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Early life adversity and health-risk behaviors: proposed psychological and neural mechanisms

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Abstract

Early life adversity (ELA) is associated with poorer health in adulthood, an association explained, at least in part, by increased engagement in health-risk behaviors (HRBs). In this review, we make the case that ELA influences brain development in ways that increase the likelihood of engaging in HRBs. We argue that ELA alters neural circuitry underpinning cognitive control as well as emotional processing, including networks involved in processing threat and reward. These neural changes are associated psychologically and behaviorally with heightened emotional reactivity, blunted reward responsivity, poorer emotion regulation, and greater delay discounting. We then demonstrate that these adaptations to ELA are associated with an increased risk of smoking cigarettes, drinking alcohol, and eating high-fat, high-sugar foods. Furthermore, we explore how HRBs affect the brain in ways that reinforce addiction and further explain clustering of HRBs.

Graphical abstract

Early life adversity (ELA) involves exposure to environmental circumstances during childhood or adolescence that are likely to require significant psychological, behavioral, or neurobiological adaptation by an average child. It is associated with poorer health in adulthood, an association explained, at least in part, by increased engagement in health-risk behaviors (HRBs). In this review, we make the case that ELA influences brain development in ways that increase the likelihood of engaging in HRBs.

Keywords

health neuroscience; early life adversity; health-risk behaviors; emotional reactivity; reward responsivity; emotion regulation; delay discounting

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Competing interests

The authors declare no competing interests.

Introduction

Early life adversity (ELA) involves exposure to environmental circumstances during childhood or adolescence that are likely to require significant psychological, behavioral, or neurobiological adaptation by an average child and that represent a deviation from the expected environment.[1] A wide range of experiences meet this definition of ELA, ranging from physical, emotional, and sexual abuse, to prolonged emotional or physical neglect, to chronic material deprivation association with poverty. Exposure to ELA is common. Population-based studies indicate that 40–50% of children both in the U.S. and cross-nationally will experience some form of ELA.[2–4] In addition to being common, ELA is strongly associated with morbidity and mortality. Greater exposure to ELA is associated with elevated risk of a wide range of mental and physical health outcomes across the lifespan, including depression, anxiety, substance abuse, cardiovascular disease, cancer, type 2 diabetes, respiratory diseases, chronic pain, gastrointestinal and metabolic disorders, and neurological and musculoskeletal problems,[4–14] as well as premature mortality.[15,16] The mechanisms underlying these associations remain poorly understood, although evidence is accumulating that ELA influences mental health by altering the developing brain in ways that contribute to the onset of psychopathology,[1,17,18] and interest is increasing in the neural mechanisms underlying the links between ELA and physical health.[19,20] In this review, we advance a conceptual model arguing that altered patterns of brain development among children exposed to ELA might contribute to the onset of chronic diseases, in part by increasing the tendency to engage in health-risk behaviors (HRBs).

The burden of chronic disease

A recent analysis of the National Health Interview Survey data revealed that 50% of adults had at least one chronic disease and 25% had two or more of the ten leading causes of death and disability in the U.S.[21] Social determinants and socially patterned HRBs including tobacco and alcohol use, unhealthful eating patterns, and physical inactivity drive the chronic disease burden observed in the U.S.[21–26] Often initiated during childhood, adolescence, and early adulthood, these highly prevalent HRBs are known to cluster within individuals and populations.[27–29] For example, a population-based study indicated that more than half of U.S. adults report engaging in two or more HRBs, including smoking cigarettes, engaging in risky drinking, being physical inactive, and being overweight.[30] Compared to those in the general population, those who are dependent on alcohol are three times more likely to be smokers and those who are dependent on tobacco are four times more likely to be dependent on alcohol.[31] Exposure to ELA is associated with a clustering of health risks, with increasing exposure related to an increasing number of HRBs.[32] Given that the presence of multiple HRBs can have an interactive effects on chronic disease occurrence,[33–35] this clustering increases the burden of chronic disease in vulnerable populations, such as those exposed to ELA. As noted above, multiple epidemiological studies have documented an association between ELA and elevated risk of chronic diseases such as cardiovascular disease,[36–38] cancer,[39–42] diabetes,[36,37] and premature mortality.[15,16] We argue that these associations are explained, at least in part, by increased vulnerability to engage in HRBs conferred by ELA. Indeed, ELA is associated with a greater likelihood of

smoking cigarettes,[32,43,44] abusing alcohol and drugs,[32,45–47] eating a poor diet,[48] and being obese.[32,49]

Given the prevalence of chronic diseases, a greater understanding of the mechanisms linking ELA to HRBs and risk for chronic disease has the potential to make a significant contribution to public health by highlighting novel targets for intervention. Building on existing theoretical perspectives,[50–52] systematic reviews,[53–55] meta-analyses,[53] and observational studies of ELA and health across the lifespan,[40,56] we posit that ELA affects brain development in ways that predispose people to engage in HRBs. The three HRBs that we focus on are: (1) smoking cigarettes and nicotine dependence; (2) drinking alcohol heavily and alcohol use disorders; and (3) eating an energy-dense diet high in sugar and fat as well as excessive food consumption.[57] Because light to moderate alcohol use is associated with improved health outcomes for certain chronic diseases, such as cardiovascular disease,[58,59] we focus on excessive alcohol consumption as a risk factor for chronic diseases. According to the U.S. Department of Health and Human Services and the U.S. Department of Agriculture, moderate alcohol use among adults of legal drinking age is defined as one drink per day for women and two drinks per day for men.[57] Excessive alcohol consumption among women of legal drinking age is defined as 4 or more drinks within 2 hours (binge drinking), 4 or more drinks on any day, and 8 or more drinks per week.[57] Excessive alcohol consumption among men of legal drinking age is defined as 5 or more drinks for men within about 2 hours (binge drinking), 5 or more drinks on any day, and 15 or more drinks per week.[57] Regarding food intake, excessive food intake is defined as excessive caloric intake relative to calories expended.[57] The reason we focus on excessive food intake and the consumption of energy-dense foods such as those high in sugar and fat is because both types of eating behaviors appear to be driven by reward processes.[60] Although these neural processes evolved when such foods were scarce, in the modern context, such foods have become abundant. Thus, the drive to consume energy-dense foods and to eat beyond immediate need has become maladaptive and excessive caloric intake has contributed to an epidemic of obesity.[60] Given that certain types of eating behaviors such as those that we focus on in the paper closely fits an addiction model[60,61] and that ELA is associated with eating a poor diet[48] as well as obesity,[32,49] we focus on unhealthy eating behavior as a pathway to obesity despite the fact that physical inactivity as well as other factors also contribute to obesity. Because obesity is often used as a proxy for eating behavior, in this paper, the neurobiological evidence that we present includes both eating behaviors as well as differences between obese vs. non-obese populations. In delineating our conceptual model, we first articulate a model of the neurodevelopmental mechanisms linking ELA with HRBs. Next, we review existing evidence of how ELA influences these neurodevelopmental processes and discuss how these neural adaptations are associated with psychological and behavioral factors that may increase the likelihood of engaging in HRBs. We end by pointing to directions for future research on the neural mechanisms underlying chronic disease risk following early-life adversity.

Neural adaptations following early life adversity

We posit that adverse early life environments influence brain and behavioral development in ways that are adaptive in the short term by promoting survival[62] but are maladaptive in the

long term to physical health. Below, we focus on three neural networks that are influenced by ELA and have relevance to HRBs. These neural networks include the salience network and prefrontal–amygdala circuits involved in detecting and responding to threat, the frontostriatal reward-processing network, and the frontoparietal network involved in cognitive control. For each of these neural networks, we discuss how altered function following ELA reflects both adaptations and trade-offs.

Threat detection processes

In threatening environments, the ability to quickly identify threats and rapidly mobilize behavioral responses that promote safety likely promotes survival.[62] Thus, exposure to threatening environments, especially early in development, should lead to neural adaptations that enhance threat detection. Indeed, existing evidence suggests that children exposed to forms of ELA characterized by threat (e.g., exposure to violence) exhibit heightened neural response to signals of threat, particularly in the amygdala and other nodes of the salience network.[63–66] Although these adaptations likely help children avoid danger, they come at a cost. For example, specificity is traded for sensitivity, leading to higher emotional reactivity to a wide range of potential threats and more false alarms among children raised in threatening environments.[63]

Reward-related processes

Multiple forms of ELA, particularly experiences of neglect and caregiver deprivation, are associated with blunted responsivity to reward.[67–71] Perhaps counterintuitively, blunted reward responsivity can actually induce reward-seeking behavior,[72,73] potentially because more intense rewards are needed to feel pleasure. In deprived environments, reward seeking is likely adaptive, particularly if resources are scarce and reward seeking helps secure resources. Unfortunately, enhanced reward seeking also increases susceptibility to substance use and pursuit of other highly rewarding stimuli (e.g., high-sugar, high-fat foods)—rewards in the modern environment that co-opt evolved reward pathways.

Cognitive control

Some forms of ELA, in particular, deprivation-related experiences, are associated with alterations in the frontoparietal executive control network,[17,74–76] which has implications for decision-making as well as threat- and reward-related processes. Impairments in the executive control network lead to a shift from reflective responding that is flexible and goal-directed to reflexive responding that is inflexible and stimulus–response driven.[77] These impairments can make it more difficult to regulate emotions[66,78] and delay immediate gratification despite long-term consequences. Although reflexive responding may be adaptive in an adverse environment when it is advantageous to be able to rapidly respond to aversive and appetitive cues, the shift away from reflective responding may make it more difficult to make goal-directed decisions that focus on long-term benefits over short-term rewards.

Existing work on ELA, HRBs, and chronic disease has largely relied on a cumulative risk model.[32,79] This approach tallies the number of adversities experienced to create a risk score. For example, a child who experienced physical abuse, sexual abuse, and domestic

violence would have a risk score of three; a child who experienced food insecurity, neglect, and parental loss would also have a risk score of three. The cumulative risk approach has been useful for highlighting the public health significance of ELA, and risk scores can be used as a screening tool to identify children in greatest need of intervention.[80] However, such an approach implicitly assumes that all forms of adversity influence health outcomes through the same neurodevelopmental pathways outlined in the paper. Increasing evidence indicates that the neurodevelopmental consequences of different forms of adversity are at least partially distinct. Indeed, a recent conceptual model distinguishes between experiences of threat that reflect harm or threat of harm to the child (e.g., exposure to violence) and experiences of deprivation that reflect an absence of some type of expected social or cognitive input during development (e.g., an absence of cognitive or social stimulation resulting from neglect or parental unavailability).[17,18,80] Research evaluating the neurodevelopmental mechanisms that are shared versus distinct across these dimensions of adversity is ongoing and this approach has yet to be applied to work examining ELA and HRBs. To stimulate progress in the search for mechanisms linking ELA and physical health outcomes, we highlight throughout our review whether empirical studies focused on adversities characterized by threat, deprivation, or a risk score.

Psychological and behavioral consequences of neural adaptations

Below, we review evidence for the associations of ELA with threat-related, reward-related, and cognitive control processes. We propose that there are four primary psychological and behavioral consequences of these neural adaptations to ELA that have relevance for health risk: increased emotional reactivity, blunted reward responsivity, difficulties with emotion regulation, and increased delay discounting. Drawing upon experimental studies in animals and observational studies in humans, we explore how these neurobiological, psychological, and behavioral adaptations to ELA might increase engagement in HRBs. We propose that these adaptations increase the tendency for those exposed to ELA to smoke cigarettes, drink alcohol, and overeat highly palatable foods, leading to obesity. Understanding these pathways might provide novel targets for chronic disease prevention efforts.

Early life adversity and emotional reactivity

Children exposed to adversity characterized by both threat and deprivation exhibit greater sensitivity to signals of threat both behaviorally and neurobiologically. Behaviorally, children exposed to violence identify facial expressions of anger faster and with less perceptual information and have greater difficulty disengaging from threat cues[81–85] compared to typically developing children. At the neural level, adversity experiences characterized by both threat and deprivation have been associated with greater amygdala reactivity in response to signals of threat, such as fearful faces or negative emotional images.[63–66,86–89] This effect is present in childhood[64,65,86] and persists through adolescence[66,86] into adulthood.[87,88] A recent meta-analysis confirms that childhood maltreatment, including abuse and neglect, is associated with greater amygdala reactivity to threat.[63] Amygdala reactivity to threat increases in a dose-response manner based on the severity of threat and deprivation.[66,86]

Greater amygdala reactivity to threat may result in greater emotional reactivity, or the tendency to experience frequent and intense emotional arousal and responses to environmental events[90] and research has demonstrated a robust link between ELA and heightened emotional reactivity.[62] This association has been found across multiple measurement methods—from self-reported emotional reactivity[91] to cardiovascular responses[92,93] and amygdala reactivity.[90] Children exposed to adversity characterized by threat (e.g., abuse) are not only more emotionally reactive to facial signals of threat (e.g., expression of anger), but also show heightened amygdala reactivity to a wide range of negative and neutral stimuli,[66,94,95] indicating increased neural sensitivity to a wider range of environmental cues. Amygdala hyperreactivity does not simply reflect concurrent psychopathology as this effect is observed in those exposed to abuse even after adjustment for the presence of psychopathology.[66,95]

Emotional reactivity and health-risk behaviors

Nicotine—Given the anxiolytic[96] and antidepressive[97] effects of nicotine, it is not surprising that the primary reason smokers report smoking is to reduce distress.[98] Smoking initiation is predicted by a tendency to experience negative emotions[98] and the perception that smoking is a good way to control negative emotions predicts smoking maintenance and escalation.[99] Therefore, those exposed to ELA who have a tendency to experience strong negative emotions may smoke in order to reduce distress. Neural evidence supports the notion that nicotine is effective at reducing emotional reactivity. In one study, amygdala activation was lower in response to negative stimuli in smokers compared to non-smokers and an exploratory analysis among smokers revealed that higher carbon monoxide levels (indicative of smoking) predicted lower amygdala activation.[100] This finding suggests that amygdala reactivity is reduced by smoking, providing neural evidence that nicotine helps people cope with negative emotions.

Alcohol—Given the anxiolytic properties of alcohol,[101] those exposed to childhood adversity may use alcohol in order to decrease emotional reactivity.[102] Although extensive evidence shows that multiple forms of ELA predicts higher amygdala response to signal of threat, in those exposed to ELA (assessed using a risk score) with alcohol dependence the opposite pattern occurs: signals of threat are associated with lower amygdala response compared to those exposed to ELA without alcohol dependence.[102] In social drinkers, intravenously administered alcohol attenuates amygdala response to fearful faces while activating striatal reward circuits,[103] providing further evidence that alcohol decreases threat-related emotional reactivity. These findings suggest that alcohol dampens emotional reactivity at the neural level, which provides an explanation for why those exposed to ELA may use and even abuse alcohol. However, more research is needed to elucidate the neural mechanism underlying the association between ELA with both tobacco and alcohol use and whether greater emotional reactivity mediates this link.

Food—Childhood maltreatment predicts a greater likelihood of obesity in adulthood[104,105] and this relationship is partially explained by using food to cope with stress.[49] This finding suggests that those with higher emotional reactivity due to ELA may be more likely to overeat in order to deal with difficult emotions. ELA is associated not only with greater

emotional reactivity, but also heightened perceptions of stress in response to daily events and hassles.[106,107] Although findings are mixed,[108] perceptions of stress are associated with greater consumption of energy dense foods, such as those high in sugar and fat.[109,110] In a cross-sectional study, people who reported greater perceived stress had a higher fat diet.[109] People eat more calories and more fat on days when they experience greater levels of perceived stress than on days when they are less stressed.[110] Thus, ELA may increase perceptions of stress and, in order to cope, lead to the consumption of foods high in sugar and fat. Furthermore, amygdala activation may increase the reward value of certain foods. In an animal model, inactivation of the amygdala is associated with reduced fat intake, presumably by reducing its hedonic value.[111] Stress and reward pathways are integrally linked in ways that likely facilitate reward-seeking behaviors when experiencing strong emotions.

Early life adversity and reward responsivity

Behavioral and neurobiological studies indicate that ELA leads to blunted reward responsivity (i.e. lower neural response to reward in reward-processing brain regions such as the ventral striatum (VS)), an effect that persists across the lifespan.[67–70] Behaviorally, those exposed to childhood maltreatment (either abuse or neglect) rate monetary reward-predicting cues less positively in adulthood compared with healthy controls,[67] and children who experience material deprivation in the form of food insecurity exhibit poor performance on tasks assessing reward responsivity.[112] Neurobiologically, the VS plays a prominent role in reward processing. In adolescents[69] and in adults,[68] exposure to adversity—particularly deprivation involving neglect—is associated with lower VS reactivity in response to reward and the effect is stronger if exposure occurs earlier in development.[68] The VS shows blunted responsivity to reward as well as a lack of sensitivity to differing reward values in adolescents who experienced early maternal deprivation.[70] Furthermore, blunted reward responsivity in the VS predicts depression following emotional neglect.[69] As also shown with blunted reactivity of the VS, lower dopamine D2 receptor (D2R) availability leads to a blunted reward response[113] and is also affected by early deprivation in animal models.[114] For example, rodents exposed to maternal separation demonstrate decreased expression of D2Rs compared with control rats.[114] Thus, evidence suggests that adversity characterized by deprivation dampens responsivity to rewards both behaviorally and neurobiologically and may increase the likelihood of using substances like nicotine, alcohol, and highly palatable foods to overcome blunted reward responsivity.

Blunted reward responsivity and health-risk behaviors

Nicotine—Anhedonia—or difficulty experiencing pleasure—is associated with blunted neural response to reward.[115] Furthermore, anhedonia is higher in adolescents who have smoked a cigarette in the past month compared to those who have not, suggesting that anhedonia could be involved in smoking initiation.[116] Furthermore, at age 15, anhedonia is a strong predictor of smoking escalation over the next 1.5 years.[116] This effect is present even when controlling for other depressive symptoms, suggesting that smoking escalation may be specifically related to blunted experience of reward.[116] Moreover, smokers show lower neural responses in the VS when anticipating reward compared to non-smokers and, among smokers, lower VS activation predicts greater smoking frequency.[117] The prior study

included young and generally light smokers who had not smoked for long, which suggests that lower responsivity of the reward system may increase the likelihood of early nicotine use as well as the severity of nicotine dependence. Given that nicotine is a potent modulator of the reward system because it stimulates mesolimbic dopamine release,[118] nicotine may counteract blunted reward responsivity in those exposed to ELA.

Alcohol—For those exposed to ELA, lower VS responsivity to reward predicts higher risk for anhedonia, which is associated with problematic alcohol use through substance-related coping.[119] As previously mentioned, early deprivation in an animal model lowers D2R availability,[114] which is associated with a blunted reward response.[113] Lower D2R availability may be associated with greater vulnerability to alcohol abuse. As evidence of a causal role of D2Rs in alcohol use, upregulation of D2Rs in the VS reduces alcohol intake in rats previously trained to self-administer.[120] Thus, those exposed to ELA may be particularly vulnerable to alcohol abuse due to blunted reward responsivity.

Food—Obesity is associated with lower striatal D2R availability, such that a higher body mass index (BMI) predicts lower receptor availability.[121] Given the relationship between ELA and lower D2R availability, one of the neural mechanisms linking ELA to obesity may be via blunted reward responsivity. Specifically, lower D2R availability may lead to compensatory overconsumption of food in order to overcome blunted reward responses.[121] Furthermore, stress modulates the effect of D2R availability on eating behavior such that lower availability of D2Rs increases the likelihood that someone will eat if emotionally stressed.[122] Thus, a combination of high-perceived stress and stress reactivity with low responsivity to reward may make those exposed to ELA particularly vulnerable to overeating as a coping mechanism to deal with stress. However, experimental studies are needed in order to establish a causal link between blunted reward responsivity and overeating.

Early life adversity and emotion regulation

Emotion regulation involves the ability to recognize emotions and use effective strategies to modulate the expression or experience of an emotion. Emotion regulation occurs through numerous processes acting at multiple points in the generation, expression, and experience of emotion.[123] Connectivity between the prefrontal cortex (PFC) and amygdala play a critical role in emotion regulation. Whereas the amygdala detects and responds to threats from the environment, the PFC modulates activity in the amygdala in order to alter the experience of emotion.[78] Regions in the medial PFC are involved in forms of emotion regulation that are automatic or implicit, such as habituation or extinction of fear responses,[124] whereas regions in the dorsolateral and ventrolateral PFC are involved in more effortful forms of emotion regulation, including cognitive reappraisal.[125] Successful emotion regulation is associated with greater functional coupling of the PFC and amygdala.[126] Exposure to ELA, particularly experiences of abuse and violence that are characterized by threat, is associated with poor emotion regulation ability across numerous studies.[91,127,128] This pattern is likely explained by alterations in prefrontal–amygdala connectivity following ELA. Multiple studies have shown that adversity involving threat is associated with reduced prefrontal–amygdala connectivity at rest.[129,130] In studies focused on effortful forms of emotion regulation, children exposed to threat-related early adversity require greater PFC

activation to successfully modulate amygdala responses to negative cues than children never exposed to adversity.[66]

Emotion regulation and health-risk behaviors

Nicotine—In a conceptual model, the need to regulate negative emotions is proposed as a contributing factor in smoking initiation.[131] Furthermore, neural evidence links the regulation of emotions to the regulation of cravings.[132] In smokers, less successful down-regulation of craving is associated with lower activation in the PFC and regions associated with regulating emotion and higher activation in limbic regions associated with craving.[132] This finding shows that the neural activation patterns underlying emotion regulation are similar to those underlying regulation of cravings. Although causal evidence is still lacking, we speculate that ELA may hinder the ability to regulate cravings through its effect on emotion regulation, leading to greater difficulty regulating cravings and a greater propensity for addiction. However, experimental studies are needed in order to draw clear causal conclusions.

Alcohol—One of the primary motives for drinking alcohol is to cope with negative emotions.[133] Thus, poor emotion regulation skills may predispose people to rely on alcohol to cope. Indeed, meta-analytic evidence indicates greater difficulties with emotion regulation among people who abuse alcohol.[134] In a group with alcohol dependence, poorer ability to regulate emotions after undergoing cognitive behavioral therapy predicted higher alcohol use at the three-months follow-up even after controlling for potential confounds such as symptom severity, number of comorbid disorders, cognitive capacities, and negative affect.[135] This study suggests the need to target emotion regulation skills as a way to lessen alcohol use and prevent relapse in those with alcohol use disorders. Given that ELA is associated with difficulties regulating emotions and differences in prefrontal–amygdala circuitry and these same differences in prefrontal–amygdala circuitry have been proposed to underlie substance use disorders,[136] this may be a psychological and neurobiological mechanism by which ELA increases the likelihood of abusing alcohol.

Food—Emotion regulation plays a central role in obesity.[137] In toddlers, poor emotion regulation skills prospectively predict higher BMI, even after controlling for baseline BMI and behavioral problems.[138] This relationship may be explained by emotional eating to cope with negative emotions.[139] In a sample of obese 10- to 16-year-olds, maternal rejection was associated with increased emotional eating, which was mediated by maladaptive emotion regulation strategies.[139] In another study, emotional dysregulation mediated the relationship between childhood trauma (i.e., threat) and obesity.[140] Reduced activation in the PFC may be the neural substrate for this effect. Indeed, research shows that obesity is associated with lower activation in the left dorsolateral prefrontal cortex (DLPFC) following a meal[141] and higher BMIs predict lower metabolic activity in the PFC.[142] Furthermore, lower baseline metabolism in the PFC is associated with poorer executive function.[142] Therefore, ELA may lead to obesity through its influences on emotion regulation, which may increase the likelihood of using food to regulate negative emotions.

Early life adversity and delay discounting

Delay discounting is the tendency to choose smaller sooner rewards over larger later rewards. ELA characterized by both threat and deprivation is associated with higher delay discounting rates.[143–145] For example, childhood abuse[145] as well as low socioeconomic status (SES)[143,144] both predict a tendency to choose immediate rewards. This psychological orientation to the present likely exists because the future is more uncertain under conditions of threat and deprivation. As evidence of this, mortality cues increase preference for immediate rewards for those who grew up poor, but not for those who grew up wealthy.[146] The context associated with low SES may perpetuate a decision-making style of choosing immediate rewards despite long-term consequences, which may contribute to the SES gradient in health behaviors.[147]

At a neural level, greater delay discounting is related to lower activation in the DLPFC when selecting smaller sooner rewards over larger later rewards.[148] Causal evidence that activation in the DLPFC affects delay discounting comes from a neurostimulation study.[149] While increased activation enhances preference for larger later rewards, decreased activation enhances preference for smaller sooner rewards.[149] Although ELA has not been specifically tied to this neural pattern of activation, behavioral evidence indicates an association between ELA and delay discounting, and we speculate that the DLPFC may be a neural pathway for this effect.

Delay discounting and health-risk behaviors

Nicotine—Extensive evidence links smoking with greater delay discounting in adolescents[150,151] and adults.[152–158] A longitudinal study tested whether delay discounting is a cause or consequence of smoking and found that baseline delay discounting increased the odds of smoking uptake, but smoking did not significantly impact delay discounting.[159] However, other studies have found that smoking is associated with increased delay discounting,[157,160,161] evidence we review later in the paper. In addition to smoking initiation, when attempting to quit smoking, delay discounting predicts poorer treatment response[162,163] and higher likelihood of relapse.[163] Smokers have the psychological as well as the neurobiological profile of greater delay discounters given that decreased activation in the DLPFC predicts increased cigarette craving[132] and heavier nicotine dependence.[164] Although causal evidence is still needed ELA may increase smoking and the severity of nicotine addiction through delay discounting.

Alcohol—People who abuse alcohol show higher rates of delay discounting compared to healthy controls.[165] Furthermore, those with alcohol abuse show neural patterns associated with delay discounting. Specifically, more severe alcohol dependence predicts lower activation of the DLPFC and higher activation of the ventromedial PFC when making impulsive reward decisions in a delayed discounting task.[166] Given the role of lower DLPFC activation on delay discounting, the fact that alcohol dependence predicts lower DLPFC activation suggests that this may reflect a predisposing neural vulnerability for alcoholism. However, given the cross-sectional design of this study, causality cannot be determined.

Food—Compared with healthy-weight women, obese women show greater delay discounting,[167] which may be driven by neural differences associated with obesity. Compared to healthy-weight controls, obese people show significantly reduced DLPFC activation in response to food cues.[168] In another study, less activation in executive function brain regions during a delay discounting task predicted greater weight gain 1–3 years later in obese women.[169] Thus, delay discounting associated with lower activation in the DLPFC may contribute to compulsive eating in obesity, but more causal evidence is still needed.

Reciprocal effects of behaviors on the brain

So far, we have discussed how ELA is associated with psychological and neurobiological vulnerabilities that increase the likelihood of smoking cigarettes, drinking alcohol, and eating high-sugar, high-fat foods. These behaviors, however, can also influence the brain. As the use of drugs and alcohol progresses from initiation to maintenance, frontostriatal reward-processing circuits are downregulated while amygdala circuits are upregulated, with these neuroadaptations of addiction primarily affecting the amygdala, striatum, and PFC.[170,171] Thus, smoking, drinking, and eating highly palatable foods affect the same brain regions that predict whether someone engages in these behaviors in the first place. Below, we discuss how smoking, drinking, and eating highly palatable food further heighten emotional reactivity, blunt reward responsivity, hinder emotion regulation, and increase delay discounting.

Emotional reactivity

Although drugs and alcohol are initially sought for their positive effects, over time, they are taken to avoid negative consequences such as withdrawal.[171,172] During abstinence, addictive substances increase emotional reactivity by recruiting an amygdala-driven anti-reward system that leads to aversive states.[171,172] Nicotine abstinence, alcohol withdrawal, and intermittent consumption of highly palatable foods induce a negative emotional state that perpetuates intense cravings.[171,173] Although withdrawal effects for nicotine and alcohol are well-studied, the negative emotional state due to restriction of highly palatable foods has not been as extensively researched, particularly in humans.[171,173] However, one study demonstrated that after switching from a high-fat to a low-fat diet, participants reported greater anger and hostility than those who continued to eat the high-fat diet.[174] Thus, intake of addictive substances leads to increased negative emotional states in the absence of the substance.

Reward responsivity

Drugs and alcohol increase feelings of reward in the short term but decrease it in the long term.[175–179] This happens because drugs stimulate reward circuitry so intensely that populations of D2Rs in the striatum downregulate, resulting in the need for higher intake to experience the same degree of reward.[72] Thus, addictive substances lead to further blunting of the reward response,[180] particularly in the VS. Nicotine withdrawal is associated with decreased striatal dopamine release[181] and blunted reward responsivity, which predicts an increased likelihood of relapse.[176] Eating highly palatable foods predicts blunted reward responsivity as well. In rodents, regular intake of high-fat and high-sugar foods leads to

downregulation of postsynaptic D2 receptors.[177–179] In humans, weight gain over a six-month period is predicted by a reduction in striatal response to palatable food consumption over this same time period.[182] This finding suggests that overeating may downregulate reward responsivity to palatable foods, inducing blunted reward responses as have been observed with other substances of abuse.[175]

Emotion regulation

Less evidence exists to suggest that smoking cigarettes, drinking alcohol, and eating highly palatable foods influence emotion regulation and the brain regions involved. Nicotine abstinence, alcohol withdrawal, and high-sugar, high-fat food restriction increase the tendency to experience negative emotions and people may attempt to regulate emotions by giving in to cravings. Using substances or food to regulate negative emotions can produce self-control failure in other domains.[183] While difficulties regulating emotions may lead people to cope by smoking, drinking, and eating, these behaviors may ultimately induce more negative emotions, further perpetuating negative coping strategies.

Delay discounting

Delay discounting is both a cause and consequence of substance use.[184,185] While higher delay discounting predicts a greater likelihood of engaging in multiple HRBs,[186] in animal models, nicotine[160] and ethanol[187] both increase delay discounting. Nicotine produces a long-lasting but eventually reversible effect on delay discounting[160] and alcohol use increases delay discounting.[187] In human studies, adolescents exposed to nicotine prenatally exhibit weaker responsivity in anticipation of reward[161] and children of smokers discount delayed rewards more than children of non-smokers.[157] Although it is difficult to know whether those exposed to nicotine are different from those not exposed in critical ways that explain this relationship, these findings provide tentative evidence that nicotine exposure may increase delay discounting. As further evidence, adult smokers discount delays at a higher rate than adolescent smokers, which might suggest that, over time, nicotine increases delay discounting,[188] especially given that this result is opposite of what might be expected based on the fact that younger people tend to exhibit higher delay discounting than older people.[189]

While few meta-analyses have been conducted, one meta-analysis on the relationship between delay discounting and addictive behaviors found an overall medium effect size with acceptable heterogeneity between studies.[190] Another meta-analysis showed that greater delay discounting is associated with more severe addictive behaviors, with comparable effect sizes found across different types of addictive behaviors.[191] Furthermore, evidence across studies suggests that delay discounting predisposes people to addictions rather than the reverse causal direction.[190] Finally, in a meta-analysis on inhibitory control and obesity, inhibitory control is significantly impaired in obese adults and children and lower PFC activity is associated with poorer inhibitory control as well as higher BMIs.[192] Thus, although delay discounting is a stronger predictor of HRBs, it is also an outcome and future research should focus on understanding this reciprocal relationship.

In sum, the psychological and neural causes and consequences of smoking cigarettes, drinking alcohol, and eating high-sugar, high-fat foods have substantial overlap and these behaviors affect the brain in ways that reinforce alcohol and drug abuse and further explain the clustering of HRBs. In fact, cross-sensitization—whereby one addictive substance leads to taking another—occurs for these behaviors. For example, in rats, access to sugar followed by forced abstinence enhances alcohol intake,[193] suggesting that sugar consumption could be a gateway to alcohol use. Thus, the common psychological and neurobiological mechanisms underlying HRBs as well as the effect of these behaviors on emotional reactivity, reward responsivity, emotion regulation, and delay discounting likely explain clustering of HRBs.

Discussion

ELA is associated with higher risk for a range of chronic disease and an increased likelihood of smoking cigarettes, drinking alcohol, and eating high-sugar, high-fat foods, leading to obesity. We present a model arguing that neurodevelopmental mechanisms involving heightened emotional reactivity, blunted reward responsivity, poor emotion regulation, and increased delay discounting are key pathways that explain the greater tendency to engage in HRBs and, ultimately, increased risk of chronic diseases associated with ELA. We focus on three HRBs that share underlying neurobiological mechanisms,[194] although, other HRBs associated with ELA are worth noting, such as risky sexual behavior[195] as well as sleep difficulties,[196] which may further increase the burden of chronic diseases. Furthermore, due to parallels with addiction, we have focused on eating high sugar and high fat foods as well as excessive food consumption as a pathway to obesity, however, ELA has also been associated with physical inactivity, which likely also contributes to the link between ELA and obesity.[32]

We have focused on how psychological, behavioral, and neurobiological adaptations to ELA confer vulnerability across a broad range of HRBs. The reason for the broad focus is to emphasize the shared mechanisms underlying these HRBs. In this way, emotional reactivity, reward responsivity, emotion regulation, and delay discounting can be considered trans-disease processes,[197] which help explain the clustering of HRBs within individuals. These psychological and neurobiological processes underlie each phase of the progression to addiction—initiation, maintenance, and relapse. Furthermore, nicotine, alcohol, and highly palatable foods themselves lead to further psychological and neural changes that intensify vulnerability to addiction, resulting in a positive feedback loop.

Previous reviews have considered how low SES affects health behaviors through psychological mechanisms,[147] how ELA affects health and health behaviors through neuroimmune processes,[20] and how lower SES affects health through neurobiological pathways.[198] However, our paper takes a broader approach than previous reviews, focusing on how multiple forms of ELA might influence HRBs that are involved in the etiology of a wide range of chronic diseases through a set of interrelated psychological and neurobiological processes that are strongly influenced by exposure to adversity in childhood. We situate these psychological and neurobiological changes within an evolutionary framework. In doing so, we consider how adverse early life environments influence brain

and behavioral development in ways that are adaptive in the short term by promoting survival but are maladaptive in the long term to physical health.

Given that the evidence we present in this paper is largely based on observational studies and cross-sectional or short-term longitudinal designs, longitudinal studies that track participants from childhood into adulthood are needed to provide stronger evidence for the proposed mechanisms, and experimental studies are needed in order to establish causal relationships. In particular, causal evidence is still lacking for the psychological and neurobiological mechanisms underlying HRBs. While the evidence is compelling that ELA influences brain development in ways that predispose people to engage in HRBs, an alternative pathway by which early life environments may influence HRBs is through modeling of parent HRBs and adopting the social norms of the broader community. Parental smoking,[199] drinking,[200] and obesity[201] predict the smoking, drinking, and obesity of their offspring. Therefore, HRBs may be transmitted intergenerationally through modeling of parent behavior. It is well-established that the constraints of low SES make it difficult to afford a high-quality diet, and that people growing up in households with low SES are more likely to eat a diet high in sugar and fat.[202] Therefore, children exposed to ELA may also have parents and communities who are more likely to engage in HRBs. Although this pathway is not mutually exclusive from the pathways in our conceptual model given that the social norms in adverse environments may be different for the reasons that we propose, it is important to consider this alternative pathway as it may be confounded with the proposed pathways. In order to control for potential confounds that are present in human studies, future studies should use experimental models to test whether our proposed psychological and neural mechanisms explain the relationship between ELA and HRBs.

Given that some of the links in our conceptual model are still tentative, the model should be considered a theoretical perspective from which hypotheses can be generated and tested. We hope that our conceptual model advances the literature by providing an organizing framework for how ELA may affect health-risk behaviors. Furthermore, because the relationships between neural circuitry and HRBs are almost certainly bidirectional, more research is needed to determine which direction is stronger. Until further research is conducted, it remains possible that the reverse causal direction (i.e. that HRBs alter neural circuitry) is stronger than the direction on which our paper focuses. Given the lack of studies as well as meta-analyses, for now, the consistency of findings, moderators of effects, and overall effect sizes remain largely unknown, highlighting a need for more quantitative assessments of the link between psychological factors, neurobiological circuits, and HRBs. Furthermore, those exposed to ELA may initiate smoking and drinking at a younger age during critical neurodevelopmental periods that may increase the likelihood of addiction in adulthood[203,204] or lead to more severe addictions in adulthood.[205] More research is needed to understand how and why ELA may lead to earlier initiation of smoking and drinking and how this might affect the brain in ways that lead to more intractable addictions.

Some researchers contend that initiation of substance use is more associated with vulnerability factors (i.e. psychopathology, SES, stressful life events) and that transition to addiction is more associated with neurobiological factors.[206] However, in this paper, we argue that environmental risk factors (i.e., ELA) directly influence neurobiological

development in ways that contribute to HRBs. In line with others who have called for a need to focus on the social and environmental context leading to substance abuse,[207] we argue that a neuroscience perspective on the link between ELA and HRBs suggests that this is a social justice issue: under this perspective, engaging in HRBs becomes not a question of choice, but a question of development. Vulnerable people do not simply "choose" to engage in HRBs because they do not know that these behaviors are harmful, but rather, their early environmental experiences influence psychological and neurobiological development in ways that make it more difficult to regulate negative emotions and delay immediate rewards. These psychological and neurobiological vulnerabilities explain why intractable cases of addiction remain even as policy changes have been implemented and social norms have shifted. Thus, chronic disease prevention should focus not only on HRBs, but also on which populations are most vulnerable to engaging in these behaviors due to environmental, psychological, and neurobiological vulnerabilities. Furthermore, future research should focus on how to mitigate neurobiological vulnerabilities in cases of smoking, heavy alcohol use, and excessive food intake that cannot be remedied with existing methods and treatments.

Our conceptual model fits well within the purview of health neuroscience, a new field that aims to understand how the brain affects and is affected by physical health.[208] Health neuroscience merges well-studied top-down processes (e.g. how the brain affects behavior) with less researched bottom-up processes (e.g. how behavior affects the brain). Given the interest of health neuroscience in explaining health with bidirectional brain-behavior relationships, our conceptual model advances the field by providing a framework for how early environmental experiences shape psychological and neurobiological factors that influence and are affected by HRBs. These bidirectional relationships facilitate a positive feedback loop in which preexisting vulnerabilities are intensified by nicotine and alcohol use as well as excessive food intake.

Future directions

A critical next step for research on adversity is to determine whether sensitive periods exist when exposure to adversity is more strongly related to certain psychological or neurobiological processes when it is experienced during a particular developmental period. Sensitive periods are challenging to study because they require precise information about the timing of exposure to adversity. In retrospective studies, obtaining accurate information on the timing of exposure is difficult and these reports are associated with substantial recall biases.[209] As a result, most research on ELA does not even report the age of exposure for their sample. Most of what we know about sensitive periods comes from studies of children who have grown up in institutional settings since it is straightforward to determine the precise period of time during which a child lived in the institution. Studies of institutional rearing have identified sensitive periods in the first two years of life for the development of a secure attachment relationship to a caregiver[210] and for the development of the hypothalamic–pituitary–adrenal (HPA) axis.[66] However, research on sensitive periods of emotional and social development remains in its infancy, and sensitive periods for the psychological and neurobiological processes that are the focus of our review are largely unknown. Future research should identify sensitive periods for which exposure to adversity

has the greatest impact on the psychological and neurobiological mechanisms that are the focus of our conceptual model.

Furthermore, future research should examine whether different types of adversities have differential influences on HRBs and the psychological and neurobiological processes that mediate these associations. Evidence is accumulating that different types of adversities have at least partially distinct associations with brain development. Threat and deprivation are two dimensions of ELA that provide a framework for conceptualizing the neural impact of these experiences.[17,18] While both types of experiences appear to influence the salience of negative emotional cues (e.g., heightened amygdala reactivity, fronto–amygdala connectivity),[63,66,211] distinct patterns of neural development have been associated with threat and deprivation in the domains of reward processing in the frontostriatal network and cognitive control in the frontoparietal network,[75,76,112] and threat is uniquely associated with some aspects of threat-related information processing and neural correlates.[81,83,212,213] Although threat and deprivation may influence neural development in different ways, they still may lead to the same downstream health outcomes. For example, high amygdala reactivity paired with low VS reactivity comprises a distinct neural phenotype of alcohol use disorders, in which alcohol use is particularly likely following exposure to stress.[214] Experiences of deprivation may be more likely to lead to blunted VS reactivity to reward than experiences of threat,[112] while both types of ELA can produce a pattern of heightened amygdala reactivity to threat.[63,86,94,95] Both threat and deprivation exposures could disrupt the balance between amygdala and VS activation, leading to the high amygdala–low VS phenotype associated with increased risk of using alcohol to cope with negative emotions.[214] Future research should consider the ways in which different types of early life adversities affect the brain in ways that confer general versus unique vulnerabilities to HRBs.

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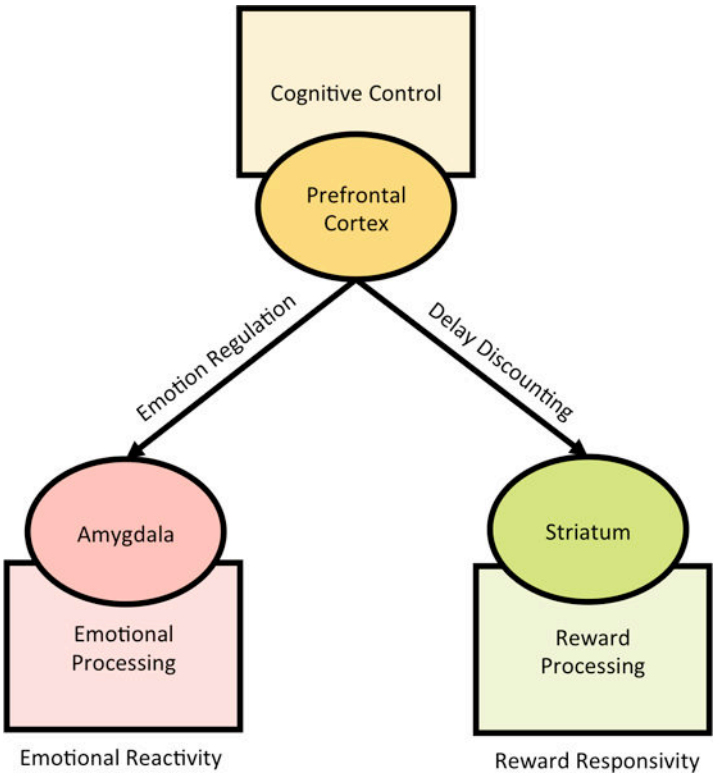

Figure 1.

Conceptual diagram of the psychological processes affected by early life adversity and their underlying neural substrates. We highlight the role of the amygdala in emotional reactivity, the ventral and dorsal striatum in reward responsivity, prefrontal–amygdala connectivity in emotion regulation, and prefrontal–ventral striatum connectivity in delay discounting.

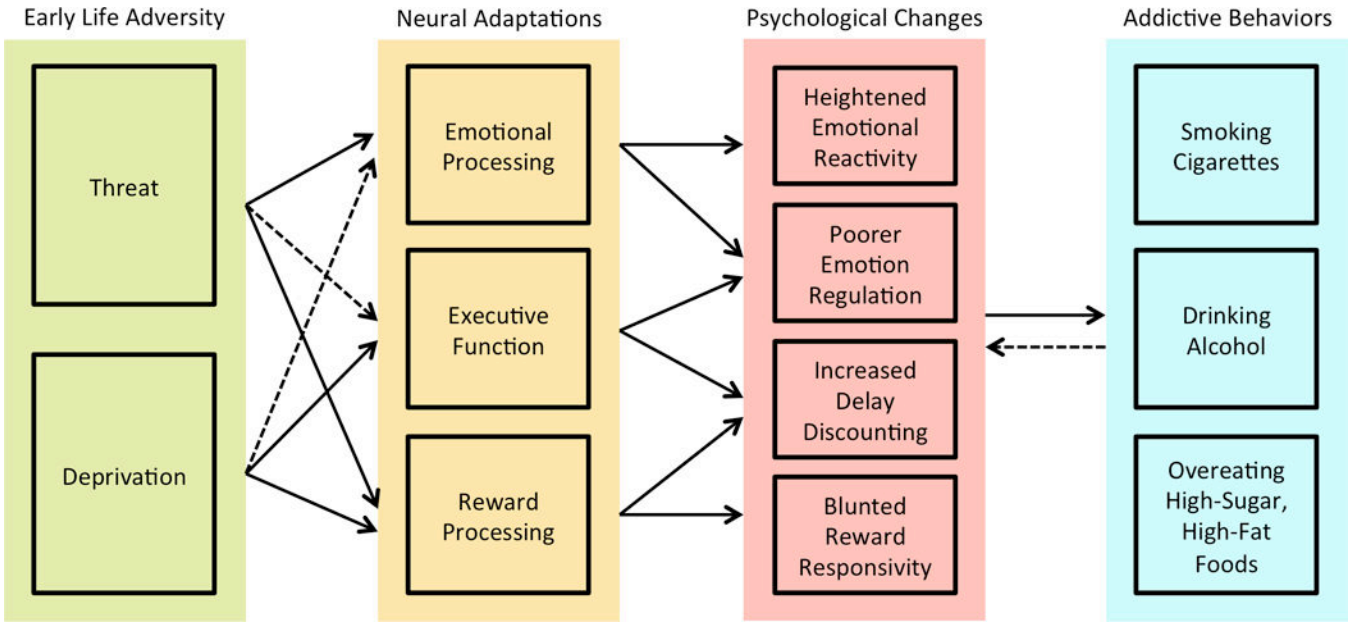

Figure 2.

The effect of two dimensions of early life adversity (ELA)—threat and deprivation—on brain development. Neural adaptations to ELA affect emotion, reward, and cognitive networks. These neural adaptations affect four psychological processes that have downstream consequences for health-risk behaviors. Smoking cigarettes, drinking alcohol, and overeating highly palatable foods further heighten emotional reactivity, hinder emotion regulation, increase delay discounting, and blunt reward responsivity, leading to a positive feedback loop for addictive behaviors.