discounting of future rewards in adulthood (36, 37) and have higher PLEs (1, 2, 38). Comparative studies have demonstrated that individuals with psychosis discount future rewards more steeply than healthy controls (31, 34, 35), a pattern that is uniquely pronounced in psychosis compared to other psychopathologies such as primary mood disorders (34), major depressive disorder (34), and bipolar disorder (35). Crucially, the same mesocorticolimbic dopaminergic systems that regulate reward anticipation are heavily implicated in the pathophysiology of psychosis (1, 2, 38). This shared neurobiological foundation suggests that individual differences in these reward circuits could be a key mechanism determining how environmental stress translates into psychiatric symptoms.

This raises the central puzzle in developmental science: why do some children exhibit

remarkable resilience to adversity while others are exquisitely vulnerable? Answering this requires dissecting individual-level heterogeneity, which likely arises from a complex interplay of genetic predispositions and neurodevelopmental factors (39-41). Traditional linear models are ill-equipped for this task, as they struggle to capture the high-dimensional, nonlinear gene-environment interactions that likely define a child's vulnerability (42, 43).

Here, we address this challenge by applying a causal machine learning framework to rich, longitudinal, multi-modal data—including genomics, structural and functional MRI, and behavior—from children aged 9-12 years old in the Adolescent Brain Cognitive Development (ABCD) Study. Using instrumental variable (IV) random forests (henceforth IV Forest) (30, 44), we move beyond population-level associations to characterize the specific neuro-genetic patterns associated with vulnerability to the psychiatric risks of socioeconomic adversity. We focus specifically on neighborhood socioeconomic deprivation because it represents a critical environmental layer beyond individual family status. Neighborhood adversities during childhood have been associated with maladaptive neurocognitive development (6, 45, 46), psychiatric disorders (28, 29), and unfavorable social outcomes such as decreased income, reduced probability of college attendance, and limited employment opportunities (47, 48). This phenomenon is particularly pronounced in societies where housing discrimination based on family income or race/ethnicity restricts underprivileged families from selecting neighborhoods that present greater opportunities for upward social mobility, as observed in the United States (47).

This study first estimates the IV-based association between neighborhood socioeconomic deprivation, steeper delay discounting, and elevated PLEs. We then document heterogeneity in this link and observe a multi-modal pattern of vulnerability characterized by specific genetic

predispositions, and limbic system structures and functions. Within this pattern, we found a paradoxical finding: a higher genetic predisposition for cognitive achievement is positively—rather than negatively—related to the psychiatric risks of a deprived socioeconomic environment.

Methods

Study Participants

The ABCD Study recruited participants from 21 research sites across the nation, utilizing a stratified, probability sampling method to capture the sociodemographic variation of the US population (49). We used the baseline, first year, and second year follow-up datasets included in ABCD Release 4.0, downloaded on February 10, 2022.

To ensure the highest quality of data and internal validity for our analyses, we implemented the standardized preprocessing and quality control pipelines recommended by the ABCD Study consortium (50, 51). Of the initial 11,876 ABCD samples, participants not meeting the ABCD Study's MRI quality control standards (N=3,275) were excluded. Similarly, for the delay discounting task, we applied the Johnson-Bickel validation criterion (52), as recommended by the ABCD behavioral workgroup (51), to exclude participants with inconsistent responses (i.e., indifferent point for a given delay larger than that of an indifference point for a longer delay) (N=5,293). We also removed participants without genotype data, MRI data, NIH Toolbox Cognitive Battery, delay discounting, residential address, ADI, and PLEs (N=1,173). Missing values of covariates were imputed using k-nearest neighbors. The final samples included 2,135 children from a variety of race/ethnic groups (**Fig. 1**).

Data

Our primary exposure was neighborhood socioeconomic adversity, measured at baseline using the national percentile scores of the Area Deprivation Index (ADI) (2, 45). The primary outcomes were delay discounting, a model-free measure of reward impulsivity assessed at the

1-year follow-up (51), and PLEs, measured using the Prodromal Questionnaire-Brief Child version at 1- and 2-year follow-ups (53). A lower value of delay discounting denotes steeper discounting of future rewards; a higher value of PLE score indicates greater severity of PLEs. To identify moderators of vulnerability, we utilized a rich, multi-modal dataset including genome-wide polygenic scores (GPS) for cognitive and psychiatric traits, structural MRI measures of brain morphometry (50), and functional MRI data from a monetary incentive delay (MID) task (50). Detailed descriptions of all measures, tasks, and MRI processing pipelines are provided in the **Supplementary Information**.

To adjust for the potential confounding effects, sociodemographic covariates were included. Consistent with existing research on psychiatric disorders in ABCD samples (2, 53-55), we controlled for the child's sex, age, race/ethnicity, caregiver's relationship to a child, BMI, parental education, marital status of the caregiver, household income, parent's age, and family history of psychiatric disorders. The family history of psychiatric disorders, measured as the proportion of first-degree relatives who experienced psychosis, depression, mania, suicidality, previous hospitalization, or professional help for mental health issues (2) was included as a covariate. Given that delay discounting and PLEs are associated with an individual's neurocognitive capabilities (56-58), NIH Toolbox total intelligence was used as a covariate. All covariates were from baseline year observations.

Statistical Analyses

Given the non-randomized, observational nature of the ABCD Study, potential confounding factors, such as genetic, environmental variables, and their unobserved common

causes, can lead to biased estimations (59). A powerful and effective way to adjust such bias is the IV regression. Designed to isolate a quasi-random source of variation in the treatment/exposure variable, IV regression is an effective method to conduct quasi-experimental analysis using non-randomized, observational data for research in various domains, including economics (60, 61), psychology (62), neuroscience (63), and psychiatry (64).

Our instrument is the presence of state-level source of income (SOI) laws at baseline year assessment, which prohibit housing discrimination against voucher holders. These laws increase the landlords' acceptance of housing vouchers, aiding low-income families in securing quality housing. As such, SOI laws are critical in enabling better residential environments by mitigating neighborhood socioeconomic adversity. That is, the implementation of these laws provides a *natural experiment*: it strongly predicts a family's neighborhood adversity (i.e., ADI) but is plausibly unrelated to the unobserved confounding factors that typically bias estimates. The IV analysis leverages this exogenous variation from SOI laws to estimate the associations of ADI with delay discounting and PLEs while mitigating bias from unobserved confounders (see **Fig. 2A**). We present theoretical explanations of the IV method and detailed justification of SOI laws as valid instrument in the **Supplementary Information**.

We used IV Forest (65, 66)—a random forest-based IV regression (60)—to adjust for unobserved confounding bias in identifying the potential relationship of ADI with delay discounting and PLEs. The IV Forest method provides nonparametric, doubly robust estimates of the average (group-level) and heterogeneous (individual-level) associations of ADI with these outcomes, interpreted under the IV assumptions (see **Fig. 2B**). This method is noted for delivering estimates with significantly lower mean-squared error compared to conventional k-

nearest neighbor methods (65, 66). Furthermore, its use of independent subsamples for model construction and validation ensures honest, overfitting-resistant estimates of average and heterogeneous relationships (65-67). Notably, this method is particularly useful for analyzing the complex, nonlinear interactions between genetic and environmental factors and their link with neurocognitive development and PLEs, even within the confines of observational data (65). We used cluster-robust inference with the ABCD Study site as the clustering unit for IV Forest estimates. The technical description of the IV Forest algorithm is detailed in the **Supplementary Information**.

Fig. 1 presents the analytical framework of our study, examining the associations of neighborhood socioeconomic adversity with children's decision-making and mental health. ADI, recorded in the baseline year, serves as an indicator of this socioeconomic adversity. We assessed the potential link between ADI and children's intertemporal decision-making through delay discounting at a 1-year follow-up. PLEs, encompassing distress, delusional, and hallucinational symptoms, were evaluated at both 1-year and 2-year follow-ups. Our analysis spans multiple follow-up periods and PLE indicators to investigate the sustained influence of ADI over time and to explore differential associations with various PLE symptoms, particularly delusional versus hallucinational.

Results

The demographic characteristics of the final sample (N=2,135) are presented in **Table 1**. Within the sample, 46.14% were female, 76.63% of participants had married parents, the mean household income was $116,538, and 65.57% identified their race/ethnicity as white.

In our initial exploratory analysis, partial correlations were used to examine the relationship between psychopathological symptoms and delay discounting. Among the symptoms assessed (e.g., depression, anxiety, ADHD), only PLEs showed significant correlation with delay discounting (Spearman ρ = -0.067, p-FDR= 0.024 ~ ρ = -0.057, p-FDR= 0.035) (**Table S1**). This finding underscores the unique association between PLEs and delay discounting, laying the groundwork for subsequent investigations into how delay discounting—along with its genetic and neural correlates—may be associated with the heterogeneous relationship of neighborhood socioeconomic adversity with PLEs.

Neighborhood Socioeconomic Adversity is Associated with Steeper Delay Discounting and Higher PLEs

IV Forest analyses suggested that a higher ADI has significant associations with a steeper delay discounting (β= -1.73, p-FDR= 0.048) and a higher PLEs (distress score 1-year follow-up: β= 1.872, p-FDR= 0.048; distress score 2-year follow-up: β= 1.504, p-FDR= 0.039; delusional score 1-year follow-up: β= 5.97, p-FDR= 0.048; delusional score 2-year follow-up: β= 4.022, p-FDR=0.048; hallucinational score 1-year follow-up: β= 3.761, p-FDR= 0.048; hallucinational score 2-year follow-up: β= 4.786, p-FDR=0.039) (**Table 2**).

To evaluate the robustness of our findings from the IV Forest, we calculated the E-values for the average relationships from the IV Forest. The E-values quantify the minimum strength of association that unobserved confounders would need to possess with both ADI and the outcomes, conditional on the observed covariates in the IV Forest model, to nullify the observed relationships (68). E-values indicated that unobserved confounders would need to have a relative risk greater than 9.13 for delay discounting and between 7.32 and 457.03 for PLEs to account entirely for the observed effects (**Table S2**). This suggests a high threshold for unobserved confounding effects, thereby strengthening the validity of our analyses.

Supplementary analyses employing a conventional linear IV regression (60) and an alternative causal machine learning method, i.e., *Double ML* (69, 70), corroborated these findings. The conventional IV regression also showed that ADI has negative relationship with childhood delay discounting (β= -0.468, p-FDR= 0.03) and positive PLEs (distress score 1-year follow-up: β= 0.609, p-FDR= 0.011; distress score 2-year follow-up: β= 0.78, p-FDR= 0.003; delusional score 1-year follow-up: β= 0.486, p-FDR= 0.028; delusional score 2-year follow-up: β= 0.578, p-FDR= 0.013; hallucinational score 1-year follow-up: β= 0.604, p-FDR= 0.011; hallucinational score 2-year follow-up: β= 0.827, p-FDR= 0.003). The partial-linear IV model of the Double ML algorithm showed significant associations of ADI with children's delay discounting (β= -0.429, p-FDR= 0.044), distress score PLEs (1-year follow-up: β= 0.495, p-FDR= 0.023; 2-year follow-up: β= 0.609, p-FDR= 0.005), hallucinational score PLEs (1-year follow-up: β= 0.498, p-FDR= 0.018; 2-year follow-up: β= 0.683, p-FDR= 0.002), and 2-year follow-up delusional score PLEs (β= 0.417, p-FDR= 0.044). The negative relationship of ADI with 1-year follow-up delusional score PLEs were marginally significant (β= 0.393, p-FDR= 0.051). These results of the conventional linear IV regression (**Table S3**) and Double

ML partial-linear IV regression (**Table S4**) are consistent with the findings obtained from the IV Forest, further supporting the primary analyses and conclusions drawn from the study.

Genetic and Neural Correlates of Delay Discounting Moderates Vulnerability to Neighborhood Socioeconomic Adversity

Next, we moved beyond the average relationships to test for heterogeneous associations of neighborhood socioeconomic deprivation: i.e., whether the associations of ADI with PLEs varies systematically across children, and, if so, whether the heterogeneity is linked to individual's neurodevelopmental characteristics and the relevant genetic factors correlated to intertemporal valuation. Conceptually, this is analogous to testing for an interaction, where the associations of ADI with PLEs is moderated by, or differ as a function of a child's individual genetic and neural markers. Unlike traditional models might test a few pre-specified interactions, our IV Forest approach allows us to explore this heterogeneity in a data-driven manner across a high-dimensional set of potential moderators, including GPS and structural MRI and MID task functional MRI data.

To identify the best subset of genetic and neural correlates of delay discounting, we first selected GPS and MRI brain regions of interest (ROIs) specifically related to delay discounting. To analyze the nonparametric correlations of multiple input variables, we used a random forest-based feature selection *Boruta* algorithm (71). Its robustness and effectiveness in selecting relevant features in high dimensional, intercorrelated biomedical data (e.g., MRI) has been validated (71) and consistently applied in genetics and neuroscience research (72-74). The variables significantly correlated with delay discounting (p-Bonferroni<0.05) were GPS of

cognitive performance, IQ, and education attainment; morphometric features (e.g., surface area, volume) in the limbic system (temporal pole, parahippocampal gyrus, caudate nucleus, rostral anterior cingulate, isthmus cingulate), inferior frontal gyrus (pars opercularis), and fusiform gyrus; mean beta activations of rewards/losses versus neutral feedback in the subcortical areas (thalamus proper, ventral diencephalon), precentral gyrus, supramarginal gyrus, temporal lobe (transverse temporal gyrus, superior temporal gyrus), and insula (**Table S5**).

We then assessed the heterogeneous associations of ADI with PLEs using three distinct IV Forest models: (i) the Delay Discounting model, incorporating sociodemographic features and delay discounting; (ii) the Gene-Brain model, which included sociodemographic features and genetic and neural correlates of delay discounting (i.e., GPS and brain ROIs identified using the Boruta algorithm); and (iii) the Integrated model which combined all the variables from the previous two models (**Fig. 1**). All three models satisfied the overlap assumption (i.e., the estimated propensity scores are not close to one or zero), which is crucial for the validity of the estimated heterogeneous relationships (**Fig. S1**). In line with prior studies (75, 76), we obtained conditional average effects, divided subjects into deciles (Q1: most vulnerable; Q10: most resilient) based on the conditional average effects, and conducted three hypothesis tests (77) on each model to determine the most effective model for capturing the individual differences (heterogeneity) in the associations of ADI with PLEs: monotonicity, alternative hypothesis, and ANOVA.

Among the three models, only the Integrated model showed significant individual differences in the associations of ADI with PLEs. This was evident in the associations of ADI with 1-year follow-up distress score PLEs (monotonicity test: p-FDR=0.011; alternative hypothesis test: p=0.002; ANOVA test: p<0.001) and 1-year follow-up hallucinational score

PLEs (monotonicity test: p-FDR=0.038; alternative hypothesis test: p=0.004; ANOVA test: p<0.001), as presented in **Fig. 3 and Table S6**. In contrast, the Delay Discounting model and Gene-Brain model failed to pass the heterogeneity tests (monotonicity test: p-FDR≥0.05; alternative hypothesis and ANOVA test: p≥0.05).

To elucidate the role of specific genetic and neural correlates within the heterogeneous associations of ADI with PLEs, we obtained Shapley additive explanation (SHAP) scores (78). SHAP scores provide insights into how each variable correlates positively or negatively to the differential associations of ADI with 1-year follow-up observations of distress score and hallucinational score PLEs. These scores help differentiate the roles of these factors across subgroups, ranging from low to high conditional average effects, thereby providing a nuanced understanding of how ADI is correlated with PLEs through various genetic and neural pathways.

In both distress score and hallucinational score PLEs, children who showed higher levels of ADI's negative relationship with PLEs exhibited distinct neuroanatomical and functional brain patterns, particularly in the limbic system. These patterns included reduced neuroanatomical features such as smaller white matter and surface area in the right temporal pole, reduced area and volume in the right parahippocampal region, decreased left white surface area, smaller area in the right isthmus cingulate, reduced intracranial volume, smaller caudate nucleus volume, and lower total grey matter volume. Functionally, greater activation during MID tasks was observed in several areas including the posterior cingulate, right ventral diencephalon, right insula, left thalamus proper, and left precentral gyrus. Additionally, children more adversely affected by ADI, as indicated by higher conditional average effects on PLEs, exhibited larger right fusiform volume, decreased activation in the left superior temporal

gyrus, younger parental age, and lower BMI (**Fig. S2**).

The analysis also revealed that higher conditional average effects on distress score PLEs was associated with higher cognitive performance GPS and a lower likelihood of being Hispanic. In contrast, for hallucinational score PLEs, greater importance was attributed to increased activation in the left supramarginal gyrus during MID tasks and more pronounced discounting of future rewards. These nuanced associations are depicted in **Fig. S2**.

To further characterize this gene-environment interaction underlying these relationships, we obtained conditional average effects of ADI on 1-year follow-up distress score PLEs, conditioned on GPS for cognitive traits (i.e., cognitive performance, IQ, and education attainment). Within the model, the estimated conditional average effects tended to increase with higher values of GPSs (**Fig. 4**). This suggests that individuals with a higher genetic predisposition for academic and cognitive achievement are paradoxically more vulnerable to the psychotogenic effects of a deprived socioeconomic environment.

Given that quality control procedures reduced a large proportion of participants from the initial ABCD Study cohort, we conducted sensitivity analysis using inverse probability weighting to adjust for potential selection bias (see **Supplementary Information** for methodological details). After inverse probability weighting adjustments, the heterogeneous associations of ADI remained statistically significant for both distress (monotonicity: p-FDR=0.011; alternative hypothesis: p-FDR=0.002; ANOVA: p-FDR<0.001) and hallucinational PLEs (monotonicity: p-FDR=0.038; alternative hypothesis: p-FDR=0.004; ANOVA: p-FDR<0.001) at 1-year follow-up (**Table S8**).

Discussion

In this study, we examined how neighborhood socioeconomic deprivation relates to children's intertemporal choice behavior (delay discounting) and PLEs, considering the multifaceted associations of neighborhood adversity and its underlying biological, environmental, and behavioral drivers. Our findings can be distilled into two main points. Firstly, there was a notable link of living in socioeconomically disadvantaged neighborhoods to the propensity for children to prefer immediate rewards over larger, delayed ones—a behavior known as steep delay discounting (indicative of lower impulse control) and to a higher rate of PLEs. This association was significant even after adjusting for a range of observed confounding factors (e.g., familial socioeconomic status) and reducing potential bias from unobserved confounders via IV approach. Secondly, the associations of disadvantaged neighborhood environments with PLEs were found to be heterogeneous. This individual variability is moderated not just by delay discounting, but also by a confluence of factors including genetic predisposition for cognitive intelligence, and brain morphometry and functioning (task activation). Causal machine learning models utilized in our study have identified a spectrum of conditions that either exacerbate vulnerability or contribute to resilience, accounting for the diverse correlations of neighborhood environments with children's PLEs.

Our findings hold implications for social science and economic theory by providing quasi-experimental evidence for the "behavioral poverty trap". Our finding that neighborhood socioeconomic adversity is linked to children's intertemporal choice toward steeper reward discounting challenges the longstanding economic assumption that time preference is a fixed

trait. This environmentally induced shift towards more impulsive decision-making, likely driven by factors such as cognitive load from resource scarcity and reduced social trust, could foster behaviors that might perpetuate socioeconomic challenges. These results suggest that policies aimed at improving childhood environments may be crucial for breaking intergenerational cycles of disadvantage. A more detailed examination of these theoretical frameworks is provided in the **Supplementary Information**.

A plausible biological mechanism for these findings involves the association of chronic stress with the neurodevelopmental trajectory of prefrontal-limbic circuits. Prior research indicates that neighborhood socioeconomic deprivation is a potent chronic stressor that elevates glucocorticoid hormones like cortisol (79-83). During the critical adolescent period of our cohort, prolonged glucocorticoid dysregulation can induce epigenetic modifications that alter the mesocorticolimbic dopaminergic system, which governs reward valuation and is heavily implicated in the pathophysiology of psychosis (33, 84-87). The neuro-genetic patterns of vulnerability we identified—characterized by reduced limbic volume and altered prefrontal-limbic reactivity during reward processing—are therefore consistent with a stress-induced disruption of the reward system that confers risk for both impulsive decision-making and PLEs (24, 88). A more detailed review of the supporting evidence is available in the **Supplementary Information**.

In our study, we discovered that children, when exposed to deprived neighborhoods and already facing the challenges of residential disadvantage, were more likely to experience PLEs. Surprisingly, these children also showed a higher GPS for cognitive performance, IQ, and education attainment (**Fig. 4**). At first glance, this finding seems to contradict prior research, which has consistently identified a negative relationship between PLEs and cognitive

performance (38, 89).

We interpret this paradox through the lens of gene-environment interaction theory, specifically the bioecological model and the Scarr-Rowe hypothesis (90-92). This framework posits that genetic influences on traits diminish under adverse environmental conditions—analogous to how nutrient-poor soil constrains plant growth regardless of genetic potential (93). In our context, residential disadvantage appears to suppress the protective effects of cognitive-related genetic variants, rendering children with higher cognitive ability GPS more vulnerable to environmental stressors that precipitate PLEs. Critically, those with the greatest genetic potential for cognitive performance lose the most protection, creating heightened susceptibility to neighborhood-level adversity.

This interaction pattern aligns with differential susceptibility theory (94, 95), which proposes that certain genetic profiles confer both vulnerability to negative environments and enhanced benefit from positive ones. While our study of neighborhood deprivation captures only the "for worse" component, our results satisfy a key theoretical prerequisite by providing evidence that genetic advantage may paradoxically increase environmental vulnerability. This challenges traditional diathesis-stress models and instead supports a genetic plasticity framework where the same variants that confer advantage in supportive contexts create risk in adverse ones.

The three GPSs examined here—encompassing cognitive performance, IQ, and educational attainment—capture accumulated learning and developmental potential (96, 97). Within the differential susceptibility framework, elevated cognitive ability GPS may index heightened neurobiological plasticity that, when confronted with resource-poor environments,

generates stress responses that increase PLE risk. Conversely, individuals with lower cognitive ability GPS may show resilience precisely because they exhibit reduced environmental reactivity, making them less sensitive to the specific stressors—such as thwarted potential or limited opportunities—that characterize deprived neighborhoods and may trigger psychotic-like experiences.

Consistent with our findings, recent large-scale studies have demonstrated that the association of genetics with brain structure, cognitive functions, and mental health disorders becomes less significant in harmful environments (e.g., abuse) (98, 99). Conversely, in more supportive and enriched settings, like those associated with higher socioeconomic status, genetic influences are more noticeable (e.g., high socioeconomic status) (91, 100, 101). Together with these findings, our study contributes to a deeper understanding of how genetic and environmental factors interact to influence the development of psychopathology in children.

Several limitations of this study warrant consideration. First, while our IV approach was employed to mitigate unobserved confounding, the observational nature of the ABCD Study necessitates a cautious interpretation of causality. While we took steps to substantiate it with prior research and sensitivity analyses (detailed in *Instrumental Variable Regression* section of the **Supplementary Information**), our interpretations should be read as associations based on IV-estimates that are compatible with a causal account but remain assumption-dependent.

Second, the stringent neuroimaging and behavioral quality-control filters necessary for internal validity yielded appreciable attrition from the ABCD Study cohort, introducing potential selection effects. The final sample was predominantly white (65.57%, self-reported race/ethnicity), which may also limit the generalizability of our specific neuro-genetic findings

to individuals from other racial and ethnic backgrounds. To formally address this challenge, we conducted a sensitivity analysis using inverse probability weighting, a rigorous method designed to account for potential selection bias. While this sensitivity analysis demonstrated that our key findings on heterogeneous associations of neighborhood adversity with PLEs were robust to reweighting on observed characteristics, this approach cannot address selection on unmeasured factors. Children excluded due to motion artifacts or task non-compliance may differ in ways correlated with both neuroimaging quality and psychiatric vulnerability. Therefore, our findings apply specifically to children capable of completing comprehensive assessments—a limitation that may exclude those at highest risk. Future studies should develop protocols enabling broader participation while maintaining data quality.

Third, the follow-up horizon is limited to baseline, 1-year, and 2-year assessments. It should be noted that additional longitudinal data from the ABCD Study were publicly released after this work was finalized, so were not included. Longer observation windows are needed to map trajectories from adversity to psychosis-spectrum outcomes and to evaluate the stability of heterogeneity signals.

Beyond neighborhood deprivation, testing other environmental risk factors as primary exposures—particularly parenting/ family environment (102) and early-life stress (99)—will clarify whether similar neuro-genetic profiles index differential susceptibility across contexts. Later ABCD releases enable (i) time-varying and cumulative-exposure models, (ii) ancestry-stratified and site-robust analyses, and (iii) external replication. Such work will help determine whether the identified moderators can support risk stratification and inform precision prevention.

This study highlights the differential associations of neighborhood disadvantage with intertemporal economic decisions and PLEs during early childhood. It underscores the importance of identifying diverse links by integrating genetic and environmental factors to guide personalized healthcare approaches. Furthermore, we propose that enhancing the childhood environment may contribute to the reduction of economic and health inequality gaps. Economic policies promoting positive intertemporal choice (e.g., increased savings, healthy diet) have predominantly focused on paternalistic welfare policies in adulthood. These policies often assume that an individual's tendency to discount future rewards is fixed ("exogenous") (24). However, our findings suggest that policies or interventions aimed at enhancing the socioeconomic environment during childhood may foster improved intertemporal choice behavior, thereby reducing economic (13, 20, 21) and health inequality (17, 103). By addressing the root of the problem, this indirect approach may assist individuals in developing the capacity to make more informed choices, ultimately promoting better outcomes.

Finally, our findings provide an empirical counterpoint to longstanding philosophical questions about human agency. Immanuel Kant, in his book *Critique of Practical Reason*, argued for an a priori capacity for reason, independent of external factors (104). Our work, however, suggests that the neuro-genetic mechanisms governing intertemporal choice and psychiatric vulnerability are profoundly associated with a child's socioeconomic environment. This link between environment and the biological substrates of decision-making challenges models of responsibility that assume unconstrained free will. Instead, our results call for a more nuanced understanding of individual agency, suggesting that societal approaches to justice, policy, and intervention must account for the powerful and heterogeneous ways in which a child's environment is related with their neurocognitive development.

Data availability

The ABCD Study dataset is openly available to all eligible researchers upon the submission of an access request via the National Institutes of Mental Health Data Archive (https://nda.nih.gov/abcd). Comprehensive written informed consent was obtained from the parents of participants, with children providing assent. The study protocols were approved by the University of California, San Diego's Institutional Review Board (IRB), under approval number 160091, in addition to receiving approval from the IRBs of the 21 participating data collection sites (105).

Code availability

All codes needed to replicate the results can be found at https://github.com/Transconnectome/DD-HTE.

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Acknowledgements

This work was supported by the National Research Foundation of Korea (NRF) grant funded by the Korea government (MSIT) (No. 2021R1C1C1006503, RS-2023-00266787, RS-2023-00265406, RS-2024-00421268, RS-2024-00342301, RS-2024-00435727, NRF-2021M3E5D2A01022515, and NRF-2021S1A3A2A02090597), by the Creative-Pioneering Researchers Program through Seoul National University (No. 200-20240057, 200-20240135). Additional support was provided by the Institute of Information & Communications Technology Planning & Evaluation (IITP) grant funded by the Korea government (MSIT) [No. RS-2021-II211343, 2021-0-01343, Artificial Intelligence Graduate School Program, Seoul National University] and by the Global Research Support Program in the Digital Field (RS-2024-00421268). This work was also supported by the Artificial Intelligence Industrial Convergence Cluster Development Project funded by the Ministry of Science and ICT and Gwangju Metropolitan City, by the Korea Brain Research Institute (KBRI) basic research program (25-BR-05-01), by the Korea Health Industry Development Institute (KHIDI) and the Ministry of Health and Welfare, Republic of Korea (HR22C1605), and by the Korea Basic Science Institute (National Research Facilities and Equipment Center) grant funded by the Ministry of Education (RS-2024-00435727). We acknowledge the National Supercomputing Center for providing supercomputing resources and technical support (KSC-2023-CRE-0568). An award for computer time was provided by the U.S. Department of Energy's (DOE) ASCR Leadership Computing Challenge (ALCC). This research used resources of the National Energy Research Scientific Computing Center (NERSC), a DOE Office of Science User Facility, under ALCC award m4750-2024, and supporting resources at the Argonne and Oak Ridge Leadership

980 Computing Facilities, U.S. DOE Office of Science user facilities at Argonne National Laboratory
981 and Oak Ridge National Laboratory.

Tables and Figures

Table 1. Socioeconomic/demographic characteristics of the participants. *Age* is rounded to chronological month. *Race/Ethnicity* denote child's self-reported racial / ethnic identity. *Household Income* is assessed as the total combined family income for the past 12 months. *Parental Education* is measured as the highest grade or level of school completed or highest degree received. *Family History of Psychiatric Disorders* represents the proportion of first-degree relatives who experienced mental illness.

Demographic Characteristics		N	Ratio (%)	Mean (SD)
Age		2,135		120.1541 (7.4658)
Sex	Male	1,150	53.86%	
	Female	985	46.14%	
Marital Status of the first caregiver	Married	1,636	76.63%	
	Widowed	12	0.56%	
	Divorced	193	9.04%	
	Separated	62	2.9%	
	Never Married	142	6.65%	
	Living with Partner	90	4.22%	
Race/Ethnicity	White	1,400	65.57%	
	Black	136	6.37%	
	Hispanic	373	17.47%	

	Asian	7	0.33%	
	Other	219	10.26%	
Parent's Identity	Biological Mother	1,848	86.56%	
	Biological Father	215	10.07%	
	Adoptive Parent	39	1.83%	
	Custodial Parent	12	0.56%	
	Other	21	0.98%	
Household Income		2,135		$116,538 (70,669)
Parental Education		2,135		17.2838 (2.3046)
BMI		2,135		18.4298 (3.8572)
Parental Age		2,135		40.8775 (6.3825)
Family History of Psychiatric Disorders		2,135		0.0958 (0.1125)

Table 2. Potential associations of neighborhood socioeconomic adversity with intertemporal valuation and PLEs. Average relationships of ADI with delay discounting and PLEs in the IV Forest models are shown. All p-values were corrected for multiple comparison using false discovery rate.

	IV Forests: Average Associations				
	Estimates	**Std. Error**	**95% Lower CI**	**95% Upper CI**	**P-FDR**
Delay Discounting (1-year follow-up)	-1.730	0.748	-3.195	-0.265	0.048
Distress Score PLEs (1-year follow-up)	1.872	0.612	0.673	3.071	0.048
Distress Score PLEs (2-year follow-up)	1.504	0.592	0.345	2.664	0.039
Delusional Score PLEs (1-year follow-up)	5.970	2.911	0.264	11.676	0.048
Delusional Score PLEs (2-year follow-up)	4.022	1.987	0.127	7.917	0.048
Hallucinational Score PLEs (1-year follow-up)	3.761	1.902	0.033	7.489	0.048
Hallucinational Score PLEs (2-year follow-up)	4.786	1.861	1.139	8.433	0.039

Fig. 1. Study flow diagram. This figure illustrates the participant selection and data processing in our study. We initially included 11,876 participants aged 9-12 years from the Adolescent Brain Cognitive Development (ABCD) Study, utilizing the release 4.0 dataset which encompasses baseline, 1-year follow-up, and 2-year follow-up observations. We excluded observations not meeting the ABCD Study's MRI quality control standards and those failing the Johnson-Bickel validation criterion for delay discounting. Participants with missing values in genotypes, MRI, NIH Toolbox Cognitive Battery, delay discounting, residential address, ADI, and PLEs were also removed. Subsequently, sociodemographic features underwent kNN imputation. This resulted in a final sample size of N=2,135. Using this cohort, our study first investigated the average associations of neighborhood socioeconomic deprivation with children's intertemporal valuation of rewards and PLEs. We then explored the individual differences of these links in relation to children's delay discounting behaviors and associated genetic and neural factors.

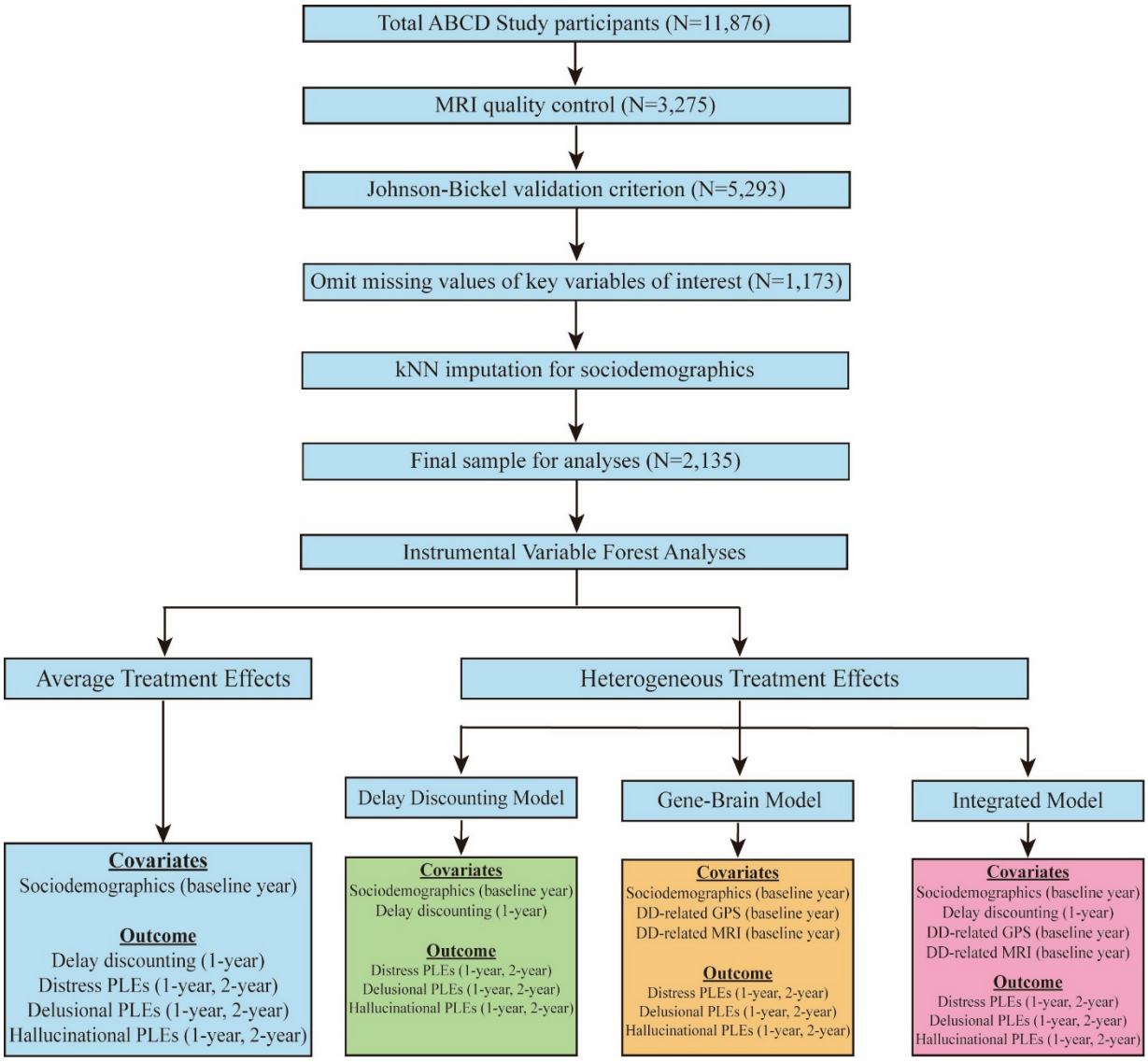
Total ABCD Study participants (N=11,876)
MRI quality control (N=3,275)
Johnson-Bickel validation criterion (N=5,293)
Omit missing values of key variables of interest (N=1,173)
kNN imputation for sociodemographics
Final sample for analyses (N=2,135)
Instrumental Variable Forest Analyses
Average Treatment Effects
Heterogeneous Treatment Effects
Delay Discounting Model
Gene-Brain Model
Integrated Model
Covariates
Sociodemographics (baseline year)
Outcome
Delay discounting (1-year)
Distress PLEs (1-year, 2-year)
Delusional PLEs (1-year, 2-year)
Hallucinational PLEs (1-year, 2-year)
Covariates
Sociodemographics (baseline year)
Delay discounting (1-year)
Outcome
Distress PLEs (1-year, 2-year)
Delusional PLEs (1-year, 2-year)
Hallucinational PLEs (1-year, 2-year)
Covariates
Sociodemographics (baseline year)
DD-related GPS (baseline year)
DD-related MRI (baseline year)
Outcome
Distress PLEs (1-year, 2-year)
Delusional PLEs (1-year, 2-year)
Hallucinational PLEs (1-year, 2-year)
Covariates
Sociodemographics (baseline year)
Delay discounting (1-year)
DD-related GPS (baseline year)
DD-related MRI (baseline year)
Outcome
Distress PLEs (1-year, 2-year)
Delusional PLEs (1-year, 2-year)
Hallucinational PLEs (1-year, 2-year)

Fig. 2. Illustration of instrumental variables analysis. (**A**) Graphical model of the IV method. This panel depicts how the IV method is applied to address the potential biases from unobserved confounders U when analyzing the effects of exposure/treatment (ADI) on outcomes (delay discounting and PLEs) within the observational context of the ABCD Study. Using the instrument (SOI laws), the IV method aims to partial out the influence of U on ADI, thus adjusting for potential confounding biases. (**B**) Graphical representation of the IV Forest algorithm. The IV Forest algorithm stratifies subjects in a manner that maximizes the individual differences in predicted conditional average effects. This panel illustrates the use of IV Forest to assess the association of ADI with delay discounting and PLEs, as well as to explore the heterogeneous relationships of ADI with PLEs, factoring in individual variations in delay discounting and its associated genetic and neural correlates.

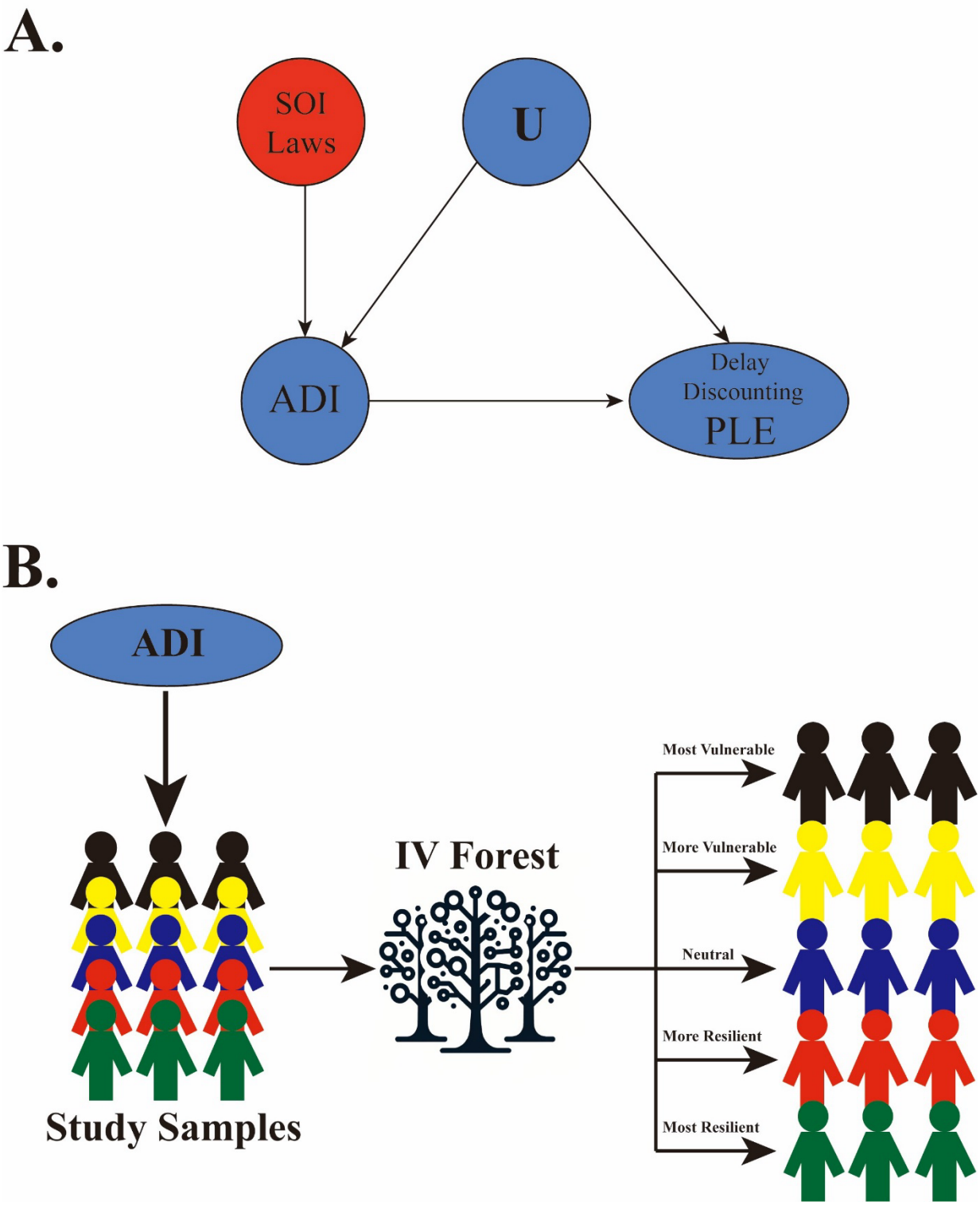

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Fig. 3. Delineation of heterogeneous associations by vulnerable/resilient subgroups. Heterogeneity in the associations of ADI with PLEs are shown as a bar plot, specifically focusing on 1-year follow-up distress score PLEs (**A**) and hallucinational score PLEs (**B**). These relationships are plotted across ten deciles, which are organized based on the relative vulnerability or resilience of the participants, with Q1 denoting the most vulnerable and Q10 indicating the most resilient. Point estimates of the conditional average effect of each decile were derived via a doubly-robust estimation method within the IV Forest algorithm. 95% confidence intervals are depicted using error bars.

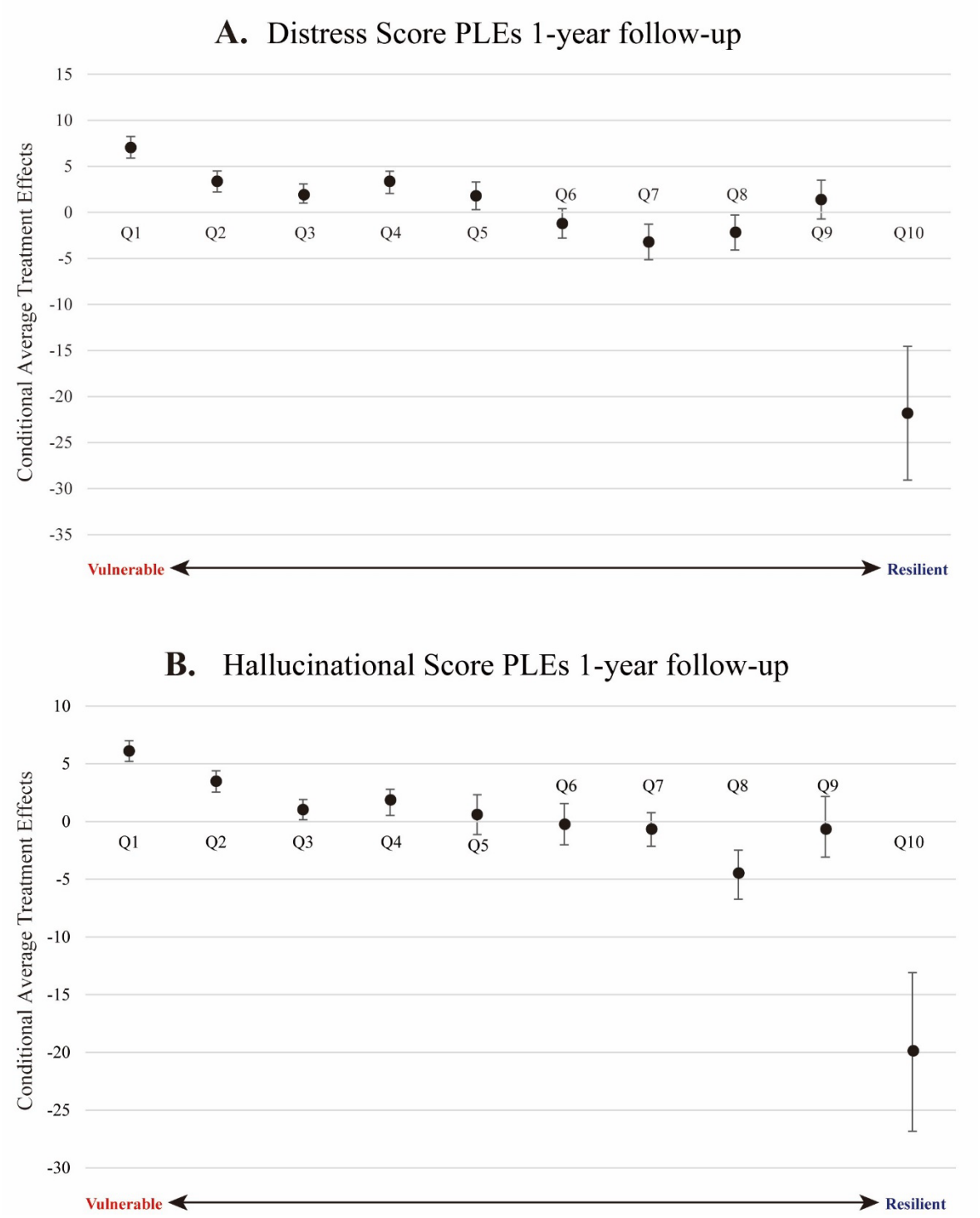
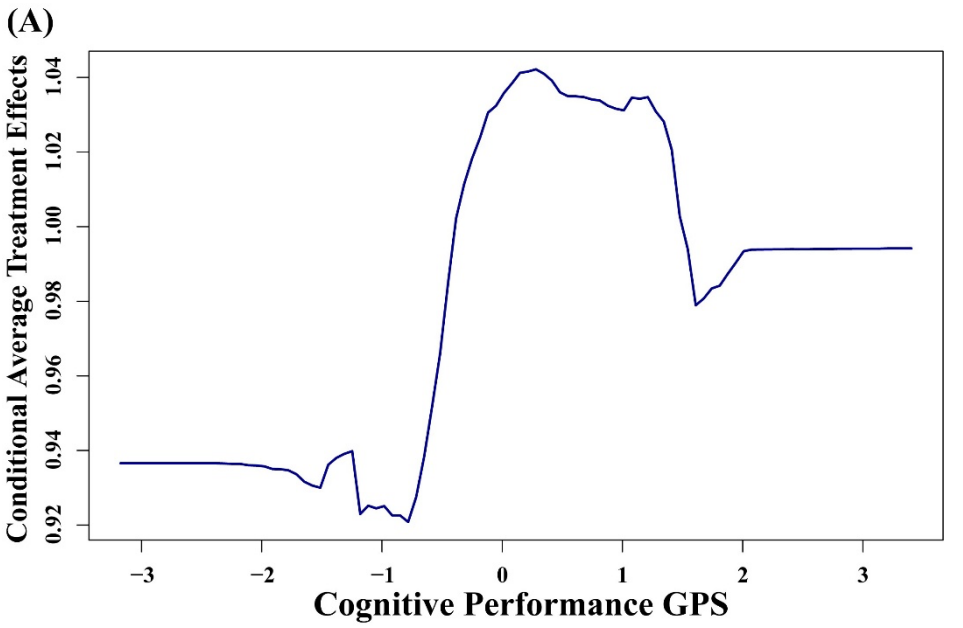
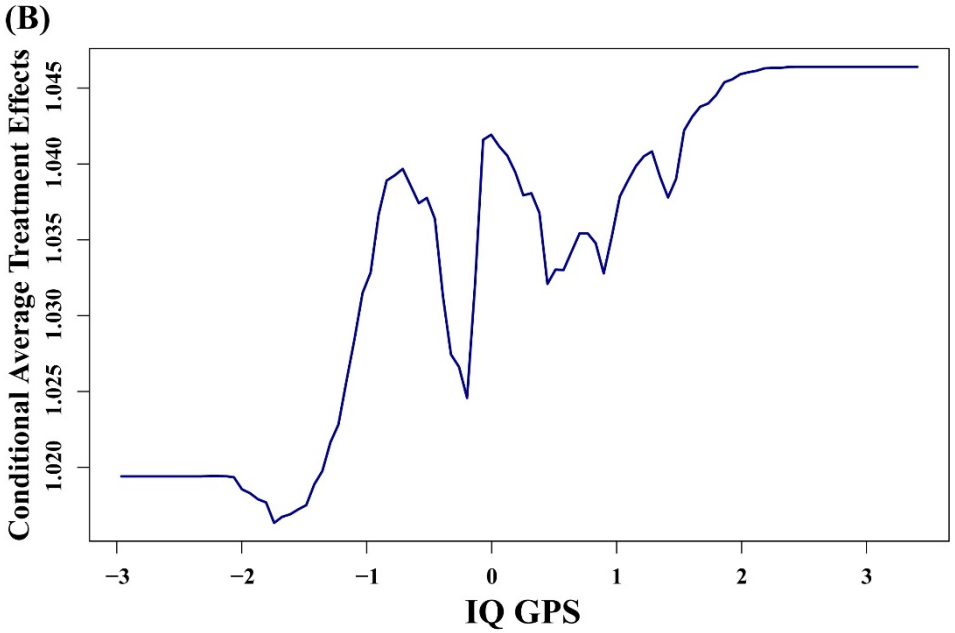
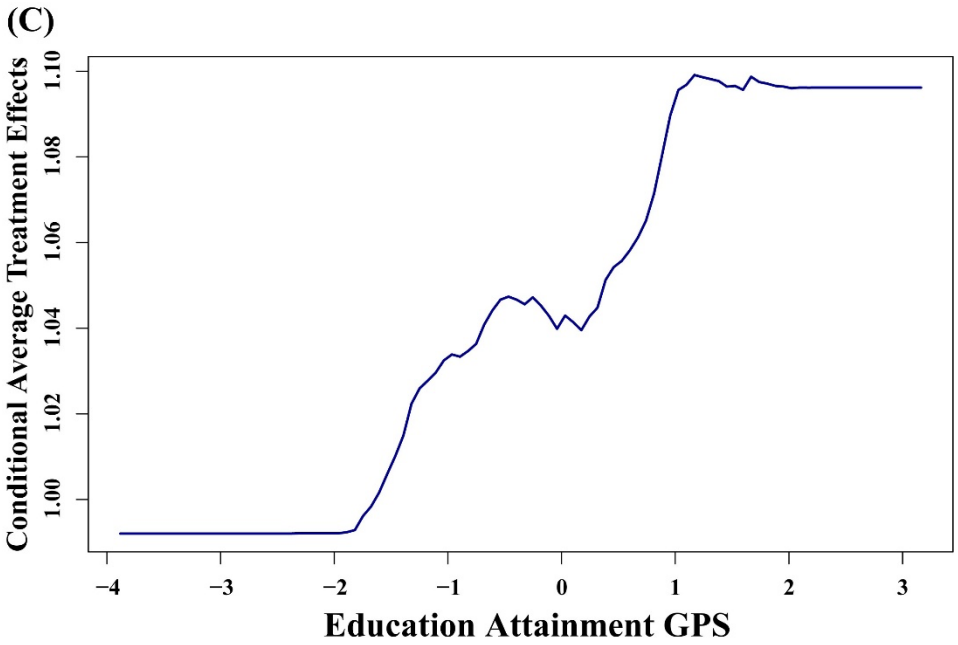

A. Distress Score PLEs 1-year follow-up
Conditional Average Treatment Effects
15
10
5
0
-5
-10
-15
-20
-25
-30
-35
Q1
Q2
Q3
Q4
Q5
Q6
Q7
Q8
Q9
Q10
Vulnerable
Resilient
B. Hallucinational Score PLEs 1-year follow-up
Conditional Average Treatment Effects
10
5
0
-5
-10
-15
-20
-25
-30
Q1
Q2
Q3
Q4
Q5
Q6
Q7
Q8
Q9
Q10
Vulnerable
Resilient

Fig. 4. GPS for cognitive traits moderate environmental risk for PLEs. Plotted is the conditional average effects of neighborhood socioeconomic deprivation (ADI) on distress score PLEs at 1-year follow-up. The effect of ADI is shown as a function of an individual's genetic predisposition (GPS) for (**A**) cognitive performance, (**B**) IQ, and (**C**) education attainment, revealing complex patterns of gene-environment interaction.


(A)
Conditional Average Treatment Effects
0.92
0.94
0.96
0.98
1.00
1.02
1.04
−3
−2
−1
0
1
2
3
Cognitive Performance GPS


(B)
Conditional Average Treatment Effects
1.020
1.025
1.030
1.035
1.040
1.045
−3
−2
−1
0
1
2
3
IQ GPS


(C)
Conditional Average Treatment Effects
1.00
1.02
1.04
1.06
1.08
1.10
−4
−3
−2
−1
0
1
2
3
Education Attainment GPS

Supplementary Information for

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Junghoon Justin Park, Minje Cho, Eunji Lee, Bo-Gyeom Kim, Gakyung Kim, Yoonjung Yoonie Joo, Jiook Cha*

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