

Claremont Colleges

Scholarship @ Claremont

Scripps Senior Theses

Scripps Student Scholarship

2022

Stress and the City: The Impacts of City Living and Urbanization on Mental Health

Natalie Akins

Follow this and additional works at: https://scholarship.claremont.edu/scripps_theses



Part of the [Behavioral Neurobiology Commons](#)

Recommended Citation

Akins, Natalie, "Stress and the City: The Impacts of City Living and Urbanization on Mental Health" (2022).
Scripps Senior Theses. 1892.

https://scholarship.claremont.edu/scripps_theses/1892

This Open Access Senior Thesis is brought to you for free and open access by the Scripps Student Scholarship at Scholarship @ Claremont. It has been accepted for inclusion in Scripps Senior Theses by an authorized administrator of Scholarship @ Claremont. For more information, please contact scholarship@cuc.claremont.edu.

Stress and the City: The Impacts of City Living and Urbanization on Mental Health

A Thesis Presented

by

Natalie A. Akins

To the Keck Science Department

of

Scripps, Pitzer, and Claremont McKenna Colleges

In Partial Fulfillment of

The Degree of Bachelor of Arts

Senior Thesis in Neuroscience

Spring 2022

TABLE OF CONTENTS

Abstract	3
Acknowledgments	4
Introduction	5
Exposure to Stress and Implication for City Living	6
The Neurobiological Mechanisms of Stress	6
Stress and Urban Living	12
Stress and Mental Illness	15
Stress and Depression	17
Stress, Schizophrenia, and Other Psychoses	20
Urban Mental Health: A Public Health Perspective	23
Urbanization and its Implications	23
Initiatives in Urban Mental Health	26
Urban Planning and City Design	26
Addressing Homelessness	28
Access to Green Space	31
Summary and Looking Forward	34
References	36

ABSTRACT

Urbanization is causing a demographic and cultural shift to the landscape of cities across the globe. Although urban living can be advantageous for both individual and societal growth, it can negatively affect mental health and wellbeing. Individuals living in urban environments have an increased risk for mental disorders like depression and schizophrenia. Certain challenges common in urban environments and associated with increased stress, may be causing the increase with mental illness. Chronic stress and the subsequent hyperactivation of the hypothalamic-pituitary-adrenal axis and sustained synthesis of glucocorticoids is detrimental to metabolic, endocrine, and immunologic processes. The overexposure to glucocorticoids can lead to pathological states like depression and increases in dopaminergic circuits common in schizophrenia. As urbanization continues to increase worldwide, how does the prolonged stress of urban living impact the brain and increase the risk of psychiatric disorders? Solutions to reduce stress like proper urban planning and design that implements green space and addresses chronic homelessness can be beneficial for improving and sustaining better mental health.

ACKNOWLEDGEMENTS

I would like to thank my family, friends, and professors for all the support and encouragement throughout the thesis process and my time at Scripps. Thank you to Scripps College and the Keck Science Department of the Claremont Colleges for providing me with the tools and education that inspired my thesis. I also would like to thank my two readers Professor Melissa Coleman, for the insight and guidance that helped me throughout my research process, and Professor Brian Duisternars, for inspiring me to learn more about neurological disorders and the factors that influence their onset in class. Thank you to my advisor Professor Tessa Soloman-Lane for the continued support and motivation throughout my academic years at Scripps. Lastly, I would like to thank my friends and family for their constant encouragement and inspiration, without them this accomplishment would not be possible. I want to give a special thank you to my parents who always cheered me on and helped me get to where I am today. I also want to thank all of my friends, especially Talia Perluss and Tess Anderson, who provided me with endless support and let me ramble about my thesis to formulate my thoughts. I love you all and thank you for everything.

INTRODUCTION

Mental disorders are characterized by a combination of abnormal thoughts, perceptions, emotions, behavior, and relationships. There are many different mental disorders with different symptomology and presentations (WHO, 2019; James et al., 2018). In middle to high income countries, mental illness is the leading cause for disability. The burden of mental health contributes to high costs to society, long lasting disability, increased mortality, and overall human suffering (Lavikainen et al., 2000; Wang et al., 2007). Globally 264 million people are estimated to be affected by depression, while schizophrenia and other psychoses affect an estimated 20 million people (WHO, 2019). Since the 18th century, scholars have discussed whether the noisy and bustling environments of cities are connected to the prevalence of mental illness (Okkels et al., 2018). With the majority of the world's population living within cities or towns, it is important to consider the impacts urbanization has on mental health and city residents. Meta analyses have indicated that current city residents in comparison to rural residents, have a 21% increased risk for anxiety disorders, 39% increased risk for mood disorders, and incidences of schizophrenia have doubled for people born and raised in cities, with an overall prevalence of all psychiatric disorders increasing by 38% (Lederbogen et al., 2011; Lederbogen et al., 2013). Although stress is fundamental for survival, chronic stress is a major risk factor for several neuropsychiatric disorders including depression, anxiety, and schizophrenia (Gody et. al, 2018). As urbanization continues to increase worldwide, how does the prolonged stress of urban living impact the brain and increase the risk of psychiatric disorders?

EXPOSURE TO STRESS AND IMPLICATIONS FOR CITY LIVING

The Neurobiological Mechanisms of Stress

Stress is a commonly used term, typically understood as feeling overwhelmed or being unable to cope with mental or emotional pressure (Mental Health Foundation, 2021). It is the body's natural response to a perceived threat and has evolutionarily helped animals respond to threats by running, hunting, or fighting (Abott, 2012). The response to stressful stimuli is triggered by the stress system, which involves many brain structures in order to detect whether stressors are real or potential threats. Key regions that integrate stress signals in situations of real or perceived threat include the paraventricular nucleus of the hypothalamus, amygdala, and several brainstem nuclei including the locus coeruleus noradrenergic system (Floriou-Servou et al., 2021). The amygdala plays a key role in emotional learning, reward processing, decision making, and specific stress related behaviors like fear responses (Ulrich-Lai and Herman, 2009). The hippocampus plays a major role in spatial relationships, and learning and memory. It has been one of the most extensively studied brain structures because of its major role in several neuropsychiatric disorders (Anand and Dhikav, 2012). Lastly, the locus coeruleus noradrenergic system plays a major role in arousal, attention, and the stress response. It contributes to long-term synaptic plasticity, pain modulation, motor control, energy homeostasis, and control of local blood flow (Benarroch, 2009).

The perception of real or potential threats leads to the release of mediating molecules like neuromodulators, neuropeptides, and hormones to restore homeostasis and promote adaptation through the stress response (Floriou-Servou et al., 2021; Godoy et al., 2018). There are two types of stressors that activate the stress response, physical and psychological. Physical stressors like chronic illness or pain put strain on the body, while psychological stressors like emotional or

mental distress are considered negative or threatening experiences (Centre for Studies on Human Stress, 2019). When the brain detects a threat, the physiological response activates the autonomic, neuroendocrine, metabolic, and immune systems (Lupien et al., 2009; **Figure 1**).

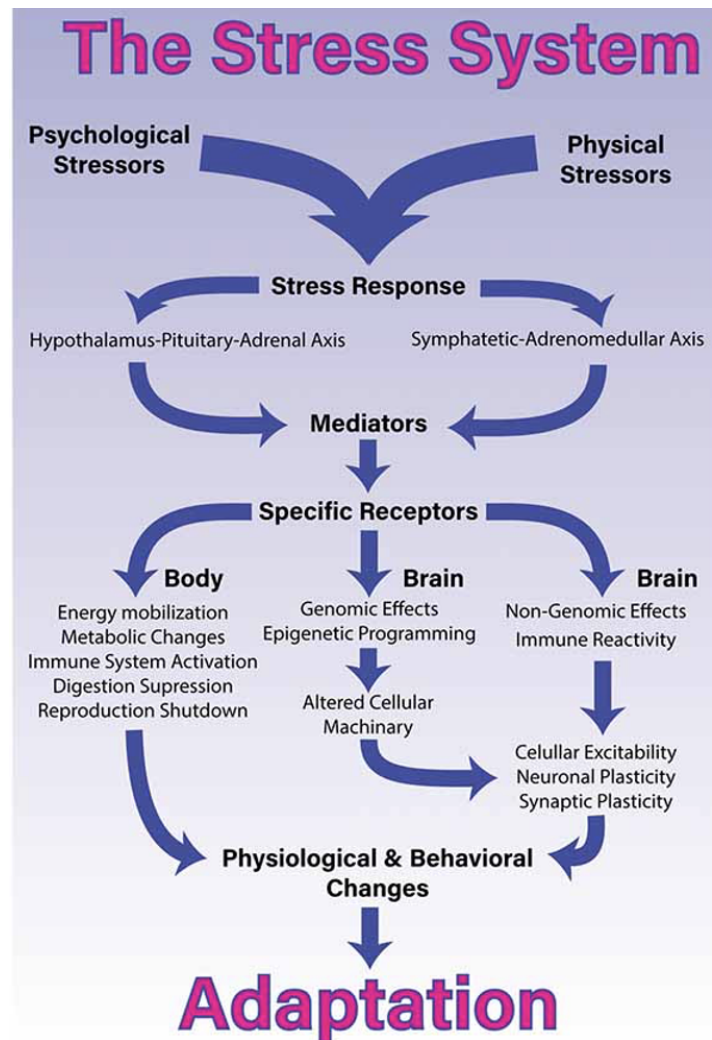


Figure 1. The Stress System (Godoy et al., 2018). The response to stressful stimuli activates two major pathways of the stress system and its release of mediating molecules. The sympathetic-adrenomedullary axis secretes noradrenaline and norepinephrine and the hypothalamus-pituitary-adrenal axis secretes glucocorticoids. In the body, the stress response promotes physical changes while genomic, epigenetic, and non-genomic effects induce short and long term effects in the brain. The mechanisms employed by the stress system mediate changes in physiology and behavior that ultimately enable adaptation and survival.

The stress response occurring as a reaction to psychological or physical stressors have distinct neural networks and cellular activity. Physical stressors, mainly processed in the

brainstem and hypothalamic regions, trigger an automatic stress response because they usually require an immediate reaction. Conversely, psychological stressors tend to cause both a physical and cognitive stress response. Initiation of the stress response activates the sympatho-adreno-medullary (SAM) system and the hypothalamic-pituitary-adrenal axis (HPA; **Figure 2**).

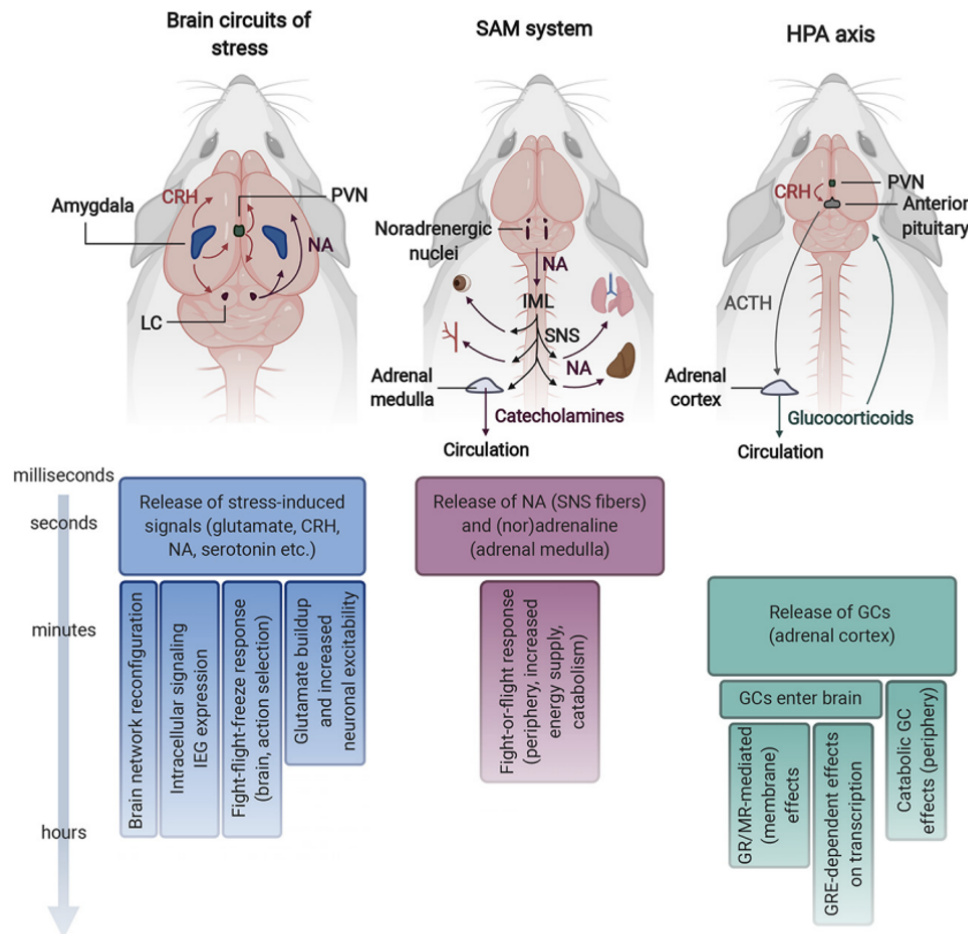


Figure 2. The three parallel stress systems (Floriou-Servou et al., 2021). Exposure to stress activates neurons mainly located in the hypothalamus, amygdala, and brainstem, which process the information and carry out the stress response. The release of stress induced signals reconfigures brain connectivity and activates the SAM system and HPA axis. The SAM and HPA axis act in conjunction to mobilize the body's energy sources in order to respond to stressors.

Short term responses are produced by the SAM axis, which causes the characteristic effects of the fight or flight response (Floriou-Servou et al., 2021). The SAM axis activates the

intermediolateral nucleus (IML), a group of preganglionic neurons in the gray matter of the spinal cord. The IML projects into cells in the adrenal medulla, triggering the release of adrenaline and norepinephrine into the bloodstream (Flourio-Servou et al., 2021; **Figure 2**). The molecules then bind to the adrenergic G protein coupled receptors and result in increased alertness, glucose production, and other physiological changes in blood vessels, glands, tissues, visceral organs, and smooth muscles (Godoy et al., 2018; Murison, 2016). At the same time, release of corticotropin-releasing hormone (CRH) from the hypothalamic paraventricular nucleus (PVN) activates the HPA axis (Flourio-Servou et al., 2021; **Figure 2**).

Long term stress is regulated by the HPA axis, which secretes glucocorticoids, mainly cortisol in humans, from the adrenal cortex after activation by the PVN (Godoy et al., 2018). The release of CRH and arginine vasopressin (AVP) acts on the anterior pituitary gland, enabling the secretion of adrenocorticotrophic hormone (ACTH), which triggers the production of glucocorticoids and release of the catecholamines adrenaline and noradrenaline from the adrenal cortex into the bloodstream (**Figure 3**). While catecholamines cannot cross the blood-brain barrier, glucocorticoids can enter the brain and affect multiple brain functions including neuron survival, neurogenesis, hippocampal size, and peripheral functions like metabolism and immunity (Flourio-Servou et al., 2021; Yang et al., 2015). Receptors for glucocorticoids are expressed throughout the brain, meaning abnormalities can have potentially long-lasting effects on the functioning of the nervous system (Lupien et al., 2009).

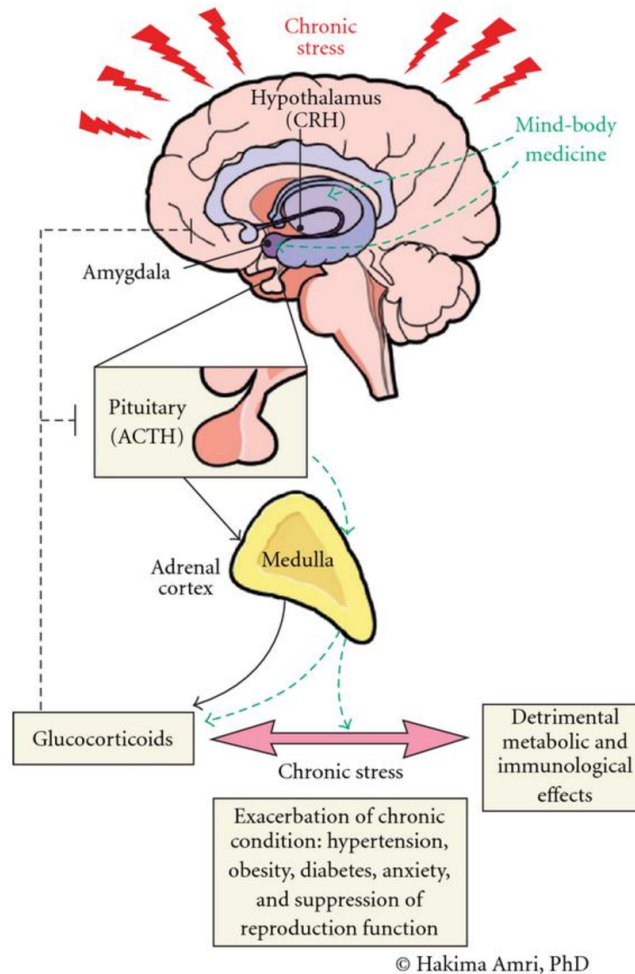


Figure 3. Schematic representation of HPA axis response to chronic stress. Chronic stress triggers the release of CRH and other hormones from the hypothalamus, which causes ACTH secretion from the pituitary gland. ACTH triggers the release of glucocorticoids from the adrenal cortex. In acute stress, glucocorticoids regulate CRH and ACTH release through a negative feedback loop. However, during chronic stress, increased cortisol levels weaken negative feedback signals and the sustained glucocorticoid synthesis becomes detrimental to bodily processes.

Both the SAM and HPA stress responses work to regulate homeostatic conditions by releasing hormones to induce physiological and behavioral changes. Following stress activation and the succeeding diffusion of the perceived stressor, negative feedback loops are triggered from the adrenal gland, hypothalamus, hippocampus, and frontal cortex, to shut down the SAM and HPA axis and return to a set homeostatic state (Lupien et al., 2009). The optimal response to a stressor is rapid activation followed by rapid deactivation once the threat is no longer present

(Murison, 2016). Although stress is a necessary response for survival, problems arise when the stress response is continually active. Sustained long term activation of the stress response system, known as chronic stress, overexposes the body to cortisol and other stress hormones, disrupting the body's functions (**Figure 3**). Chronic stress can also lead to brain mass atrophy and decreases in brain weight, which in turn causes changes in the stress response, cognition, and memory (Yaribeygi et al., 2017). The volume and intensity of these structural changes are influenced by the level and duration of exposure to stress.

Although the interaction between stress and the CNS has been shown to cause structural changes in the brain, with long term effects on the nervous system, the role stress plays in mental disorders is not as well known. The relationship between stress and mental illness is complex because the susceptibility to stress varies from person to person (Salleh, 2008). However there is evidence that prolonged exposure to stress can increase the risk of psychiatric disease and contribute to its onset, especially in individuals who are predisposed or still developing (Paykel, 1978; Abott, 2012). For children living in urban environments, the prolonged stress of urban living can be detrimental to their development. Numerous animal and human studies have shown that children are particularly sensitive to stress as they undergo important age-related changes. During the prenatal period, exposure to stress affects the development of brain regions that help regulate the HPA axis including the hippocampus, prefrontal cortex, and amygdala (Lupien et al., 2009). Exposure to prenatal and early life stress has long lasting effects on the HPA axis, the brain, and adult behavior. Learning impairments, enhanced sensitivity to drugs of abuse, and increased anxiety and depression related behaviors are all effects of increased stress on hippocampal functions and increases in CRH in the amygdala (Lupien et al., 2009). Prenatal

glucocorticoid exposure also affects the developing dopaminergic system, which is involved in reward or drug seeking behavior, as well as schizophrenic symptomatology (Lupien et al., 2009).

Stress and Urban Living

Living in an urban environment has been repeatedly established as a risk factor for developing psychiatric disorders and to the increase in incidences of schizophrenia (Kelly et al., 2010). Urban living is associated with chronic stress from more demanding and stressful social environments, environmental stressors like overcrowding, and greater social disparities (Lederbogen et al., 2011). Longitudinal studies even suggest a causal relationship between the effects of urban environments on mental health, not one mediated by other epidemiological variables (Yates, 2011). The stimulation, deprivation, and discrepancy (SDD) model accounts for the structural characteristics of urban environments that are likely to contribute to chronic stress (**Figure 5**). Environmental stressors associated with city living like “street exposure” to busy, noisy urban environments, high population density, crime exposure, and victimization can be attributed with increased risk for psychiatric disorders (Freeman et al., 2014; Kirkbride et al., 2012; Newbury et al., 2017). It is important to note that structural stressors overlap frequently rather than appearing as isolated incidences.

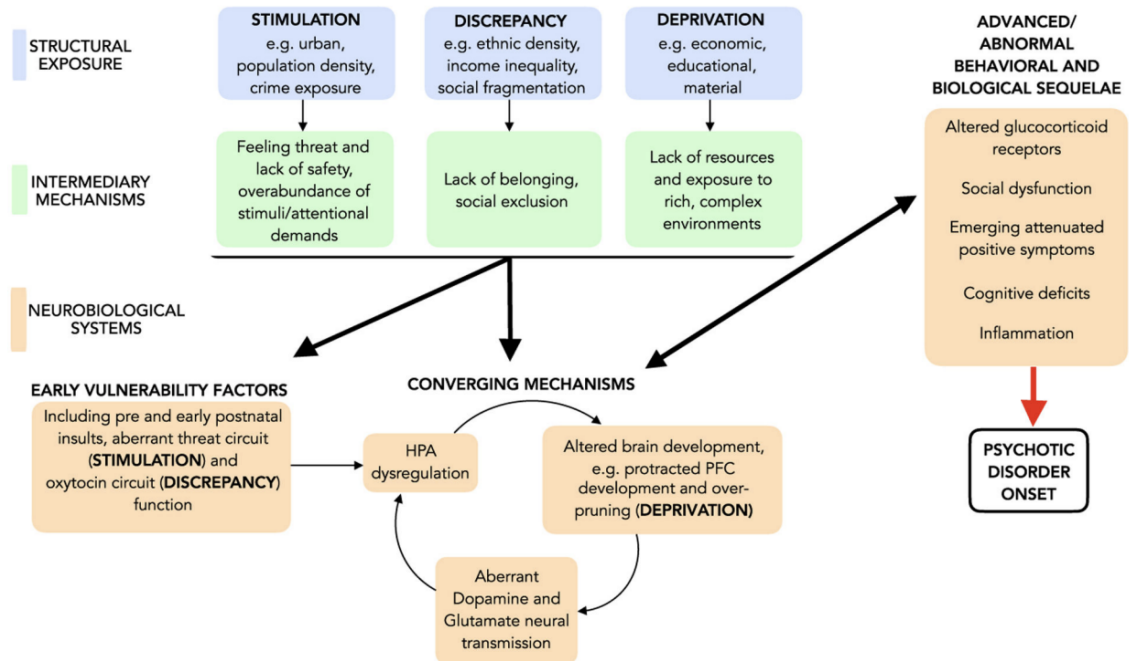


Figure 5. The stimulation, deprivation, and discrepancy (SDD) model with structural exposures, intermediary mechanisms, and biological mechanisms in relation to psychotic disorder onset (Vargas et al., 2020). Partially inspired by the diathesis-stress model of psychosis, the SDD model highlights the importance of considering chronic stress exposure at a systems level and assessing for pre-existing biological vulnerabilities.

Stimulation

Stimulation describes environments that activate neural threat systems and present feelings of lack of safety and an excess to sensory inputs (Vargas et al., 2020). Chronic exposure to environments that evoke feelings of threat and lack of safety affect the structure, function, and connectivity of the threat circuit including the amygdala, hippocampus, and ventromedial prefrontal cortex (McLaughlin et al., 2014). During critical periods of development, continuous exposure to these stressors can negatively impact neural circuitry related to fear conditioning, threat detection, identification, and learned fear (McLaughlin et al., 2014; Johansen et al., 2011). Additionally, the chronic exposure to highly stimulated and populated urban environments may impact fear learning, resulting in hypervigilance, a lower threshold for experiencing fear, and eventually abnormal amygdala function (van Marle et al., 2009). Increased amygdala activity has

been found in those living in urban environments, and hyperactivity of the perigenual anterior cingulate cortex responsible for regulating the amygdala, has been linked to urban upbringing (Lederbogen et al., 2011).

Discrepancy

Discrepancy describes environments that foster a sense of social exclusion, isolation, or lack of belonging (Vargas et al., 2020). Social, political, and economic structural factors have contributed to racial, ethnic, and class division, as well as social and economic disadvantage (Hutson et al., 2012). Studies have found associations between psychosis incidence and income inequality, ethnic density, and social fragmentation. Rapid urbanization caused by violence and forced displacement have contributed to growing income disparity, isolation, poverty, and discrimination, as people migrate to cities for better opportunities and to start new lives (López-Jaramillo et al., 2017; Robertson and Szabo, 2017). Income inequality represents the variation in income distribution within a neighborhood with high income inequality meaning heterogeneity across incomes, and low income inequality having a relatively homogenous income distribution (Vargas et al., 2020). Ethnic density is defined as the similarity in ethnic background with higher ethnic density entailing more individuals sharing a similar ethnic background, and low ethnic density meaning a low proportion of individuals share an ethnic background. In immigrant groups, research has shown that living in lower ethnic density neighborhoods accounts for an increase in psychosis incidence (Schofield et al., 2017; Vargas et al., 2020). Lastly, social fragmentation leads to experiences of social isolation, resulting in feelings of lack of trust and belonging, along with reduced social support (Eliacin, 2013). Social fragmentation is characterized by the stability and structure of one's social environment. It can be operationalized by proportion of rented housing, frequency of change to living arrangements,

proportion of single and divorced individuals, as well as shared neighborhood values, trust, and stable relationships between neighbors. Studies have found higher social fragmentation is associated with higher rates of psychosis (Allardyce et al., 2005).

Deprivation

Deprivation is defined as environments that have a lack of the necessary stimuli for brain health and normative maturation including lack of resources with regards to employment, income, education, health, living conditions, and barriers to housing and services (Vargas et al., 2020). While exposure to resource lacking environments has been associated with many negative health outcomes, high deprivation has been specifically linked to increased risk for developing a psychotic disorder (Kirkbride et al., 2012). Ultimately, the structural exposures of stimulation, deprivation, and discrepancy, along with neural underpinnings, and intermediary mechanisms are all associated with increased psychotic disorder incidence (**Figure 5**). Chronic structural exposures can cause the previously mentioned HPA dysregulation, abnormal dopamine and glutamate transmission, inflammation, and altered brain functioning, development, and other factors associated with the onset of psychotic symptoms (Vargas et al., 2020).

Stress and Mental Illness

Urban living is linked to increased vulnerability to mental illness through long term activation of the stress response (**Figure 6**). Abnormal glucocorticoid synthesis overexposes the body to cortisol and other hormones that disrupt bodily functions and cause changes in the brain structure and function. Decreased hippocampal volume, increased amygdala activity, and hyperactivity in the perigenual anterior cingulate cortex (pACC) are some characteristics

associated with chronic stress and pathological states like depression and psychosis (Lederbogen et al., 2011; Anand and Dhikav, 2012).

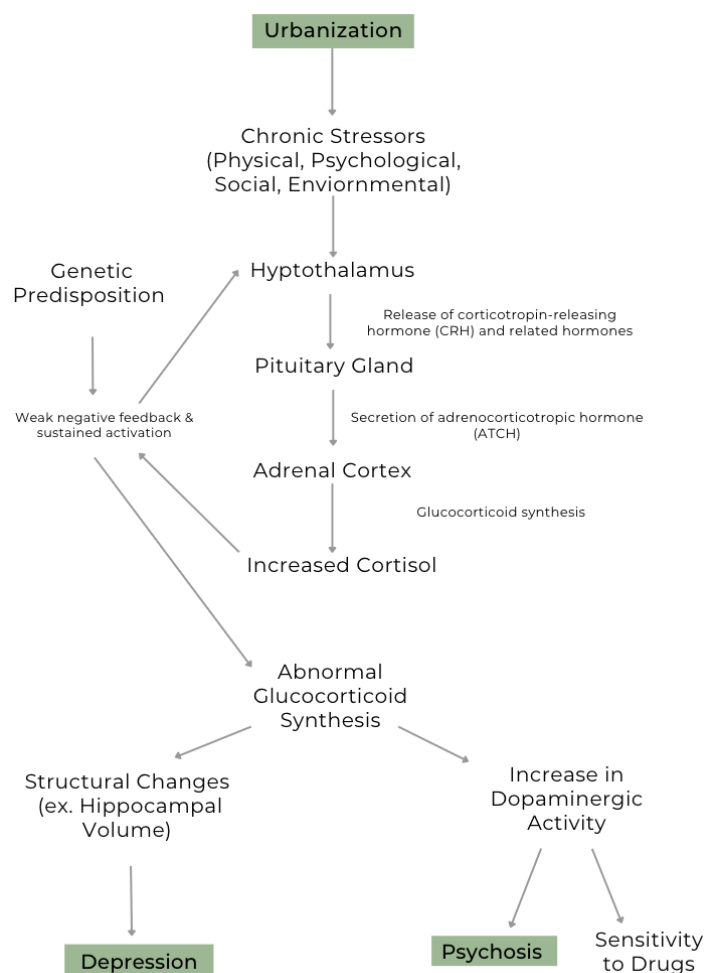


Figure 6. Diagram illustrating the pathway linking urbanization to vulnerability of psychiatric conditions like depression and psychosis. Urban living exposes one to chronic physical, psychological, social, and environmental stressors that trigger the stress response. Overexposure to glucocorticoids is considered the main reason for pathological states like depression and psychosis as well as increased sensitivity to drugs.

Living in urban environments and urban upbringing causes increased amygdala activity from social stress and hyperactivity of the pACC (Lederbogen et al., 2011). The pACC is a major part of the limbic stress regulation system and exhibits high neuronal glucocorticoid receptor expression, modulates HPA axis activation during stress, and is connected in chronic social stressors like social defeat (Lederbogen et al., 2011). Although the effects of urban living on the

pACC and amygdala are different, these two structures are closely linked in function and important to the stress response and related disorders. The amygdala is implicated in anxiety and depression, while the pACC is linked to schizophrenia (Yates, 2011). Numerous studies also link the hippocampus with several neuropsychiatric disorders and inhibition of the HPA axis (Anand and Dhikav, 2012). The hippocampus is one of the most extensively studied regions of the brain because it is the earliest and most severely affected structure in several neuropsychiatric disorders like anxiety, depression, and psychosis (Dhikav and Anand, 2011). It is particularly vulnerable to stress and chronic stress has been reported to alter hippocampal networks (Dhikav and Anand, 2011). Thus, stress has a major effect on numerous structures in the brain which not only play an important role in the stress system, but also the onset of psychiatric disorders.

Stress and Depression

Major Depressive Disorder (MDD) is one of the most common mental disorders with symptoms that negatively affect how one feels, thinks, and acts (National Institute for Mental Health, 2018). It affects 1 in 15 adults, and 1 in 6 people are estimated to experience depression at some point in their life. Depression causes feelings of sadness, loss of interest, motivation, and a variety of other emotional and physical problems that decrease one's ability to function (National Institute for Mental Health, 2018). Symptom severity and frequency varies individually and by stage of illness, and in order to be diagnosed, several persistent symptoms in addition to low mood are required (American Psychiatric Association, 2020). Depression can occur at any time, during a person's life, but on average appears in the late teens to mid 20s, with women more likely to experience depression than men (American Psychiatric Association, 2020). Current research suggests that the onset of depression is caused by a combination of genetic, biological, environmental, and psychological factors (National Institute for Mental

Health, 2018). Stressful life events, for example, could induce a series of psychological and physiological changes including the activation of the HPA axis and sympathetic nervous system (Yang et al., 2015).

Hyperactivity of the HPA axis is one of the most consistent neurobiological findings in depressed patients, affecting about 70% of people with depression (Yang et al., 2015). In depression, elevated concentrations of cortisol, increased activity of the adrenal gland, and changes in pituitary volume are all considered markers of both MDD and hyperactivation of the HPA axis (Yang et al., 2015; Jurena et al., 2004). Under normal conditions, glucocorticoids contribute to the termination of the stress response through feedback loops involving the hippocampus and paraventricular nucleus (**Figure 3**), but abnormalities in the feedback loop change the ability of glucocorticoids suppress CRH and ACTH secretion (Jurruena et al., 2004).

The hypersecretion of cortrophic hormone-releasing factor (CRF) plays a significant role in MDD. As HPA axis activity is regulated by secretion of CRF and vasopressin (AVP) from the hypothalamus, numerous studies provide evidence that the hypersecretion of CRF induces behavioral effects seen in depressed patients including changes in activity, appetite, and sleep (Jurruena et al., 2004). CRF is an important neuropeptide responsible for HPA alterations in depression including increased numbers of CRF expressing neurons in the hypothalamic paraventricular nucleus, increased levels of CRF in cerebrospinal fluid, and later discovery that increased concentrations of CRF in spinal fluid decreases with long term treatment from fluoxetine or amitriptyline. Additionally depressed patients who have committed suicide have been found to have a decreased number of CRF binding sites in the frontal cortex. Thus, researchers have hypothesized that stress hormone dysregulation of CRF may be a cause of depression and suggest that antidepressants can stabilize HPA dysregulation through

glucocorticoid receptors (Jurueña et al., 2004). Numerous studies in humans, animals, and cellular models have demonstrated that antidepressants increase glucocorticoid receptor expression, enhance glucocorticoid receptor function, and promote glucocorticoid receptor nuclear translocation (Jurueña et al., 2004). These changes are associated with enhanced glucocorticoid receptor mediated negative feedback by glucocorticoids and the subsequent reduction of HPA activity (Jurueña et al., 2004). Antidepressant treatment has also proven to prevent and restore hippocampal volume loss (Conrad, 2008). Reduction of hippocampal volume by 10-15% in patients with MDD is one of the most consistent neuroanatomical findings (Godoy et al., 2018; Sapolsky, 2000).

The Glucocorticoid Cascade Hypothesis and Glucocorticoid Vulnerability Hypothesis both propose that overexposure to glucocorticoids from chronic stress or genetic predisposition to HPA hyperactivity may make the hippocampus vulnerable to potential injury. The Glucocorticoid Cascade Hypothesis proposes that glucocorticoids secreted during periods of stress desensitize the hippocampus to glucocorticoid exposure by downregulating glucocorticoid receptors (Sapolsky et al., 1986; Conrad, 2008). Eventually this downregulation leads to further glucocorticoid hypersecretion until there is permanent loss of receptors in the hippocampus and a feed forward cycle of elevated glucocorticoid and hippocampal damage is created (Conrad, 2008). This hypothesis describes the mechanism underlying the shift from reversible glucocorticoid receptor downregulation to permanent cell death in the hippocampus (Sapolsky, 1992; Sapolsky et al., 1986). However, the Glucocorticoid Cascade Hypothesis has conflicting findings on how prolonged glucocorticoid elevation permanently damages the hippocampus and if the hippocampus of rodents versus primates respond to glucocorticoids in the same way. When the Glucocorticoid Cascade Hypothesis was proposed, supporting studies were utilized in rats,

but subsequent studies using rats and other models did not consistently find hippocampal damage with prolonged glucocorticoid and stress exposure (Conrad, 2008).

The Glucocorticoid Vulnerability Hypothesis was proposed as an alternative to the Glucocorticoid Cascade Hypothesis, theorizing that glucocorticoids may not be necessary for hippocampal damage, but contribute to the hippocampus's vulnerability to damage (Conrad, 2008). In other words, a history of chronic stress makes the hippocampus more susceptible to damage, which increases vulnerability to glucocorticoids even when levels are not elevated due to stress. As a consequence, chronic stress and glucocorticoids play a critical role in priming the hippocampus to be more susceptible to damage from neurotoxic and metabolic challenges like depression (Conrad et al., 2008). The continuous exposure to glucocorticoids contributes to the reduction in hippocampal volume and vulnerability to developing stress related disorders. This then affects the function of brain areas related to emotion and reward circuitry implicated not only in depression, but also drug addiction and psychosis like schizophrenia (Yang et al., 2015; Conrad, 2008).

Stress, Schizophrenia, and Other Psychoses

Schizophrenia affects 20 million people worldwide, and typically begins in late adolescence or early adulthood. Psychoses, including schizophrenia, are characterized by distorted thinking, perceptions, emotions, language, sense of self, and behavior. Psychoses are commonly distinguished from other psychiatric disorders by hallucinations, defined as hearing, seeing, or feeling things that are not there, and delusions, which are fixed false beliefs or suspicions despite evidence they are incorrect (WHO, 2019). Risk factors for developing a psychotic disorder include genetic and biological pre-existing vulnerabilities. Additionally, psychological factors are thought to influence the onset, course, and severity of psychosis

(Phillips et al., 2007; van Winkel et al., 2008). Exposure to chronic stress is a factor in the pathogenesis of schizophrenia (Vargas et al., 2020; Holtzman et al., 2012).

The association between stress and psychosis may be a consequence of underlying vulnerability from stress sensitization. Stress sensitization refers to the increased emotional and psychotic response to stress (van Winkel et al., 2008). These increased reactions occur when previous exposures to severe or chronic stressors cause increased responses to smaller stressors in daily life. The current hypothesis surrounding the biological mechanisms involved in sensitization include involvement of the HPA axis because it mediates the stress response, and the dopamine system because it is considered important in the development of psychosis (Kapur, 2003).

There is strong evidence supporting the involvement of the HPA axis in the onset, exacerbation, and relapse of schizophrenia (van Winkel et al., 2008). Walker and Diforio's "neural diathesis-stress model" proposes that HPA axis dysfunction may activate a cascade of events that triggers dysfunctional dopaminergic neural circuitry underlying psychotic symptomatology (van Winkel et al., 2008; Holtzman et al., 2012). This model is based on the following evidence that supports the association between HPA dysregulation and psychosis (Walker and Diforio, 1997). First, patients with schizophrenia and other psychotic disorders have increased baseline levels of cortisol and ACTH, and increased cortisol response to pharmacological challenge (Venkatasubramanian et al., 2010; Holtzman et al., 2012). Second, antipsychotic medications that reduce cortisol and ACTH secretion have been shown to reduce dopamine activity and consequently psychotic symptoms, while those that increase HPA activity increase dopamine activity and psychotic symptoms (Walker et al., 2008; Venkatasubramanian et al., 2010). Third, neuroimaging studies have consistently revealed volumetric reduction in

cortical and subcortical brain regions. Reduced hippocampal volume is one of the most consistent findings in patients with schizophrenia. As seen in patients with depression, reduced hippocampal volume is an indicator of HPA axis dysfunction. Neuroimaging studies have also revealed increased volume in the pituitary gland of schizophrenic patients, which is hypothesized to also reflect HPA axis hyperactivity (Holtzman et al., 2012; van Winkel et al., 2008). Fourth, there may be a synergistic relationship between HPA axis activation and dopaminergic circuits. Evidence suggests abnormal glucocorticoid secretion may increase glutamate release and subsequent dopamine activity, especially in the mesolimbic system (Marinelli et al., 2006; van Winkel et al., 2008; Holtzman et al., 2012; Popoli et al., 2012). One PET investigation on healthy human subjects found significant release of dopamine in the ventral striatum after being exposed to psychosocial stress. The amount of dopamine released was highly correlated to the cortisol response from the task (Pruessner et al., 2004). Cortisol is known to have a facilitating effect on dopamine firing neurons by acting via glucocorticoid receptors in the ventral tegmental area (VTA) to increase dopamine neuron firing in response to glutamatergic stimulation (Cho and Little, 1999)

The sustained activation of glucocorticoid secretion from chronic stress induces changes in glutamate neurotransmission in the prefrontal cortex, amygdala, and hippocampus (Popoli et al., 2012). There is substantial evidence implicating dysfunction of the glutamate system in the pathogenesis of schizophrenia (McCutcheon et al., 2020). Glutamate influences the activity of dopaminergic cells in the VTA and enhances dopamine release in the nucleus accumbens (Tzschantke and Schmidt, 2003). Chronic stress has been associated with a loss of glutamate receptors, increased glutamate release, impaired cycling and suppression, and changes in metabolism in cortical and limbic areas, ultimately influencing cognitive and emotional

processing and behavior (Popoli et al., 2012). Thus, changes in glutamate transmission from chronic stress may also increase activity in dopamine neurons, which in turn influence psychotic symptoms (McCutcheon et al., 2020).

Dopamine dysregulation is closely linked with the positive symptoms of hallucinations and delusions, and glutamate transmission is associated with negative symptoms and cognitive dysfunction (Vargas et al., 2020). Additionally, interneurons are a key mechanism for downstream dopamine dysregulation and most vulnerable to harm from oxidative stress. They are some of the last components developed during neurodevelopment and exposure to prenatal and early life stress may lead to more interneuron loss during multiple critical periods of growth (Grace, 2016). Thus, urban upbringing and urban living are linked to increased risk of chronic dopamine dysregulation and the development of psychotic disorders (Grace, 2016).

URBAN MENTAL HEALTH: A PUBLIC HEALTH PERSPECTIVE

Urbanization and its Implications

The rapid expansion of urban environments is causing a major shift in the economy, ecology, and the health of city residents. By the year 2050, it is estimated that 69% of the global population will live in urban areas (United Nations, 2012). Urbanization is characterized by the demographic shift where people, most notably young people, migrate from rural areas to more urban areas (Okkels et al., 2018). Urban areas are distinguished by population density and physical features like limited green space, high noise levels, graffiti, increased trash, traffic, and hazardous waste sites (Weich et al., 2002). Thus, both the physical and mental health of city residents will be affected by exposure to the aforementioned physical features as well as changes in social interaction and physical activity (Lederbogen et al., 2013). Urbanization is associated with growth, socioeconomic transformation, and increased wealth, with urban environments

generally having better access to education, health care, and higher rates of employment (Dye, 2008; Lederboden et al., 2013; Okkels et al. 2017). However, the health benefits of urbanization are not uniform and may not apply for specific diseases and populations (Dye, 2008). Cities offer a wide range of opportunities but they are also places of increased access to drugs, crime, violence, poverty, homelessness, and isolation. (Lecic-Tosevski et al., 2019). Urbanization in its current form is highly unsustainable and closely related to many of the world's major problems (UN-Habitat, 2016). Cities thus pose as unique landscapes for challenges, especially psychological challenges, not found in other environments.

The challenges surrounding urbanization include rising inequalities, insecurity, and housing issues. There is an increasing number of people living in informal housing settlements or slums, which are characterized by nondurable or overcrowded housing that lack access to basic needs like water, sanitation, and security against eviction (Okkels et al., 2018). People living in poor urban areas statistically have worse mental and physical health, presenting a challenge to sustainable development and access to basic urban services. Related to mental health, informal settlements also present high levels of stress exposure from increased violence, drug trafficking, and extreme poverty (de Magalhães Narvaez et al., 2017).

Historically, urbanization has been related to positive economic development and health outcomes. It was a process that started in North America and Western Europe, but is now mainly occurring in developing nations (Lederbogen et al., 2011). Therefore it is not possible to generalize the historical experiences of North American and Western European urbanization to the current urbanization characterized by the rapid and unstructured migration of people to cities in low income countries. This migration can be attributed to mass displacement produced by the interwoven systems of globalized capitalism and imperialism that have exploited land and labor

of developing nations and contributed to increases in climate disasters (Walia, 2021). 90% of the increase in the world's urban population is expected to take place in Asia and Africa, places impacted by land dispossession from foreign investment, cash crops, mining and energy extraction, and biofuel production (Okkels et al., 2018; Walia, 2021). The financialization of land devastates local food production, impoverishes and displaces farmers, destroys social ecosystems, and erodes women's access to common land (Walia, 2021). Land dispossession is further exacerbated by climate disasters like submerging islands, desertification, raging fires, soil erosion, hurricanes, ocean acidification, pollution, and strip mining, that are resulting in the fastest growing displacement (Walia, 2021). Without proper infrastructure and governmental programs addressing public health issues, the rapid urbanization occurring from mass displacement will have increasingly negative consequences (Okkels et al., 2017).

Meta-analytic studies have repeatedly observed the association between living in urban environments and increased psychological distress, along with risk for mental illness including anxiety, depression, and psychosis (Vargas et al., 2020). A meta-analysis published in 2010 concluded that occurrence of mental illness is 38% higher in cities (Peen et al. 2010). Although living in urban vs rural environments is established as a risk factor for mental illness, epidemiological evidence is inclusive (Lecic-Tosevski, 2019). Findings have varied considerably depending on the city or country examined. Most studies on urban mental health as well as mental health research comes from high income countries. Thus, a vast majority of studies on prevalence of mental disorders are published in Europe and North America where trends indicate increased risk for developing mental disorders for people born and raised in urban environments. However, in studies conducted in low- and middle-income countries this trend does not always hold. Several studies have actually reported higher occurrences of certain mental illnesses in

rural areas compared to urban areas (Breslau et al., 2014). In an international population based study sampling adults in 42 low income and middle income countries, results provide evidence that urbanicity was not associated with increased incidence of psychosis like in developing countries. Findings suggest that urban living may contribute to psychosis risk in high income countries because of different urban-rural patterns like cannabis use, racial discrimination, and socioeconomic disparities, all of which vary between developing and developed nations (DeVylder et al., 2018). Therefore, findings from high income countries cannot be generalized and more research needs to be conducted in low-and middle-income countries where a majority of urbanization is occurring today.

Initiatives in Urban Mental Health

Despite increasing urbanization and the growing number of people with mental health issues living in cities, there is no specific plan that clearly addresses the issues and needs of urban mental health, or strategies in place to improve and promote the health of city residents. Addressing needs like urban planning and city design, homelessness, and access to green and blue space are all solutions that could improve urban mental health (Okkels et al., 2018).

Urban Planning and City Design

Mental health issues have a large range of onset and symptomatology, and urban design can play a role in prevention, support, and promotion of health and wellbeing. With the growth of city populations, increase of people living with mental illness, and general risk factors city living poses for mental illness, the link between urban design and mental health is an important consideration for healthier cities. Urban mental health is a growing interdisciplinary field extending beyond the traditional psychiatrists and psychologists. Today it includes policymakers,

architects, urban planners, and engineers to name a few, in order to address the growing need for urban mental health interventions that support, improve, and prevent mental health and well-being through the built environment (McCay et al., 2017). Additionally, urban planning and urban design can help combat the rapid and unplanned urban growth that leads to informal settlements and slums as these conditions are associated with worse mental health outcomes, extreme poverty, violence, and drug abuse (Okkels et al., 2018). Urban planning deals with how and where houses, roads, institutions, parks, and sidewalks are built, as well as public transportation, access to green space, and opportunities for physical activity and social interaction (Okkels et al., 2018). How an urban environment is planned can either promote or complicate one's health. As cities continue to grow, urban designers should keep in mind the four themes that provide a framework for better mental health: green, active, prosocial, and safe spaces (McCay et al., 2017).

As described by the SDD model of psychosis, structural stressors from urban environments play a significant role in the onset of psychiatric disorders. Proper urban design and planning combat stimulation from lack of safety, discrepancy associated with lack of belonging, and deprivation from a lack of resources that urban environments produce. Whether it be creating spaces where people feel safe and confident, reducing noise to improve sleeping, facilitating access to nature, promoting social interactions, or reducing stress from commuting, designing urban environments is essential for encouraging better health outcomes (McCay et al., 2017). Access to green space helps improve and maintain mental health and well-being (Hartig et al., 2014). Physical environments can impact a sense of community. Designing cities with active spaces that are accessible like parks, outdoor gyms, and places to play for children and allow the integration of physical activity like walking or biking, helps integrate exercise and

social interactions in people's day to day (McCay et al., 2017). Prosocial spaces facilitate positive and safe interactions to create a sense of community, integration, and belonging. This is especially beneficial for vulnerable populations like refugees, migrants, young, and older populations. Lastly, safe spaces that promote a sense of safety and security. Sufficient street lighting, surveillance, sidewalks, transportation, and distinct landmarks are some examples of important urban design interventions that contribute to feelings of safety (McCay et al., 2017).

Addressing Homelessness

Homelessness is a growing problem accompanying urbanization linked to many causes like gentrification and rising rent, deinstitutionalization, worsening inequality, and the deterioration of social networks and safety nets (Okkels et al., 2018). Although it remains mostly an urban phenomenon, the influence of capitalism continues to increase income disparity, poverty, and the number of people who are homeless. The disparity between earned income, housing costs, and lack of affordable housing has priced many out of the rental market and into homelessness (Tsemberis et al., 2017). For individuals with severe psychiatric disorders, the rising rent has resulted in a disproportionate increase in homelessness as they are at risk for remaining homeless for months or years compared to those facing homelessness due to economic or personal crises (Culhane et al., 2002). Untreated mental illness co-occurring with addiction also contributes to increased vulnerability to chronic homelessness (Bharel et al., 2013). A study in Boston reported that in a sample of 6,494 patients in the Boston Health Care for the Homeless Program, two thirds reported a psychiatric diagnosis and 60% had a substance use disorder; almost half had both diagnoses and it was common to be diagnosed with other chronic diseases like hypertension, asthma, diabetes, an infectious disease, or HIV (Bharel et al., 2013). These comorbidities tend to impede recovery and prolong the time spent homeless.

Over the years, policies and strategies have emerged to address chronic homelessness. The decision about which root cause of homelessness to address, economic or clinical, has resulted in two different systems of care. The “Staircase Model” supporting treatment first and then housing, or the “Housing First Model” addressing housing first and then treatment (Tsemberis et al., 2017; **Figure 7**). The Staircase Model developed in the early 1980s offers housing to an individual after they have successfully completed a series of program steps beginning with low demand outreach or drop in, followed by treatment, sobriety, adherence to program rules, and then reaching shelters, transitional housing, and finally permanent housing (Ridgway and Zippel, 1990; Tsemberis et al., 2017). However, the approach that a person who is both homeless and has mental health and addiction issues must be treated first before they can be offered individual housing is unrealistic. For people experiencing homelessness, addressing their addiction and clinical problems do not often take priority over concerns about their hunger, safety, and other matters of survival. Additionally, stress, withdrawal, negative emotions and challenges, and environmental triggers can all cause relapse, which requires a fresh start from the bottom stair (Buena Vista Recovery, 2021). For individuals with complex problems, the Staircase Model can take years to climb and only has a 40% chance of success (Atherton and Nicholls, 2008). The Housing First Model on the other hand offers immediate access to housing and support services that reduce stress related to survival and make their housing and recovery more successful (**Figure 7**).

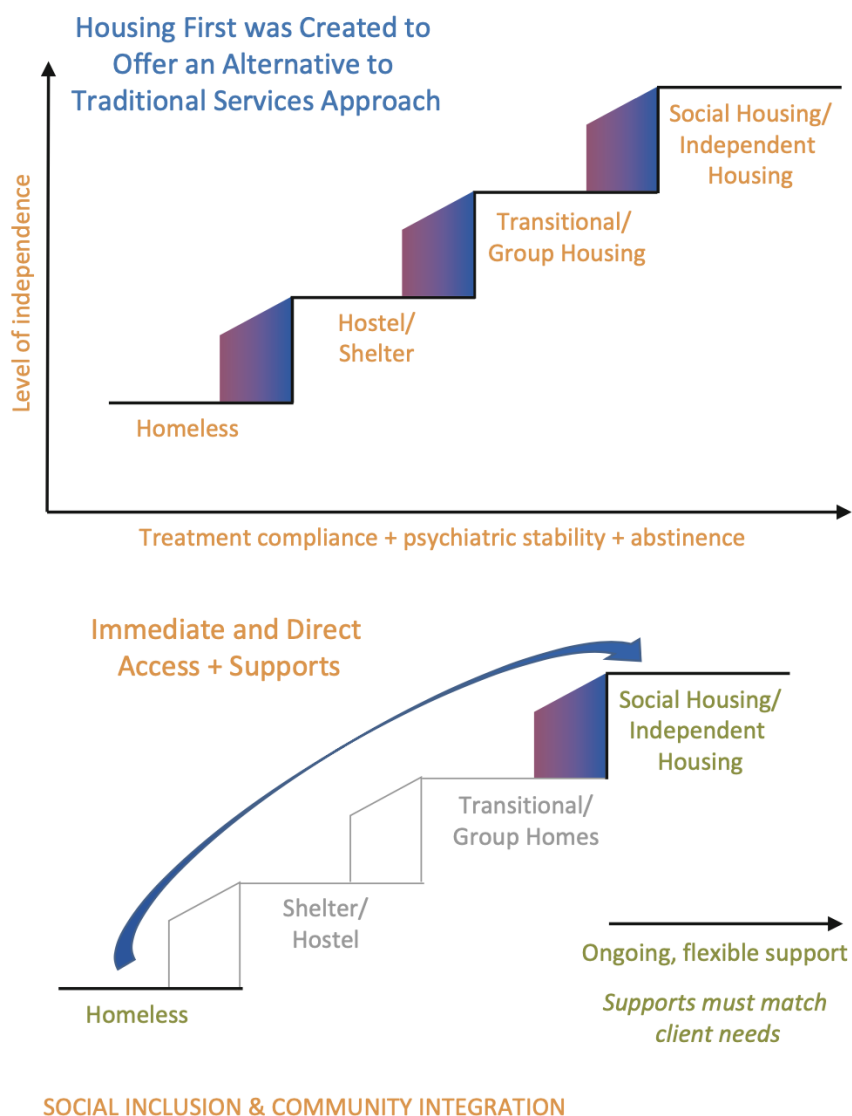


Figure 7. Traditional Staircase Model vs Housing First Model (Tsemberis et al., 2017). The staircase model has participants complete a series of program steps before being able to access housing. The housing first model on the other hand provides immediate and direct access to housing in addition to individual support that increases the success of treating chronic homelessness.

The Housing First Model, also known as the Pathway Housing First (PHF) model, emerged as an alternative to the Staircase Model. It has proved the most successful initiative for housing people with comorbid drug addiction and mental illness because stress related to finding housing is reduced (Tsemberis et al., 2017). Under this program, housing is viewed as a right and not something that should be earned through compliance with psychiatric treatment or abstinence

from drugs. The goal of the PHF program is to provide support services that assist with maintaining housing and address problems determined by the individual. Individuals are not evicted from their apartments if they relapse or need hospitalization and they are assisted with obtaining treatment and returning home upon completion (Tsemberis et al., 2017). Additionally, the PHF uses a harm reduction approach to address problems of addiction, mental illness, health, troubling relationships, apartment maintenance, budgeting, and other aspects essential to life (Tsemberis et al., 2017). Since its emergence, a growing number of cities in Canada, Europe, Australia, Europe, and the United States have declared reducing homelessness by using the PHF model to address chronic homelessness related to mental health and addiction problems (Okkels et al., 2018).

Access to Green Space

Urbanization, resource exploitation, and lifestyle changes have diminished access to nature in many societies (Hartig et al., 2014). Today urban living is associated with stationary lifestyles and exposure to chronic stress, contributing to the increase in burden of diseases like diabetes, obesity, and depression (Vos et al., 2015). Compared to those with sufficient access to green areas, people in densely populated cities without access to green space have a higher risk of developing mental illness. They have reduced opportunity for the stress reducing benefits of nature and increased exposure to environmental stressors (Okkles et al., 2017; Hartig et al., 2014). Contact with nature affects health through pathways involving air quality, physical activity, social cohesion, and stress reduction (Hartig et al., 2014; **Figure 8**). Contact with natural environments is proposed to act through two theoretical models of psychological restoration (Roe et al., 2013). Kaplans' Attention Restoration Theory suggests that natural settings invoke involuntary attention which supports restoration from mental fatigue, while Ulrich's model

suggests that stress reduction arises from an immediate, positive response to visual stimulus from a natural setting impacting the brain and stress system (Kaplan and Kaplan, 1989; Ulrich et al., 1991; Roe et al., 2013). Thus, access to green space plays a significant role in reducing stress, critical in urban settings where chronic stressors continually activate the stress response.

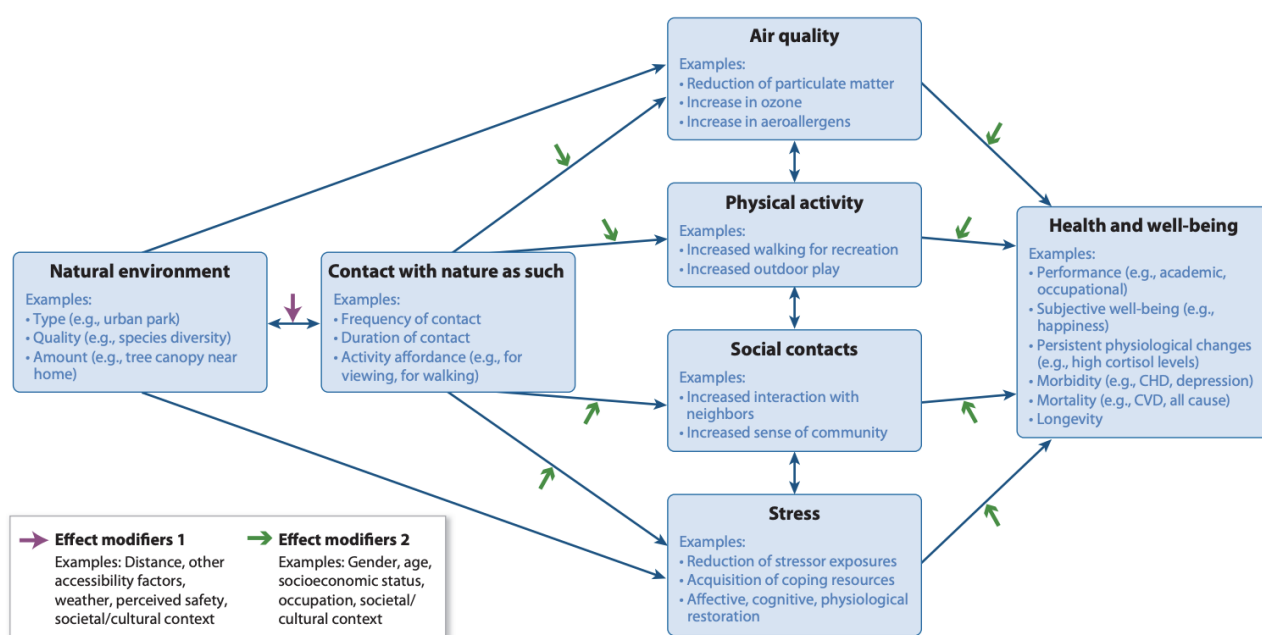


Figure 8. Model detailing the pathways through which the natural environment can affect the health in a range of populations (Hartig et al., 2014). Natural environments can affect health even without directly engaging with nature and beneficial outcomes to air quality, physical activity, social contact, and stress. Ultimately access to green space and contact with nature can reduce the risk of illnesses and promote general subjective well-being.

Access to green space positively influences psychological and physiological factors like physical activity, increased social interaction, stress reduction and relaxation, and overall better health and well-being (Okkels et al., 2017; Thomas et al., 2015). The presence of natural spaces like parks has shown greater levels of meaning to life, and experiences with nature are known sources of positive feelings that contribute to better quality of life (Chiesura, 2004). Besides the aesthetic, psychological, and health benefits, urban green space offers social benefits by promoting social relationships with neighbors and community members (Kuo et al., 1998). Lack of green zones is a known factor on how social stress may negatively affect mental health in

urban areas (van den Berg et al., 2010). Access to green space may reduce levels of perceived stress and combat the physical and mental impacts of long lasting social isolation associated with increased risk for depression, anxiety, coronary heart disease, and death (House, 2001; Lederbogen et al., 2013). Nature can help individuals escape from social and physical stressors that are often described as motives for recreation in natural spaces (Home and Hunziker, 2012). However, gender does play a role in the perceptions and usage of urban green space and creates differences in the relationship between environmental factors and health outcomes (Roe et al., 2013). Fear of safety is a common barrier experienced by women accessing urban green space, making it important to create green spaces that promote feelings of safety as well (Richardson and Mitchell, 2010).

Societal interventions in green space for physical activity and recreation can also prevent the onset of many diseases including depression, diabetes, and obesity (World Health Organization, 2012). Investment in green space would be especially beneficial for children, as health behavior and environments during critical growth periods can affect health across the entire life course (Van Landeghem et al., 2002). Growing evidence supports access or exposure to natural environments contributes to health and well-being by promoting health, encouraging healthy behaviors, and even decreasing risk factors like air pollution (Carrus et al., 2013). Additionally, the integration of Nature Based Solutions (NBS) in urban design and planning can improve the health conditions of city residents and make urban regions more sustainable and resilient to climate disasters. NBS are defined as solutions that are inspired and supported by nature (Raymond et al. 2017). The incorporation of NBS and urban green space will be beneficial for reducing stress, improving mood, and increasing physical activity, ultimately contributing to the better mental health and well-being of city residents.

SUMMARY AND LOOKING FORWARD

Urbanization is causing a demographic and cultural shift to the landscape of cities across the globe. Urban living can be advantageous for education, work, social communication and acceptance, health services, and culture. It is a chance for both individual and societal growth. However, while there are many benefits to urban living, it can also be a threat to mental health and wellbeing. Recent trends indicate that city environments are connected to the prevalence and severity of mental illnesses. Does the prolonged stress of city life impact the brain and increase the risk of psychiatric disorders? The answer is yes and no. Like cities, mental illnesses are diverse. Generalizing if mental illnesses are more prevalent in cities because of prolonged stress exposure is not an entirely accurate assumption. While some mental illnesses are more frequent in cities, others are more prevalent in rural areas. Prevalence depends on both the illness and the city. However, that is not to say that certain challenges common in urban environments are not associated with increased stress. Environmental stressors like lack of green space, homelessness, high rates of crime and violence, and easier access to drugs can cause chronic stress, which is a major risk factor for several neuropsychiatric disorders including depression and schizophrenia.

On a positive note, the city may offer opportunities for the prevention and treatment of mental illness that rural areas cannot (Okkels et al., 2018). However, the increasing number of psychiatric patients does pose a challenge to community mental health services, especially in low-and middle-income countries. In these locations with the steepest increase of urbanization, the current mental health services are not prepared to support the increase in mental disorders. People with mental illness in low-and middle-income countries hardly receive any healthcare, with an estimated 90% of patients with mental illness not receiving proper mental healthcare (Gureje et al., 2015). Thus, in addition to creating proper urban infrastructure that supports and

improves mental health, establishing better mental health services is essential for enhancing the mental health and well-being of city residents. Solutions like increased access to green space, supportive urban design, and addressing homelessness with the housing first model, can reduce some of the stress associated with city living. Lastly, for neuropsychiatric disorders like depression and schizophrenia, the use of antidepressants and antipsychotics may prove beneficial not only for symptoms, but for regulating HPA axis dysfunction. Overall, there is much to consider regarding city landscapes and mental health as urbanization continues to rise around the world. However, with the cooperation of city makers it is possible to address the needs that have arisen due to the rise of urbanization in order to combat the stress of city living and reduce the burden of mental illness.

REFERENCES

- Abbott, A. (2011). City living marks the brain. *Nature*, 474(7352), 429–429.
<https://doi.org/10.1038/474429a>
- Abbott, A. (2012). Stress and the city: Urban decay. *Nature*, 490(7419), 162–164.
<https://doi.org/10.1038/490162a>
- Alcock, I., White, M. P., Wheeler, B. W., Fleming, L. E., & Depledge, M. H. (2014). Longitudinal Effects on Mental Health of Moving to Greener and Less Green Urban Areas. *Environmental Science & Technology*, 48(2), 1247–1255.
<https://doi.org/10.1021/es403688w>
- Allardyce, J., Gilmour, H., Atkinson, J., Rapson, T., Bishop, J., & McCreadie, R. G. (2005). Social fragmentation, deprivation and urbanicity: Relation to first-admission rates for psychoses. *The British Journal of Psychiatry*, 187(5), 401–406.
<https://doi.org/10.1192/bjp.187.5.401>
- Amari, H. (n.d.). *Schematic representation of the regulation of the HPA axis under...* ResearchGate. Retrieved April 12, 2022, from
https://www.researchgate.net/figure/Schematic-representation-of-the-regulation-of-the-HPA-axis-under-chronic-stress-CRH-and_fig2_51531100
- American Psychiatric Association. (2020). *What Is Depression?*
<https://www.psychiatry.org/patients-families/depression/what-is-depression>
- Anand, K. S., & Dhikav, V. (2012). Hippocampus in health and disease: An overview. *Annals of Indian Academy of Neurology*, 15(4), 239–246.
<https://doi.org/10.4103/0972-2327.104323>

Atherton, I., & Nicholls, C. (2008). “Housing First” as a means of addressing multiple needs and homelessness. *Undefined*.

<https://www.semanticscholar.org/paper/%27Housing-First%27-as-a-means-of-addressing-multiple-Atherton-Nicholls/8054281d02a1e92b787abd6a59076b1c8e6fe69c>

Benarroch, E. E. (2009). The locus ceruleus norepinephrine system: Functional organization and potential clinical significance. *Neurology*, 73(20), 1699–1704.

<https://doi.org/10.1212/WNL.0b013e3181c2937c>

Bharel, M., Lin, W.-C., Zhang, J., O’Connell, E., Taube, R., & Clark, R. E. (2013). Health care utilization patterns of homeless individuals in Boston: Preparing for Medicaid expansion under the Affordable Care Act. *American Journal of Public Health*, 103 Suppl 2, S311-317. <https://doi.org/10.2105/AJPH.2013.301421>

Bloemsma, L. D., Wijga, A. H., Klompaker, J. O., Hoek, G., Janssen, N. A. H., Oldenwening, M., Koppelman, G. H., Lebret, E., Brunekreef, B., & Gehring, U. (2021). Green space, air pollution, traffic noise and saliva cortisol in children. *Environmental Epidemiology*, 5(2), e141. <https://doi.org/10.1097/EE9.0000000000000141>

Breslau, J., Marshall, G. N., Pincus, H. A., & Brown, R. A. (2014). Are mental disorders more common in urban than rural areas of the United States? *Journal of Psychiatric Research*, 56, 50–55. <https://doi.org/10.1016/j.jpsychires.2014.05.004>

Buena Vista Recovery. (2021, May 28). Why Do Addicts Relapse Even If Things Are Good? | Buena Vista Arizona. *Buena Vista Recovery*.

<https://buenavistarecovery.com/why-do-addicts-relapse-even-if-things-are-good/>

- Carrus, G., Laforteza, R., Colangelo, G., Dentamaro, I., Scopelliti, M., & Sanesi, G. (2013). Relations between naturalness and perceived restorativeness of different urban green spaces. *PsyEcology*, 4(3), 227–244. <https://doi.org/10.1174/217119713807749869>
- Centre for Studies on Human Stress. (2019). Stressors. *CESH / CSHS*.
<https://humanstress.ca/stress/what-is-stress/stressors/>
- Chiesura, A. (2004). The role of urban parks for the sustainable city. *Landscape and Urban Planning*, 68(1), 129–138. <https://doi.org/10.1016/j.landurbplan.2003.08.003>
- Cho, K., & Little, H. J. (1999). Effects of corticosterone on excitatory amino acid responses in dopamine-sensitive neurons in the ventral tegmental area. *Neuroscience*, 88(3), 837–845. [https://doi.org/10.1016/S0306-4522\(98\)00264-4](https://doi.org/10.1016/S0306-4522(98)00264-4)
- Conrad, C. D. (2008). Chronic Stress-Induced Hippocampal Vulnerability: The Glucocorticoid Vulnerability Hypothesis. *Reviews in the Neurosciences*, 19(6), 395–411.
- Culhane, D. P., Metraux, S., & Hadley, T. (2002). Public service reductions associated with placement of homeless persons with severe mental illness in supportive housing. *Housing Policy Debate*, 13(1), 107–163.
<https://doi.org/10.1080/10511482.2002.9521437>
- Day, L. L. (2000). Choosing a House: The Relationship between Dwelling Type, Perception of Privacy and Residential Satisfaction. *Journal of Planning Education and Research*, 19(3), 265–275. <https://doi.org/10.1177/0739456X0001900305>
- de Magalhães Narvaez, J. C., Moreira, C. G., & da Rosa, F. R. (2017). Crime, Illegal Drugs, and Mental Health. In N. Okkels, C. B. Kristiansen, & P. Munk-Jørgensen (Eds.),

Mental Health and Illness in the City (pp. 169–190). Springer Singapore.

https://doi.org/10.1007/978-981-10-2327-9_3

DeVylder, J. E., Kelleher, I., Lalane, M., Oh, H., Link, B. G., & Koyanagi, A. (2018).

Association of Urbanicity With Psychosis in Low- and Middle-Income Countries.

JAMA Psychiatry, 75(7), 678–686. <https://doi.org/10.1001/jamapsychiatry.2018.0577>

Dhikav, V., & Anand, K. (2011). Potential predictors of hippocampal atrophy in Alzheimer's disease. *Drugs & Aging*, 28(1), 1–11.

<https://doi.org/10.2165/11586390-000000000-00000>

Dragoş, D., & Tănăsescu, M. (2010). The effect of stress on the defense systems. *Journal of Medicine and Life*, 3(1), 10–18.

Dye, C. (2008). Health and Urban Living. *Science*, 319(5864), 766–769.

<https://doi.org/10.1126/science.1150198>

Eliacin, J. (2013). Social Capital, Narratives of Fragmentation, and Schizophrenia: An Ethnographic Exploration of Factors Shaping African-Caribbeans' Social Capital and Mental Health in a North London Community. *Culture, Medicine and Psychiatry*, 37(3), 465–487. <https://doi.org/10.1007/s11013-013-9322-2>

Floriou-Servou, A., Ziegler, L. von, Waag, R., Schläppi, C., Germain, P.-L., & Bohacek, J. (2021). The Acute Stress Response in the Multiomic Era. *Biological Psychiatry*, 89(12), 1116–1126. <https://doi.org/10.1016/j.biopsych.2020.12.031>

Freeman, D., Emsley, R., Dunn, G., Fowler, D., Bebbington, P., Kuipers, E., Jolley, S., Waller, H., Hardy, A., & Garety, P. (2015). The Stress of the Street for Patients With Persecutory Delusions: A Test of the Symptomatic and Psychological Effects of Going

Outside Into a Busy Urban Area. *Schizophrenia Bulletin*, 41(4), 971–979.

<https://doi.org/10.1093/schbul/sbu173>

Godfrey, R., & Julien, M. (2005). Urbanisation and health. *Clinical Medicine*, 5(2), 137–141. <https://doi.org/10.7861/clinmedicine.5-2-137>

Godoy, L. D., Rossignoli, M. T., Delfino-Pereira, P., Garcia-Cairasco, N., & de Lima Umeoka, E. H. (2018). A Comprehensive Overview on Stress Neurobiology: Basic Concepts and Clinical Implications. *Frontiers in Behavioral Neuroscience*, 12.

<https://www.frontiersin.org/article/10.3389/fnbeh.2018.00127>

Grace, A. A. (2016). Dysregulation of the dopamine system in the pathophysiology of schizophrenia and depression. *Nature Reviews Neuroscience*, 17(8), 524–532.

<https://doi.org/10.1038/nrn.2016.57>

Gruebner, O., A. Rapp, M., Adli, M., Kluge, U., Galea, S., & Heinz, A. (2017). Cities and Mental Health. *Deutsches Ärzteblatt International*, 114(8), 121–127.

<https://doi.org/10.3238/arztebl.2017.0121>

Gureje, O., Thornicroft, G., & FundaMentalSDG Steering Group. (2015). Health equity and mental health in post-2015 sustainable development goals. *The Lancet. Psychiatry*, 2(1), 12–14. [https://doi.org/10.1016/S2215-0366\(14\)00094-7](https://doi.org/10.1016/S2215-0366(14)00094-7)

Hartig, T., Mitchell, R., de Vries, S., & Frumkin, H. (2014). Nature and Health. *Annual Review of Public Health*, 35(1), 207–228.

<https://doi.org/10.1146/annurev-publhealth-032013-182443>

Holtzman, C. W., Shapiro, D. I., Trotman, H. D., & Walker, E. F. (2012). Stress and the prodromal phase of psychosis. *Current Pharmaceutical Design*, 18(4), 527–533.

<https://doi.org/10.2174/138161212799316280>

- Holtzman, C. W., Trotman, H. D., Goulding, S. M., Ryan, A. T., Macdonald, A. N., Shapiro, D. I., Brasfield, J. L., & Walker, E. F. (2013). Stress and Neurodevelopmental Processes in the Emergence of Psychosis. *Neuroscience*, 249, 172–191.
<https://doi.org/10.1016/j.neuroscience.2012.12.017>
- Home, R., & Hunziker, M. (2012). Psychosocial Outcomes as Motivations for Visiting Nearby Urban Green Spaces. *Leisure Sciences*, 34, 350–365.
<https://doi.org/10.1080/01490400.2012.687644>
- House, J. S. (2001). Social Isolation Kills, But How and Why? *Psychosomatic Medicine*, 63(2), 273–274.
- Hutson, M. A., Kaplan, G. A., Ranjit, N., & Mujahid, M. S. (2012). Metropolitan Fragmentation and Health Disparities: Is There a Link? *The Milbank Quarterly*, 90(1), 187–207. <https://doi.org/10.1111/j.1468-0009.2011.00659.x>
- James, S. L., Abate, D., Abate, K. H., Abay, S. M., Abbafati, C., Abbasi, N., Abbastabar, H., Abd-Allah, F., Abdela, J., Abdelalim, A., Abdollahpour, I., Abdulkader, R. S., Abebe, Z., Abera, S. F., Abil, O. Z., Abraha, H. N., Abu-Raddad, L. J., Abu-Rmeileh, N. M. E., Accrombessi, M. M. K., ... Murray, C. J. L. (2018). Global, regional, and national incidence, prevalence, and years lived with disability for 354 diseases and injuries for 195 countries and territories, 1990–2017: A systematic analysis for the Global Burden of Disease Study 2017. *The Lancet*, 392(10159), 1789–1858.
[https://doi.org/10.1016/S0140-6736\(18\)32279-7](https://doi.org/10.1016/S0140-6736(18)32279-7)
- Johansen, J. P., Cain, C. K., Ostroff, L. E., & LeDoux, J. E. (2011). Molecular mechanisms of fear learning and memory. *Cell*, 147(3), 509–524.
<https://doi.org/10.1016/j.cell.2011.10.009>

- Judd, F. K., Jackson, H. J., Komiti, A., Murray, G., Hodgins, G., & Fraser, C. (2002). High Prevalence Disorders in Urban and Rural Communities. *Australian & New Zealand Journal of Psychiatry*, 36(1), 104–113.
<https://doi.org/10.1046/j.1440-1614.2002.00986.x>
- Juruena, M. F., Cleare, A. J., & Pariante, C. M. (2004). *The Hypothalamic Pituitary Adrenal axis, Glucocorticoid receptor function and relevance to depression*. 13.
- Kabisch, N., van den Bosch, M., & Laforzezza, R. (2017). The health benefits of nature-based solutions to urbanization challenges for children and the elderly – A systematic review. *Environmental Research*, 159, 362–373.
<https://doi.org/10.1016/j.envres.2017.08.004>
- Kaplan, R., & Kaplan, S. (1989). *The Experience of Nature: A Psychological Perspective*.
<https://doi.org/10.1037/030621>
- Kapur, S. (2003). Psychosis as a state of aberrant salience: A framework linking biology, phenomenology, and pharmacology in schizophrenia. *The American Journal of Psychiatry*, 160(1), 13–23. <https://doi.org/10.1176/appi.ajp.160.1.13>
- Kelly, B. D., O’Callaghan, E., Waddington, J. L., Feeney, L., Browne, S., Scully, P. J., Clarke, M., Quinn, J. F., McTigue, O., Morgan, M. G., Kinsella, A., & Larkin, C. (2010). Schizophrenia and the city: A review of literature and prospective study of psychosis and urbanicity in Ireland. *Schizophrenia Research*, 116(1), 75–89.
<https://doi.org/10.1016/j.schres.2009.10.015>
- Kirkbride, J. B., Jones, P. B., Ullrich, S., & Coid, J. W. (2012). Social deprivation, inequality, and the neighborhood-level incidence of psychotic syndromes in East London. *Schizophrenia Bulletin*, 40(1), 169–180. <https://doi.org/10.1093/schbul/sbs151>

- Kuo, M., Bacaicoa, M., & Sullivan, W. (1998). Transforming Inner-City Landscapes Trees, Sense of Safety, and Preference. *Environment and Behavior - ENVIRON BEHAV*, 30, 28–59. <https://doi.org/10.1177/0013916598301002>
- Lavikainen, J., Lahtinen, E., Lehtinen, V., & Sosiaali- ja terveystieteiden tutkimus- ja kehittämiskeskus. (2000). *Public health approach on mental health in Europe*. National Research and Development Centre for Welfare and Health.
- Lecic-Tosevski, D. (2019). Is urban living good for mental health? *Current Opinion in Psychiatry*, 32(3), 204–209. <https://doi.org/10.1097/YCO.0000000000000489>
- Lederbogen, F., Haddad, L., & Meyer-Lindenberg, A. (2013). Urban social stress – Risk factor for mental disorders. The case of schizophrenia. *Environmental Pollution*, 183, 2–6. <https://doi.org/10.1016/j.envpol.2013.05.046>
- Lederbogen, F., Kirsch, P., Haddad, L., Streit, F., Tost, H., Schuch, P., Wüst, S., Pruessner, J. C., Rietschel, M., Deuschle, M., & Meyer-Lindenberg, A. (2011). City living and urban upbringing affect neural social stress processing in humans. *Nature*, 474(7352), 498–501. <https://doi.org/10.1038/nature10190>
- López-Jaramillo, C., Arias, J. M. C., & Díaz Zuluaga, A. M. (2017). Mental Health and Urban Life: Experiences from Colombia. In N. Okkels, C. B. Kristiansen, & P. Munk-Jorgensen (Eds.), *Mental Health and Illness in the City* (pp. 1–17). Springer. https://doi.org/10.1007/978-981-10-0752-1_5-1
- Lundbeck Foundation. (n.d.). The Hypothalamic Pituitary Adrenal (HPA) Axis in Depression. *Neurotorium*. Retrieved April 9, 2022, from <https://neurotorium.org/image/the-hypothalamic-pituitary-adrenal-hpa-axis-in-depression-2/>

- Lupien, S. J., McEwen, B. S., Gunnar, M. R., & Heim, C. (2009). Effects of stress throughout the lifespan on the brain, behaviour and cognition. *Nature Reviews Neuroscience*, 10(6), 434–445. <https://doi.org/10.1038/nrn2639>
- Maclaughlin, B., Wang, D., Noone, A.-M., Liu, N., Harazduk, N., Lumpkin, M., Haramati, A., Saunders, P., Dutton, M., & Amri, H. (2011). Stress Biomarkers in Medical Students Participating in a Mind Body Medicine Skills Program. *Evidence-Based Complementary and Alternative Medicine : ECAM*, 2011, 950461. <https://doi.org/10.1093/ecam/neq039>
- Marinelli, M., Rudick, C. N., Hu, X.-T., & White, F. J. (2006). Excitability of dopamine neurons: Modulation and physiological consequences. *CNS & Neurological Disorders Drug Targets*, 5(1), 79–97. <https://doi.org/10.2174/187152706784111542>
- McCay, L., Bremer, I., Endale, T., Jannati, M., & Yi, J. (2017). Urban Design and Mental Health. In N. Okkels, C. B. Kristiansen, & P. Munk-Jørgensen (Eds.), *Mental Health and Illness in the City* (pp. 421–444). Springer. https://doi.org/10.1007/978-981-10-2327-9_12
- McCutcheon, R. A., Krystal, J. H., & Howes, O. D. (2020). Dopamine and glutamate in schizophrenia: Biology, symptoms and treatment. *World Psychiatry*, 19(1), 15–33. <https://doi.org/10.1002/wps.20693>
- McLaughlin, K. A., Sheridan, M. A., & Lambert, H. K. (2014). Childhood Adversity and Neural Development: Deprivation and Threat as Distinct Dimensions of Early Experience. *Neuroscience and Biobehavioral Reviews*, 47, 578–591. <https://doi.org/10.1016/j.neubiorev.2014.10.012>

- Military Health Systems. (n.d.). *Depression 101*. Retrieved April 1, 2022, from <https://health.mil/News/Gallery/Infographics/2016/05/02/Depression-101>
- Murison, R. (2016). The Neurobiology of Stress. In *Neuroscience of Pain, Stress, and Emotion* (pp. 29–49). Elsevier. <https://doi.org/10.1016/B978-0-12-800538-5.00002-9>
- National Institute of Mental Health. (2018). *Depression*. National Institute of Mental Health (NIMH). <https://www.nimh.nih.gov/health/topics/depression>
- Newbury, J., Arseneault, L., Caspi, A., Moffitt, T. E., Odgers, C. L., & Fisher, H. L. (2018). Cumulative Effects of Neighborhood Social Adversity and Personal Crime Victimization on Adolescent Psychotic Experiences. *Schizophrenia Bulletin*, 44(2), 348–358. <https://doi.org/10.1093/schbul/sbx060>
- NIMH. (2022, January). *Mental Illness*. National Institute of Mental Health (NIMH). <https://www.nimh.nih.gov/health/statistics/mental-illness>
- Okkels, N., Kristiansen, C. B., & Munk-Jørgensen, P. (Eds.). (2017). *Mental Health and Illness in the City*. Springer Singapore. <https://doi.org/10.1007/978-981-10-2327-9>
- Okkels, N., Kristiansen, C. B., Munk-Jørgensen, P., & Sartorius, N. (2018). Urban mental health: Challenges and perspectives. *Current Opinion in Psychiatry*, 31(3), 258–264. <https://doi.org/10.1097/YCO.0000000000000413>
- Paykel, E. S. (1978). Contribution of life events to causation of psychiatric illness. *Psychological Medicine*, 8(2), 245–253. <https://doi.org/10.1017/s003329170001429x>
- Peen, J., Schoevers, R. A., Beekman, A. T., & Dekker, J. (2010). The current status of urban-rural differences in psychiatric disorders. *Acta Psychiatrica Scandinavica*, 121(2), 84–93. <https://doi.org/10.1111/j.1600-0447.2009.01438.x>

- Phillips, L. J., Francey, S. M., Edwards, J., & McMurray, N. (2007). Stress and psychosis: Towards the development of new models of investigation. *Clinical Psychology Review*, 27(3), 307–317. <https://doi.org/10.1016/j.cpr.2006.10.003>
- Popoli, M., Yan, Z., McEwen, B. S., & Sanacora, G. (2012). The stressed synapse: The impact of stress and glucocorticoids on glutamate transmission. *Nature Reviews Neuroscience*, 13(1), 22–37. <https://doi.org/10.1038/nrn3138>
- Pruessner, J. C., Champagne, F., Meaney, M. J., & Dagher, A. (2004). Dopamine Release in Response to a Psychological Stress in Humans and Its Relationship to Early Life Maternal Care: A Positron Emission Tomography Study Using [11C]Raclopride. *The Journal of Neuroscience*, 24(11), 2825–2831. <https://doi.org/10.1523/JNEUROSCI.3422-03.2004>
- Raymond, C. M., Frantzeskaki, N., Kabisch, N., Berry, P., Breil, M., Nita, M. R., Geneletti, D., & Calfapietra, C. (2017). A framework for assessing and implementing the co-benefits of nature-based solutions in urban areas. *Environmental Science & Policy*, 77, 15–24. <https://doi.org/10.1016/j.envsci.2017.07.008>
- Richardson, E. A., & Mitchell, R. (2010). Gender differences in relationships between urban green space and health in the United Kingdom. *Social Science & Medicine* (1982), 71(3), 568–575. <https://doi.org/10.1016/j.socscimed.2010.04.015>
- Ridgway, P., & Zippile, A. M. (1990). The paradigm shift in residential services: From the linear continuum to supported housing approaches. *Psychosocial Rehabilitation Journal*, 13(4), 11–31. <https://doi.org/10.1037/h0099479>

- Robertson, L., & Szabo, C. (2017). *Implementing Community Care in Large Cities and Informal Settlements: An African Perspective* (pp. 1–24).
https://doi.org/10.1007/978-981-10-0752-1_16-1
- Roe, J. J., Thompson, C. W., Aspinall, P. A., Brewer, M. J., Duff, E. I., Miller, D., Mitchell, R., & Clow, A. (2013). Green Space and Stress: Evidence from Cortisol Measures in Deprived Urban Communities. *International Journal of Environmental Research and Public Health*, 10(9), 4086–4103. <https://doi.org/10.3390/ijerph10094086>
- Salleh, Mohd. R. (2008). Life Event, Stress and Illness. *The Malaysian Journal of Medical Sciences : MJMS*, 15(4), 9–18.
- Sapolsky, R. M. (1992). *Stress, the aging brain, and the mechanisms of neuron death* (pp. xi, 429). The MIT Press.
- Sapolsky, R. M. (2000). The possibility of neurotoxicity in the hippocampus in major depression: A primer on neuron death. *Biological Psychiatry*, 48(8), 755–765.
[https://doi.org/10.1016/S0006-3223\(00\)00971-9](https://doi.org/10.1016/S0006-3223(00)00971-9)
- Sapolsky, R. M., Krey, L. C., & McEwen, B. S. (1986). The neuroendocrinology of stress and aging: The glucocorticoid cascade hypothesis. *Endocrine Reviews*, 7(3), 284–301.
<https://doi.org/10.1210/edrv-7-3-284>
- Schofield, P., Thygesen, M., Das-Munshi, J., Becares, L., Cantor-Graae, E., Pedersen, C., & Agerbo, E. (2017). Ethnic density, urbanicity and psychosis risk for migrant groups – A population cohort study. *Schizophrenia Research*, 190, 82–87.
<https://doi.org/10.1016/j.schres.2017.03.032>

- Smardon, R. C. (1988). Perception and aesthetics of the urban environment: Review of the role of vegetation. *Landscape and Urban Planning*, 15(1), 85–106.
[https://doi.org/10.1016/0169-2046\(88\)90018-7](https://doi.org/10.1016/0169-2046(88)90018-7)
- Spicer, J. (2011a). *Neural Mechanisms of Social Evaluative Threat* [Columbia University].
<https://doi.org/10.7916/D8TB2DRH>
- Spicer, J. (2011b). *Neural Mechanisms of Social Evaluative Threat* [Columbia University].
<https://doi.org/10.7916/D8TB2DRH>
- Stress. (2021, September). Mental Health Foundation.
<https://www.mentalhealth.org.uk/a-to-z/s/stress>
- Thomas, F. (2015). The role of natural environments within women's everyday health and wellbeing in Copenhagen, Denmark. *Health & Place*, 35, 187–195.
<https://doi.org/10.1016/j.healthplace.2014.11.005>
- Tsemberis, S., & Macnaughton, E. (2017). Homelessness and Challenges of Community Care. In N. Okkels, C. B. Kristiansen, & P. Munk-Jørgensen (Eds.), *Mental Health and Illness in the City* (pp. 395–420). Springer.
https://doi.org/10.1007/978-981-10-2327-9_6
- Tzschentke, T. M., & Schmidt, W. J. (2003). Glutamatergic mechanisms in addiction. *Molecular Psychiatry*, 8(4), 373–382. <https://doi.org/10.1038/sj.mp.4001269>
- Ulrich, R. S., Simons, R. F., Losito, B. D., Fiorito, E., Miles, M. A., & Zelson, M. (1991). Stress recovery during exposure to natural and urban environments. *Journal of Environmental Psychology*, 11(3), 201–230.
[https://doi.org/10.1016/S0272-4944\(05\)80184-7](https://doi.org/10.1016/S0272-4944(05)80184-7)

- Ulrich-Lai, Y. M., & Herman, J. P. (2009). Neural regulation of endocrine and autonomic stress responses. *Nature Reviews Neuroscience*, 10(6), 397–409.
<https://doi.org/10.1038/nrn2647>
- United Nations. (n.d.). *World Urbanization Prospects—Population Division*. Retrieved April 1, 2022, from <https://population-un-org.ccl.idm.oclc.org/wup/>
- United Nations Human Settlements Programme (UN-Habitat). (2016). *Urbanization and development: Emerging futures*.
<https://unhabitat.org/programme/city-prosperity-initiative>
- van den Berg, A. E., Maas, J., Verheij, R. A., & Groenewegen, P. P. (2010). Green space as a buffer between stressful life events and health. *Social Science & Medicine*, 70(8), 1203–1210. <https://doi.org/10.1016/j.socscimed.2010.01.002>
- Van Landeghem, K., Curtis, D., & Abrams, M. (2002). *Reasons and Strategies for Strengthening Childhood Development Services in the Healthcare System*. 35.
- van Marle, H. J. F., Hermans, E. J., Qin, S., & Fernández, G. (2009). From specificity to sensitivity: How acute stress affects amygdala processing of biologically salient stimuli. *Biological Psychiatry*, 66(7), 649–655. <https://doi.org/10.1016/j.biopsych.2009.05.014>
- van Winkel, R., Stefanis, N. C., & Myin-Germeys, I. (2008). Psychosocial Stress and Psychosis. A Review of the Neurobiological Mechanisms and the Evidence for Gene-Stress Interaction. *Schizophrenia Bulletin*, 34(6), 1095–1105.
<https://doi.org/10.1093/schbul/sbn101>
- Vargas, T., Conley, R. E., & Mittal, V. A. (2020). Chronic stress, structural exposures and neurobiological mechanisms: A stimulation, discrepancy and deprivation model of

psychosis. *International Review of Neurobiology*, 152, 41–69.

<https://doi.org/10.1016/bs.irm.2019.11.004>

Venkatasubramanian, G., Chittiprol, S., Neelakantachar, N., Shetty, T., & Gangadhar, B. N.

(2010). Effect of antipsychotic treatment on Insulin-like Growth Factor-1 and cortisol in schizophrenia: A longitudinal study. *Schizophrenia Research*, 119(1–3), 131–137.

<https://doi.org/10.1016/j.schres.2010.01.033>

Vos, T., Barber, R. M., Bell, B., Bertozzi-Villa, A., Biryukov, S., Bolliger, I., Charlson, F.,

Davis, A., Degenhardt, L., Dicker, D., Duan, L., Erskine, H., Feigin, V. L., Ferrari, A.

J., Fitzmaurice, C., Fleming, T., Graetz, N., Guinovart, C., Haagsma, J., ... Murray, C.

J. (2015). Global, regional, and national incidence, prevalence, and years lived with

disability for 301 acute and chronic diseases and injuries in 188 countries, 1990–2013:

A systematic analysis for the Global Burden of Disease Study 2013. *The Lancet*,

386(9995), 743–800. [https://doi.org/10.1016/S0140-6736\(15\)60692-4](https://doi.org/10.1016/S0140-6736(15)60692-4)

Walia, H. (2021). *Border & Rule: Global Migration, Capitalism, and the Rise of Racist Nationalism*. Haymarket Books.

Walker, E. F., & Diforio, D. (1997). Schizophrenia: A neural diathesis-stress model.

Psychological Review, 104(4), 667–685. <https://doi.org/10.1037/0033-295x.104.4.667>

Walker, E., Mittal, V., & Tessner, K. (2008). Stress and the hypothalamic pituitary adrenal axis in the developmental course of schizophrenia. *Annual Review of Clinical*

Psychology, 4, 189–216. <https://doi.org/10.1146/annurev.clinpsy.4.022007.141248>

Wang, P. S., Aguilar-Gaxiola, S., Alonso, J., Angermeyer, M. C., Borges, G., Bromet, E. J.,

Bruffaerts, R., de Girolamo, G., de Graaf, R., Gureje, O., Haro, J. M., Karam, E. G.,

Kessler, R. C., Kovess, V., Lane, M. C., Lee, S., Levinson, D., Ono, Y., Petukhova, M.,

- ... Wells, J. E. (2007). Worldwide Use of Mental Health Services for Anxiety, Mood, and Substance Disorders: Results from 17 Countries in the WHO World Mental Health (WMH) Surveys. *Lancet*, 370(9590), 841–850.
[https://doi.org/10.1016/S0140-6736\(07\)61414-7](https://doi.org/10.1016/S0140-6736(07)61414-7)
- Weich, S., Blanchard, M., Prince, M., Burton, E., Erens, B., & Sproston, K. (2002). Mental health and the built environment: Cross-sectional survey of individual and contextual risk factors for depression. *The British Journal of Psychiatry: The Journal of Mental Science*, 180, 428–433. <https://doi.org/10.1192/bjp.180.5.428>
- WHO. (2019, November 28). *Mental disorders*.
<https://www.who.int/news-room/fact-sheets/detail/mental-disorders>
- World Health Organization. Regional Office for Europe. (2012). *Action plan for implementation of the European Strategy for the Prevention and Control of Noncommunicable Diseases 2012–2016*. World Health Organization. Regional Office for Europe. <https://apps.who.int/iris/handle/10665/352659>
- Yang, L., Zhao, Y., Wang, Y., Liu, L., Zhang, X., Li, B., & Cui, R. (2015). The Effects of Psychological Stress on Depression. *Current Neuropharmacology*, 13(4), 494–504.
<https://doi.org/10.2174/1570159X1304150831150507>
- Yaribeygi, H., Panahi, Y., Sahraei, H., Johnston, T. P., & Sahebkar, A. (2017). The impact of stress on body function: A review. *EXCLI Journal*, 16, 1057–1072.
<https://doi.org/10.17179/excli2017-480>
- Yates, D. (2011). The stress of city life. *Nature Reviews Neuroscience*, 12(8), 430–430.
<https://doi.org/10.1038/nrn3079>