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ADDICTION AS CAPABILITIES FAILURE

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Addiction has become a national crisis of morbidity, mortality, and economic and societal well-being in the United States, creating an enormous emotional and financial burden on individuals, families and society. As understanding of the neurobiology of addiction and co-morbid mental illness grows, the brain's vulnerabilities to addiction and chronic recurring relapse are anticipated to further consume the attention of biomedical sciences and society.

Paradigm-shifting discoveries to achieve a decline in incidence and prevalence of addiction and co-morbid mental illnesses will have transformative impacts on individuals and society. This is the focus of this Article. Health capability refers to a person's ability to be healthy, supporting a comprehensive strategy to create and change the external conditions and individual behaviors for optimal individual and population health. Guided by the notion that addiction is the consequence of failures to inoculate individuals with immunity from internal and external vulnerabilities to chemical dependency, we propose that it is capabilities, individual and collective, that determine individual and familial health and well-being and consequently the health and well-being of society. Grounded in recent innovative discoveries in our lab, we hypothesize that capabilities act as the master regulator of our individual and collective behavior, and hence, capabilities determine health and well-being, preventing addiction and aiding recovery.

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INTRODUCTION

Addiction has become a national crisis of morbidity, mortality, and socioeconomic well-being in the United States, creating an enormous emotional and financial burden on individuals, families and society. As understanding of the neurobiology of addiction and co-morbid mental illness grows, the brain's vulnerabilities to addiction and chronic recurring relapse are anticipated to further consume the attention of biomedical sciences and society. Paradigm-shifting discoveries to achieve a decline in incidence and prevalence of addiction and co-morbid mental illnesses will have transformative impacts on individuals and society.

Yet, current approaches to addiction and recovery have significant limitations, focusing on: (i) disease and dysfunction rather than health and well-being; (ii) reductionist, protracted and isolated scientific models under controlled circumstances rather than systematically exploring complex interactive systems in the real world where humans succeed or fail to thrive; (iii) outmoded programs and treatments with limited effectiveness rather than inventive individuals and groups with proven successes; and (iv) analytically, single elements rather than a set of elements, an object in its own right, as foundational in set theory in mathematics. Despite major advances in understanding the genetics and neurobiology of addiction and mental illnesses and hundreds of clinical trials, current prevention and treatment programs have fallen short of significantly alleviating the devastating burden of these diseases. Substantial knowledge gaps still present major impediments to addressing mental and substance use disorders. A new way to understand and approach addiction and co-morbid mental illnesses is patently needed.

Our approach seeks to break through this impasse to discover the abilities of people to be healthy and well, taking advantage of new advances in neuroscience, unavailable until now, that enable us to test previously unviable hypotheses linking capabilities, health, and well-being. We bridge etiologies of addiction and determinants of health and well-being through capabilities, associated with our previous findings in defining fundamental principles and

properties of health governance.[1] Understanding the governance principles of capabilities, what people are able to do and be, our unconventional hypothesis is that capabilities are the master regulators of health and well-being. If proven correct, this alternative approach to addiction will indicate an immediate and dramatic shift in the scientific knowledge, prevention, and treatment of substance use, co-morbid mental disorders, and major social illnesses, such as unemployment, violence, delinquency, crime, and corruption.

Capabilities promote optimal functioning in the individual and society; this promotion of health and wellness simultaneously addresses other diseases as well, such as diabetes and heart disease. Thus, a shift in our thinking with respect to the conceptual framework of the functioning of the individual and society will follow: this is because current approaches fail to address the fundamental causes of the problem, addiction as a failure of capabilities. Capable people and minds have built-in, protective neurobiological mechanisms that counteract risks for addiction; for example, resilient individuals actively recover synaptic plasticity despite initial synaptic plasticity decreases in all who use drugs.[2] A bolder approach is needed to bring people to their highest potential of human flourishing. Our work challenges enduring beliefs by distinguishing capabilities as upstream regulators of abstinence and recovery from substance use and co-morbid mental disorders. This radically improves our understanding of how to prevent and treat addiction and to do so rapidly, before it is too late; moreover, it paves the way beyond health promotion to eradicating addiction in society.

Capabilities work by training the brain to recognize and combat causes of addiction. In our view, addiction is one of the world's most dangerous problems. To combat causes of addiction, abilities to prevent the neural onset of addiction must be developed over time, training the brain to trigger an immune-like response. The antigen is the awareness of the toxicity and extreme danger of introducing substances into the central nervous system, especially a clean and early-exposed system, which serves as the basis of development of the internal and external capabilities set needed to protect the brain from addiction. Capabilities harness the natural activity of the brain, particularly executive cognitive functioning and neural pathway activation, but also positive emotion and habit and routine formation. With this view, substance use is seen as a hostile invader to the central nervous system and capabilities,

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[1] *See* Jennifer Prah Ruger, *Health Capability: Conceptualization and Operationalization*, 100 AM. J. PUB. HEALTH 41, 43 (2010) (surveying the author's conceptual model of health capability).

[2] *See* Pier Vincenzo Piazza & Véronique Deroche-Gamonet, *A Multistep General Theory of Transition to Addiction*, 229 PSYCHOPHARMACOLOGY 387, 406 (2013) ("Most drug-induced impairments in synaptic plasticity are initially observed in all individuals, but the majority . . . are able to adapt and recover from most of them.").

which are routinely developed to habitually kick in to combat relapse to chronic use in the recovering brain and the onset of substance use disorders entirely, for example, in the developing brain of individuals under 25-years-old.

Capabilities development impacts higher brain activity, including: executive and cognitive functioning; neural pathways and activation; and neurogenesis and neurodegeneration. Neurogenesis, which occurs in abstinence of drug use throughout normal lifetime brain development, refers to the growth of new neurons and brain cells.[3] Neurodegeneration, on the other hand, is associated with substance use induced by pathological processes and risk factors such as adolescence,[4] genetic predisposition to addiction,[5] and familial history of addiction,[6] and further reduces the brain's ability to withstand stress. The capabilities set develops additively over time, as a synergistic cluster, to recognize and trigger behavioral responses to immediately and aggressively protect the brain's exposure to the substance before it enters the body or becomes excessive on the path to addiction.

Capabilities do not just work at the individual level; they protect entire populations once enough people develop the capabilities to prevent addiction and potentially to eradicate it. This is because when enough people (a certain threshold) have developed capabilities sets against addiction, herd immunity keeps others safe; opportunities for the disease to spread are significantly reduced. The addiction prevention capabilities set thus consists of two categories of factors, internal and external,[7] that enable one to prevent the long-lasting changes in the brain that substance dependence creates. Each subset of internal and external factors has a neurobiological correlate,

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[3] *See* Eng-Tat Ang et al., *Neurodegenerative Diseases: Exercising Toward Neurogenesis and Neuroregeneration*, 2 FRONTIERS AGING NEUROSCIENCE, July 21, 2010, at 1, 5 (discussing the impact of exercise and caloric restriction on the creation of new neurons); *see also* Eric J. Nestler, *Is There a Common Molecular Pathway for Addiction?,* 8 NATURE NEUROSCIENCE 1445, 1448 (2005) (discussing the mysterious purpose of adult neurogenesis and noting that chronic drug use seems to reduce it).

[4] S.A. Morris et al., *Alcohol Inhibition of Neurogenesis: A Mechanism of Hippocampal Neurodegeneration in an Adolescent Alcohol Abuse Model*, 20 HIPPOCAMPUS 596, 596 (2010).

[5] *See* R.D. Mayfield et al., *Genetic Factors Influencing Alcohol Dependence*, 154 BRIT. J. PHARMACOLOGY 275, 279 (2008) ("[G]enes involved in neurodegenerative disease such as Alzheimer's were significantly altered (presenilin 1 and transferrin), suggesting a link between alcoholism and other neurodegenerative conditions.").

[6] *Id.,* at 275; D.J. Meyerhoff et al., *Effects of Heavy Drinking, Binge Drinking, and Family History of Alcoholism on Regional Brain Metabolites*, 28 ALCOHOLISM CLINICAL EXPERIMENTAL RES. 650, 658 (2004); Rohan Palmer & John McGeary, *Models of Drug Addiction: Theories and Future Applications in Prevention and Treatment*, 32 BROWN U. CHILD & ADOLESCENT BEHAV. LETTER, no. 5, 2016, at 5, 6 ("Familial transmission of genetic differences largely explains why drug use and abuse behavior runs in families.").

[7] Ruger, *supra* note 1, at 43-44 (distinguishing between internal and external "health capability elements").

creating a brain system that allows the person to prevent the chronic brain disease of addiction, which disrupts neural areas and sequences that allow us to exert free will.[8]

This Article firstly overviews recent neuroscience on the effects of drug use and the process of addiction. Next, the health capability model is outlined. Subcategories of internal factors include health status and health functioning; health knowledge; health-seeking skills and beliefs; self-efficacy; health values and goals; self-governance and self-management, effective health decision-making; intrinsic motivation; and positive expectations. External factors include social norms; social networks and capital; group membership influences; material circumstances; economic, political, and social security; access and utilization of health services; and enabling public health and health care systems. Then, internal and external capabilities of the addiction prevention capabilities set are presented and explained in terms of the relevant neurobiological correlates. By connecting capabilities to addiction neuroscience, we provide a multifaceted strategy to approach the eradication of addiction from society and to promote the ability of all people to live a flourishing life.

[8] *See* Rita Z. Goldstein & Nora D. Volkow, *Dysfunction of the Prefrontal Cortex in Addiction: Neuroimaging Findings and Clinical Implications*, 12 NATURE REVS. NEUROSCIENCE 652, 652-53 (2011) (explaining various symptoms of addiction, such as cravings, intoxication, bingeing and withdrawal which limit the ability of addicts to exercise self-control).

Figure 1. Health Capability Profile[9]

I. INTERNAL FACTORS

A. Health status and health functioning

1. Measures of self-reported health functioning (e.g., SF-36, mental functioning, and physical functioning)

2. Measures of health conditions (e.g., biomedical markers, biomedical diagnoses, disease [e.g., HIV/AIDS, tuberculosis, diabetes, depression and other mental health disorders], risk factors [e.g., smoking, exercise, diet, drug abuse or dependence, safe sex practices, obesity, interpersonal violence])

B. Health knowledge

1. Knowledge of one's own health and health conditions (e.g., does the person with HIV, tuberculosis, or diabetes know they have it and know how to manage the disease?)

2. General knowledge of health and disease, preventive measures to protect health, and risk factors for poor health (e.g., nutrition and diet, transmission of disease, and protection [from STDs], sanitation [handwashing and waste disposal and storage], immunization [to protect against onset of disease], pregnancy and child birth)

3. Knowledge of costs and benefits of health behaviors, lifestyles, exposures

4. Knowledge of how to acquire health information and knowledge (e.g., modes of information gathering [health care provider, Internet, journals and books, special interest groups])

C. Health-seeking skills and beliefs, self-efficacy

1. Beliefs about one's ability to achieve health outcomes, even under adverse circumstances

2. Ability to acquire skills (e.g., monitoring glucose levels, use of condoms) and apply them under changing circumstances to work toward positive health outcomes

3. Confidence in ability to perform or abstain from health behaviors and actions

D. Health values and goals

1. Value of health

2. Value of health-related goals (e.g., cholesterol levels)

3. Value of lifestyle choices and behaviors (e.g., moderate versus excessive drinking)

4. Ability to recognize and counter damaging social norms

E. Self-governance and self-management and perceived self-governance and management to achieve health outcomes

1. Self-management and self-regulation skills and expectations

2. Ability to manage personal and professional situations: ability to handle external pressures (e.g., children, work, household and extended family responsibilities, finances, marital and personal relationships

3. Ability to make the connection between cause and effect with regard to personal behavior and health outcomes; personal responsibility

4. Ability to draw on networks of social groups

5. Vision, direction, planning, strategy, and ability to make positive health choices

F. Effective health decision-making

1. Ability to effectively use both knowledge and resources to prevent onset or exacerbation of disease or prevent death

2. Ability to weigh the short-term and long-term costs and benefits of health behaviors and actions (e.g., smoking)

3. Ability to identify health problems (e.g., employ guidelines of prevention, recognize signs and symptoms) and pursue effective prevention and treatment

4. Ability to make healthy choices under various environmental constraints (e.g., abstain from unpotable water, use sunscreen and bed nets)

G. Intrinsic motivation to achieve desirable health outcomes: extent to which motivation for current or future behavior maintenance or change is internally (e.g., personal responsibility, personal assessment) **or externally** (e.g., mandates, rewards, requirements, peer pressure) **motivated**

H. Positive expectations about achieving health outcomes: optimistic or pessimistic viewpoint on personal life and health prospects

II. EXTERNAL FACTORS

A. Social norms

1. Extent to which health norms are scientifically valid and evidence-based

2. Extent to which health behaviors and health-seeking skills are viewed favorably (e.g., cultures of abstinence from alcohol, drugs, sexual activity) or unfavorably (e.g., cultures of alcohol abuse, obesity within family)

3. Extent to which a health behavior is adopted by a majority or minority of a population in the culture (e.g., whether circumcision is widely accepted and practiced) and by whom

4. Extent to which discrimination or antidiscrimination is the dominant norm in the provision of health care and public health services, influencing disparities in access

5. Norms about decisional latitude or power in familial and social contexts

6. Society's ability to recognize and counter damaging social norms and promote positive ones

B. Social networks and social capital for achieving positive health outcomes

1. Emotional or instrumental support from friends and family (e.g., loving and caring family and friends who help with specific tasks or needs, such as watching children, picking up children from school)

2. Existence of available networks of social groups

3. Extent to which social networks may negatively impact health (e.g., bullies and their complicit accomplices, the "old boys" network, the "in crowd")

C. Group membership influences: church, union, community membership to supplement or counterbalance social norms and social assistance in other social contexts

D. Material circumstances

1. Economic: income and employment status

2. Neighborhood and community (e.g. safety, noise, environmental pollutants, neighborhood facilities and resources)

3. Safe water and sanitation

4. Housing

5. Food security

6. Extent to which immediate environment is toxin- or disease-free (e.g. toxic air, soil, water, inundated with malaria-infected mosquitoes)

E. Economic, political, and social security: extent to which individuals and group feel secure or insecure in their immediate and broader macrosocial environment (e.g., broader changes in the national and subnational economic and political systems generating job, financial, or political insecurity and pessimistic outlook violence, criminal activity)

F. Utilization and access to health services: sought and obtained health services when care was thought needed

1. Serious symptoms of poor health conditions (e.g., shortness of breath, frequent or severe headaches, chest pain, lump in breast, fever, back or neck pain, loss of consciousness)

2. Morbid symptoms of poor health conditions (e.g., sadness, hopelessness, anxiety, pain in knee or hip, fatigue or extreme tiredness, difficulty hearing, fall or other major injury)

3. Perception of the need to see a health provider when experiencing a serious or morbid health symptom

4. Ability to obtain health services when there is a perceived need

5. Presence of barriers (e.g., geographic, financial, linguistic) to access and utilization of services

G. Enabling public health and health care systems

1. Extent to which health care and public health system environment interacts with individual to build and enable health agency (e.g., a health coach for diabetes management)

2. Extent to which health care and public health system environment protects health and safety of public (e.g., contaminated blood supply, food safety and contamination, drug regulation)

3. Health care and public health system effectiveness and accountability

[9] Reprinted with permission from Ruger, *supra* note 1, at 45-46. © AM. J. PUB. HEALTH.

I. SCIENCE OF ADDICTION[10]

Addiction is a chronic brain disease. All addictive drugs of abuse, including alcohol and marijuana, increase dopamine and produce a drug high or euphoria, over-activating the brain's reward circuit to motivate future behavior.[11] Vulnerability to addiction may be caused by lower sensitivity to dopamine:[12] addicted individuals display decreased sensitivity to natural, non-drug reinforcers,[13] which increases the relative strength of drug-induced dopamine rewards. Dopamine-enhancing effects of major illicit drugs temporarily relieves some of the symptoms of mental disorders,[14] leading to heightened vulnerability, although repeated administration triggers receptor downregulation.[15] The brain's reward circuit involves the basal ganglia,

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[10] *See generally* George F. Koob & Nora D. Volkow, *Neurocircuitry of Addiction*, 35 NEUROPSYCHOPHARMACOLOGY REVS. 217 (2010) (describing the brain regions and circuits affected by addiction); Nora D. Volkow & Marisela Morales, *The Brain on Drugs: From Reward to Addiction,* 192 CELL 712 (2015) (discussing "the circuit- and cell-level mechanisms of [addiction] and its co-option of pathways regulating reward, self-control, and affect").

[11] *See generally* George F. Koob & Michel Le Moal, *Drug Abuse: Hedonic Homeostatic Dysregulation,* 278 SCI. 52, 54 (1997) ("Studies suggest that stress-like stimuli and neuropharmacological agents that activate the mesocortico limbic dopamine system can rapidly reinstate intravenous drug self-administration that has been previously extinguished."); Nestler, *supra* note 3, at 1445 (describing how in spite of "disparate mechanisms of action and pharmacological effects, all drugs of abuse cause certain common effects after both acute and chronic exposure").

[12] *See* George F. Koob & Michel Le Moal, *Drug Addiction, Dysregulation of Reward, and Allostasis*, 24 NEUROPSYCHOPHARMACOLOGY 97, 116 (2001) ("Decreased sensitivity to a drug, including sensitivity to the initial aversive effects of a drug, can lead to increased drug intake which can set up further challenges to the reward circuits and interacting neural systems."); Nora D. Volkow et al., *Decreased Striatal Dopaminergic Responsiveness in Detoxified Cocaine-Dependent Subjects,* 386 NATURE 830, 830 (1997) ("Addicts showed reduced dopamine release in the striatum, the brain region where the nucleus accumbens is located, and also had a reduced 'high' relative to controls.").

[13] Goldstein & Volkow, *supra* note 8, at 652; *see also* Peter W. Kalivas & Nora D. Volkow, *The Neural Basis of Addiction: A Pathology of Motivation and Choice,* 162 AM. J. PSYCHIATRY 1403, 1407 (2005) ("[T]he decrease in dopamine release and reception combined with the reduced activation of the prefrontal cortex in response to biologically relevant stimuli may explain the reduced sensitivity of addicted subjects to 'natural' reinforcers.").

[14] *See* Caryn Lerman et al., *Depression and Self-Medication with Nicotine: The Modifying Influence of the Dopamine D4 Receptor Gene*, 17 HEALTH PSYCHOL. 56, 60 (1998) (concluding that the prevalence of smoking among depressed persons may be due to nicotine's roll in the neurotransmission of dopamine). *See generally* Thomas M. Kelly & Dennis C. Daley, *Integrated Treatment of Substance Use and Psychiatric Disorders*, 28 SOC. WORK IN PUB. HEALTH 388 (2013) (examining the co-morbidity of substance use disorders and other psychiatric disorders).

[15] *See* Piazza & Deroche-Gamonet, *supra* note 2, at 404 ("[R]eward systems adapt to the daily overexposure of the brain to drugs by shifting the homeostatic set point (allostasis) to adapt to

which is involved in positive forms of motivation that have pleasurable effects such as socializing, eating, and sex, as well as involvement in the formation of habits and routines.[16] In receptor downregulation, brain circuits become less sensitive to dopamine as they adapt, decreasing the relative motivation from daily healthy activities.[17] That is, the neural adaptations arising from repeated drug exposure make it difficult for individuals to gain pleasure from anything besides substances, perpetuating a cycle of drug use in increasing quantities and frequencies.[18] The extended amygdala is also involved in states of unease, irritability and anxiety, which are heightened in withdrawal after the euphoria from drugs attenuates.[19] These negative states motivate cyclical drug-seeking behavior, which in its late stages is characterized by temporary relief from the pain and distress of withdrawal, rather than desire or ability to get high.[20]

The dopamine system is fundamental to the function of the prefrontal cortex (PFC), involving abilities to think, plan, solve problems; executive function, self-control, self-regulation, working memory, decision-making, judgement; and regulating the function of the limbic system (processes emotions and stressful stimuli[21]).[22] Among brain structures, the PFC takes the longest to

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this continuous overstimulation."); Jason M. Uslaner et al., *The Attribution of Incentive Salience to a Stimulus that Signals an Intravenous Injection of Cocaine,* 169 BEHAV. BRAIN RES., 320, 323 (2006) ("We established . . . that a drug-associated cue can acquire incentive salience leading to Pavlovian conditioned approach behavior."); *see also* Nora D. Volkow et al., *Cocaine Cues and Dopamine in Dorsal Striatum: Mechanism of Craving in Cocaine Addiction*, 26 J. NEUROSCIENCE 6583, 6583 (2006) ("[W]hen neutral stimuli are paired with a rewarding drug they will, with repeated associations, acquire the ability to increase DA in NAc and in dorsal striatum (becoming conditioned cues), and these neurochemical responses are associated with drug-seeking behavior.").

[16] Peter W. Kalivas & Nora D. Volkow, *The Neural Basis of Addiction: A Pathology of Motivation and Choice*, 162 AM. J. PSYCHIATRY 1403, 1403 (2005).

[17] *Id*.; Koob & Le Moal, *supra* note 11, at 55.

[18] *See* Piazza & Deroche-Gamonet, *supra* note 2, at 404.

[19] *See generally* Michael Davis et al., *Phasic vs Sustained Fear in Rats and Humans: Role of the Extended Amygdala in Fear vs Anxiety,* 35 NEUROPSYCHOPHARMACOLOGY 105 (2010) (describing the differences in the role of the extended amygdala in phasic and sustained fear).

[20] Koob & Le Moal, *supra* note 11, at 52-53.

[21] Joanna S. Fowler et al., *Imaging the Addicted Human Brain*, 3 SCI. PRAC. & PERSP. 4, 5 (2007); Lisa M. Najavits et al., *Substance Use Disorder and Trauma*, *in* 1 APA HANDBOOK OF TRAUMA PSYCHOLOGY 195, 203 (Steven N. Gold ed., 2017).

[22] *See generally* Gareth Ball et al., *Executive Functions and Prefrontal Cortex: A Matter of Persistence?* 5 FRONTIERS SYS. NEUROSCIENCE, Jan. 2011, at 1 ("We propose that persistence [of neural activity] within the [prefrontal cortex] reflects dynamic network formation and these findings underline the importance of frequency analysis of fMRI time-series in the study of executive functions); Britta K. Hölzel et al., *How Does Mindfulness Meditation Work? Proposing Mechanisms of Action from a Conceptual and Neural Perspective,* 6 PERSP. ON

develop, increasing adolescent vulnerability to social pressure, impulsivity, and poor decision-making.[23] Addiction pathologically disrupts these areas, scrambling the sequences that enable us to exert free will.[24] This is consistent with disease progression in latter stages of addiction: not only does the reward system adapt to overexposure, shifting the homeostatic set point to recognize the normal state as involving drugs, but dopamine cells stop firing after repeated exposure to a reward, firing instead when exposed to the stimuli that predict the reward.[25] Dopamine release shifts backwards, increasing when stimuli that predict drug availability are present; the conditioning of these secondary reinforcers uses the same neural mechanisms and processes as natural reinforcers.[26] Thus, drugs hijack the brain's learning and memory systems to incentivize behaviors that lead to drug use, enhancing motivation for drug-seeking behaviors by conditioning predictive stimuli as secondary reinforcers. For example, drug use tips the reward-stress circuit balance away from the frontal lobes, toward the basal ganglia and extended amygdala, leading to compulsive drug-seeking behavior and reduced impulse control.[27] In the terminal, loss-of-control stages of addiction, the reward circuit experiences qualitative differences between drugs and natural reinforcers; coupled with a loss of synaptic plasticity in the nucleus accumbens (NAcc) and medial prefrontal cortex (mPFC), behavior crystallizes around one goal.[28]

PSYCHOL. SCI. 537, 548-49 (2011) (explaining the neurological processes in the PFC as subjects who had received mindfulness training engaged in self-reflection, self-reference, narration, and experience); Mounir Ouzir & Mohammed Errami, *Etiological Theories of Addiction: A Comprehensive Update on Neurobiological, Genetic and Behavioral Vulnerability*, 148 PHARMACOLOGY BIOCHEMISTRY BEHAV. 59, 61 (2016) (discussing the role of the PFC in decision making, planning, learning and motivation).

[23] Joanna S. Fowler et al., *Imaging the Addicted Human Brain*, SCI. & PRAC. PERSP., Apr. 2007, at 4, 6; Jay N. Giedd et al., *Brain Development During Childhood and Adolescence: A Longitudinal MRI Study*, 2 NATURE NEUROSCIENCE 861, 861-63 (1999); Marvin D. Krohn, Alan J. Lizotte & Cynthia M. Perez, *The Interrelationship Between Substance Use and Precocious Transitions to Adult Statuses,* 38 J. HEALTH SOC. BEHAV. 87, 98-99 (1997); Lindsay M. Squeglia et al., *Brain Development in Heavy-Drinking Adolescents,* 172 AM. J. PSYCHIATRY 531, 535-42 (2015).

[24] *See generally* Goldstein & Volkow, *supra* note 8 ("Disruption of the [prefrontal cortex] in addiction underlies not only compulsive drug taking but also accounts for the disadvantageous behaviors that are associated with addiction and the erosion of free will.").

[25] Piazza & Deroche-Gamonet, *supra* note 2, at 404.

[26] *Id.* at 400-01.

[27] Koob & Le Moal, *supra* note 11, at 54.

[28] Piazza & Deroche-Gamonet, *supra* note 2, at 389.

Since multiple neural networks are disrupted by drugs,[29] treatment should follow a multi-pronged strategy. This may include: enhancing motivation for non-drug behaviors, strengthening PFC circuits to improve cognitive control over desires and emotions and to predict situations where risk for taking drugs is heightened, and decreasing the strength of conditioned stimuli by decreasing sensitivity to stressors and improving negative emotions. Especially because drug use changes neural structures and connectivity, quitting is a complex and difficult process even with a strong will or the best intentions.[30] Moreover, certain populations are uniquely vulnerable to addiction. Adolescents are more vulnerable to risky behaviors which may lead to addiction,[31] and the adolescent brain is at heightened risk for addiction.[32] The brain develops throughout the twenties, alongside significant social changes in young people's lives.[33] The Longitudinal Study of Adolescent Brain Cognitive Development (ABCD Study)[34] studies the effects of social, environmental, and genetic factors on young people's neural development, cognitive development, and life trajectory. Additionally, individuals with co-morbid mental illnesses—two or more illnesses occurring simultaneously or subsequently, implying exponentially detrimental interactions between the illnesses—are at heightened risk for addiction.[35]

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[29] *See generally* Koob & Volkow, *supra* note 10 ("[M]ultiple brain regions and circuits are disrupted in drug addiction and are likely to contribute differentially to the complex phenotype observed in addicted individuals.").

[30] Golnaz Tabibnia & Dan Radecki, *Resilience Training That Can Change the Brain*, 70 CONSULTING PSYCHOL. J.: PRAC. & RES. 59, 78 (2018).

[31] *See* Hicham El Kazdouh et al., *Adolescents, Parents and Teachers' Perceptions of Risk and Protective Factors of Substance Use in Moroccan Adolescents: A Qualitative Study,* 13 SUBSTANCE ABUSE TREATMENT PREVENTION POL'Y 1, 1 (2018) (concluding, based on the results of a socio-ecological study, that adolescents in Morocco may become more susceptible to addiction based on risk and protective factors); Daniel T. L. Shek et al., *Development, Implementation, and Evaluation of a Multi-Addiction Prevention Program for Primary School Students in Hong Kong: the B.E.S.T. Teen Program,* 6 ASIAN J. GAMBLING ISSUES & PUB. HEALTH, July 8, 2016, at 1, 1 (2016) (noting that, "an increasing proportion of high risk adolescents were found to be vulnerable to risk behaviors," not just in the West but also elsewhere, including Hong Kong).

[32] Palmer & McGeary, *supra* note 6, at 5.

[33] Joanna Chambers, *The Neurobiology of Attachment: From Infancy to Clinical Outcomes*, 45 PSYCHODYNAMIC PSYCHIATRY 542, 553 (2017).

[34] *See* Editorial Staff, *NIH's Adolescent Brain Cognitive Development (ABCD) Study*, 39 ALCOHOL RES.: CURRENT REVS. 97, 97 (2017) (describing the ABCD Study).

[35] Ouzir & Errami, *supra* note 22, at 63; *see also* Robert M. Anthenelli, *Focus On: Comorbid Mental Health Disorders*, 33 ALCOHOL HEALTH 109 (2010) (suggesting "dysregulation of the brain's and body's stress system" as a possible explanation for the relationship of alcohol use disorders with mood and anxiety disorders); *see generally* Bridget F. Grant et al., *Prevalence and Co-Occurrence of Substance Use Disorders and Independent Mood and Anxiety Disorders:*

While certain populations are particularly vulnerable to drug use and addiction, everyone deserves the ability to live a life free from addiction. The addiction prevention capabilities set builds off neuroscientific research to strengthen the neural systems that act as protective factors against drug use and addiction. For example, individuals who are more resistant to addiction still experience the deleterious impairments of drugs but exhibit greater active resilience in the ability to recover synaptic plasticity,[36] suggesting an addiction-prevention role for activities that increase neurogenesis, neural plasticity, resilience, and cognitive flexibility. Addiction prevention capabilities pro-actively and positively train the brain for neural fitness, creating a strong and healthy set of capabilities that authoritatively and automatically regulate individual drug-abstinence and recovery behavior even in the presence of environmental risk factors.

II. HEALTH CAPABILITY MODEL[37]

The Health Capability Model consists of internal and external factors. Internal factors are internal capabilities to be developed. These include several categories. First, health status and health functioning are critical. These abilities are assessed through self-reported functioning (e.g., mental and physical functioning), as well as biomedical and social measures of health (biomedical markers, diagnoses, and diseases; lifestyle and social risk factors). A second category includes health knowledge. This ability is assessed through knowledge of: personal health, including how to prevent and manage health conditions; general health and disease, preventive practices for good health, and risk factors for poor health; cost-benefit analysis of different health behaviors, lifestyles, and exposures; and channels for gaining health knowledge.

A third category is health-seeking skills and beliefs, including self-efficacy. This ability is assessed through beliefs about personal abilities to achieve health outcomes, even under adverse circumstances; the ability to acquire and apply positive health skills; and confidence in personal ability to execute health behaviors. A fourth category of health values and goals is assessed by the personal value of health, health-related goals, lifestyle choices, and health behaviors. It also includes the ability to recognize and resist harmful social norms. A fifth category of internal abilities is self-governance and self-management, including one's perceived self-governance and management

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Results from the National Epidemiologic Survey on Alcohol and Related Conditions, 29 ALCOHOL RES. HEALTH 107 (2004) ("Associations between most substance use disorders and independent mood and anxiety disorders were overwhelmingly positive and significant . . . .").

[36] Piazza & Deroche-Gamonet, *supra* note 102, at 406.

[37] Ruger, *supra* note 1, at 43-48.

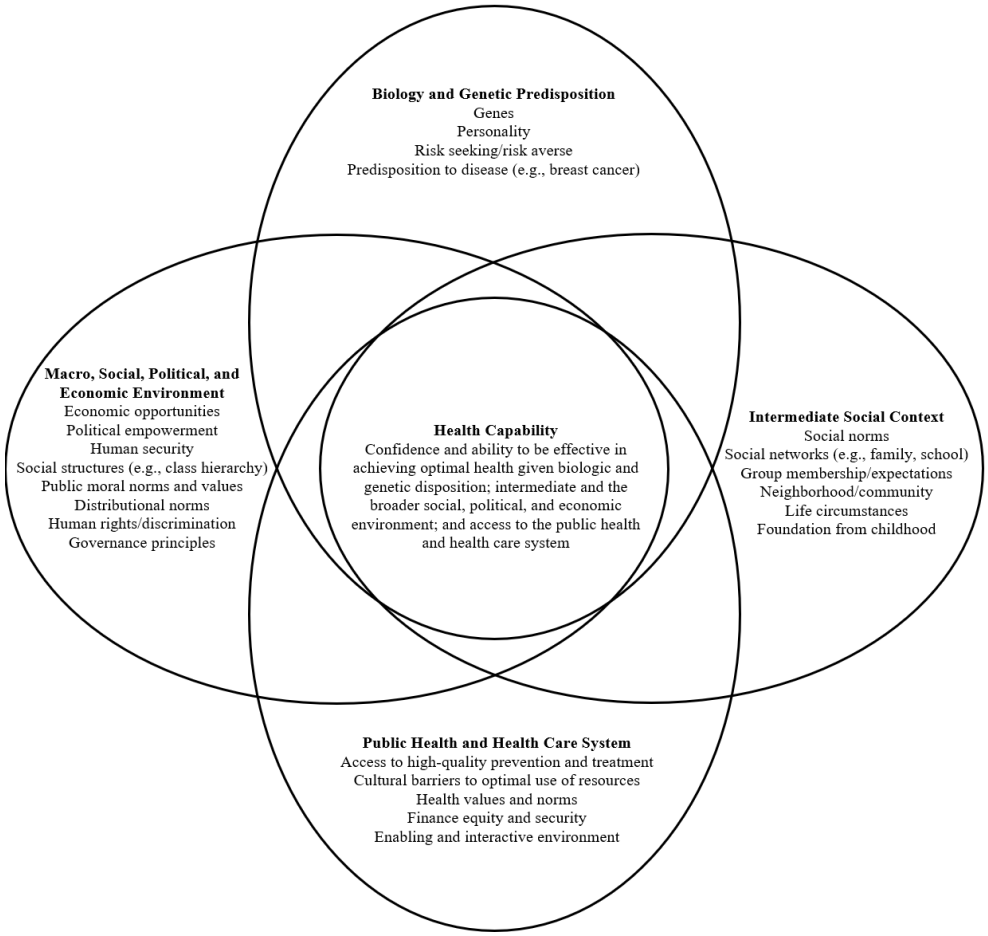
to achieve health outcomes. These abilities are developed and assessed through one's expectations and skills surrounding self-management and self-regulation, including the management of personal and professional situations, external stress and positive health choices. It also involves the ability to causally connect personal behavior to health outcomes, personal responsibility, and utilizing social networks.

A sixth category is effective health decision-making, which includes using knowledge and resources to prevent morbidity and mortality, effectively understanding the short-term and long-term trade-offs of behaviors, recognizing health problems and pursuing prevention and treatment, and making healthy choices despite environmental limitations. A seventh category of internal abilities is intrinsic motivation to attain desirable health outcomes (e.g. through personal assessment and responsibility) rather than external motivation (e.g. by rules, rewards, or peer pressure) to maintain or change one's behavior. The final category of internal abilities involves having positive, optimistic perspectives and expectations about one's life and prospects for achieving health outcomes.

The Health Capability Model also includes external capabilities to be societally developed. The first of these external abilities is social norms—scientifically valid and evidence-based norms that are perceived positively and adopted by most people, such as antidiscrimination in provision or equitable decisional power in familial and social contexts. Social norms also envelop society's ability to recognize harmful norms and counter them by promoting positive norms. A second category is the availability and existence of social networks and capital that support achieving positive health outcomes, such as friends and family. This ability recognizes and actively works to counter the negative impacts of social networks on health.

A third category of external abilities relates to influences from group memberships, which either reinforce or offset social norms, and can provide assistance in social domains. A fourth category is material circumstances: economic (income, employment status, housing, food security); neighborhood and community (safety and order, calm, resources, activities and opportunities, access to nature and green and social space, access to healthy food); and sanitation (safe water, pollution, maintained infrastructure and cleanliness). A fifth category is economic, political, and social security in immediate and broader macrosocial environment. A sixth category involves health services: seeking care when perceived as necessary, seeking a health provider for morbid health symptoms; obtaining and utilizing care; and ease of access to care. A final category of external abilities to be developed are effective and accountable public health and health care systems that enable, empower, and develop individuals' health agency while protecting public health and safety.

Figure 2. Health Capability Diagram[38]



III. ADDICTION PREVENTION CAPABILITIES SET

A. Internal Capabilities

A capabilities set specific to substance abuse prevention is the potential solution to the addiction problem. Similar to a vaccine, the addiction prevention capabilities set inoculates a person from addiction. This fundamental, influential, and critical capabilities set works to regulate behavior upstream, and is not under another regulatory influence, instead strengthening the executive

[38] Reprinted with permission from Ruger, *supra* note 1, at 45-46. © AM. J. PUB. HEALTH.

and habitual parts of the brain to create a protective structure against addiction. The capabilities set has elements that correspond to the categories of internal and external abilities noted previously. These abilities and their positive impacts on neural systems are described in the remaining paragraphs in this section.

Healthy habits such as proper sleep, nutrition, dietary restriction, and hydration, as well as energy management strategies such as meditation, controlled breathing, and progressive muscle relaxation[39] play important roles in protecting the brain against addiction vulnerability. These abilities create a wellness that obviates the need to seek short-term pleasure, improving negative emotions, decreasing sensitivity to stressors, and decreasing strength of conditioned stimuli. For example, one major psychological strategy for sustaining resilience in the nervous system includes these behaviors that boost physical health. Sleep encourages homeostasis, memory consolidation, and improved mood, impacting the serotonin system, hypothalamic-pituitary-adrenal (HPA) stress response system, mPFC-amygdala connection, and neo-cortex.[40] Food restriction (calories per meal, frequency of meals) can slow disease and benefit fear extinction while improving memory, mood, sleep, quality of life, and cognitive function over time; it impacts the BDNF and serotonin systems, the amygdala, and protects hippocampal neurons against degeneration.[41] Additionally, a high fat and sucrose diet decreases BDNF, and learning and memory ability, while omega-3 fatty acids and anti-oxidants increase hippocampal synaptic plasticity.[42] Exercising fights disease, improves mood,[43] and attenuates the stress response, cognitive function, self-efficacy,[44] learning, and memory; it increases BDNF, serotonin, neurogenesis in the hippocampus and lPFC, while decreasing activity in the posterior cingulate

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[39] *See* Karen J. Reivich & Martin E. P. Seligman, *Master Resilience Training in the US Army*, 66 AM. PSYCHOLOGIST 25, 28 (2011) (discussing, in the context of resilience training for soldiers, energy management strategies, such as meditation, controlled breathing, and progressive muscle relaxation).

[40] Fernando Gomez-Pinilla, *The Influences of Diet And Exercise On Mental Health Through Hormesis*, 7 AGEING RES. REV. 49, 55 (2008); Tabibnia & Radecki, *supra* note 30, at 76.

[41] Tabibnia & Radecki, *supra* note 30, at 66, 76; Gomez-Pinilla, *supra* note 4040, at 50-51.

[42] Gomez-Pinilla, *supra* note 40, at 51.

[43] *See, e.g.*, Yves Rolland et al., *Exercise Program for Nursing Home Residents with Alzheimer's Disease: A 1-Year Randomized, Controlled Trial,* 55 AM. GERIATRICS SOC'Y 158, 164 (2007) ("[C]ombined interventions including physical activity have led to better physical health, lower depression, or better functional mobility in [a population with Alzheimer's disease] . . . .").

[44] *See generally* Rod K. Dishman et al., *Social-Cognitive Correlates of Physical Activity in a Multi-Ethnic Cohort of Middle-School Girls: Two-year Prospective Study*, 35 J. PEDIATRIC PSYCHOL. 188, 189 (2010) (noting the correlation between physical activity and self-efficacy).

cortex (PCC).[45] Conversely, a sedentary lifestyle and overconsumption of food increases the risk of neurodegenerative diseases.[46] MAP (mental and physical) training is hypothesized to work through hippocampal neurogenesis; aerobic exercise increases the neural production in adults, while mental training keeps those cells alive.[47]

In terms of health knowledge, general knowledge of the dangers of putting a toxic substance in your brain and knowledge of the costs and benefits of drug exposure[48] and use are critical for individuals, medical doctors, and policymakers. Addiction is pathological in its chronic disruption of the areas and sequences in the brain that enable us to exert free will.[49] Cognitive affective theories and findings suggest that changing attitudes that led to drug abuse, such as self-importance and a behavior-consequence disconnect,[50] to beliefs that the effects of drugs are dangerous and irreversible are crucial to addiction prevention.[51] Indeed, despite personal and cultural factors, perceptions among young people of drug use as harmful decreases drug use.[52]

General knowledge of the limits of self-control and drug tolerance are also crucial. Specifically, understanding that the brain adapts to prolonged and increasingly higher doses to function normally when the drug is present and abnormally when absent[53] refutes experimentation and greatly increases the difficulty of successfully stopping drug use. Both structure and function

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[45] Tabibnia & Radecki, *supra* note 30, at 76; *see also* Gomez-Pinilla, *supra* note 40, at 52-53; Rod K. Dishman et al., *Neurobiology of Exercise*, 14 OBESITY 345, 346 (2006) ("Chronic physical activity improves brain health."). *See generally* Catherine L. Davis et al., *Exercise Improves Executive Function and Achievement and Alters Brain Activation in Overweight Children: A Randomized, Controlled Trial*, 30 AM. PSYCHOL. ASS'N 91, 96 (2011) (showing that exercise in overweight children led to increased PFC activity); Yves Rolland et al., *Physical Activity and Alzheimer's Disease: From Prevention to Therapeutic Perspectives*, 9 J. AM. MED. DIRECTORS ASS'N 390, 396 (2008) (discussing the measurements of neurotransmitters in response to exercise and physical activity).

[46] Ang et al., *supra* note 3, at 1.

[47] B.L. Alderman et al., *MAP Training: Combining Meditation and Aerobic Exercise Reduces Depression and Rumination While Enhancing Synchronized Brain Activity,* 6 TRANSLATIONAL PSYCHIATRY 1, 1 (2016).

[48] Shek, *supra* note 31, at 1-2 (explaining the heightened risk of addiction in adolescents).

[49] *See generally* Goldstein & Volkow, *supra* note 8 ("Disruption of the PFC in addiction underlies not only compulsive drug taking but also accounts for the disadvantageous behaviors that are associated with addiction and the erosion of free will.").

[50] J.E. SCHULENBERG ET AL., 2 MONITORING THE FUTURE: NATIONAL SURVEY RESULTS ON DRUG USE, 1975–2018: COLLEGE STUDENTS AND ADULTS AGES 19–60, at 70, 253, 256 (2018), http://monitoringthefuture.org/pubs/monographs/mtf-vol2_2018.pdf [https://perma.cc/NPT5-UHCE].

[51] Palmer & McGeary, *supra* note 6, at 6 (noting that "attitudes toward drug use" may be a factor in adolescent substance use).

[52] SCHULENBERG ET AL., *supra* note 50, at 23.

[53] Piazza & Deroche-Gamonet, *supra* note 2, at 389.

of dopamine neurons are undeniably affected by all drugs of abuse, especially the synaptic plasticity of dopaminergic cells in the ventral striatum and PFC. Moreover, these changes in the brain are long-lasting; dependence may persist for the entire life span,[54] and the neural adaptations that reinforce relapse cannot simply be undone by long periods of abstinence.[55] Additionally, knowledge of unique individual vulnerabilities is essential; for example, Adverse Childhood Experiences (ACEs) are linked to initial opioid use.[56] Trauma, stress, and periods of transition all constitute individual risk factors for substance abuse and addiction.[57]

Health-seeking skills include abilities to execute strategies to avoid addiction under changing circumstances. The loss of synaptic plasticity strips the brain of its control over neuronal circuits, which respond adaptively to shifting environmental circumstances.[58] Strengthened PFC circuits are able to predict and avoid situations where risk for taking drugs is heightened, and exert cognitive control over desires and emotions.[59] As individual behavior change and population response were more associated with neural activity in the ventromedial (vm)PFC than self-report judgments,[60] neurobiology plays a more significant role in health-seeking than beliefs about self-efficacy alone. Medial PFC activation was positively associated with smokers' successful quitting, even

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[54] *Id.* at 387, 404.

[55] Warren K. Bickel et al., *21st Century Neurobehavioral Theories of Decision Making in Addiction: Review and Evaluation*, 164 PHARMACOLOGY BIOCHEMISTRY BEHAV. 4, 10 (2016).

[56] Shanta R. Dube et al., *Childhood Abuse, Neglect, and Household Dysfunction and the Risk of Illicit Drug Use: The Adverse Childhood Experiences Study*, 111 PEDIATRICS 564, 567 (2003); David A. Wiss, *A Biopsychosocial Overview of the Opioid Crisis: Considering Nutrition and Gastrointestinal Health,* 7 FRONTIERS PUBL. HEALTH, July 9, 2019, at 1, 5 (2019).

[57] *See* Najavits et al., *supra* note 21, at 198 (describing how traumatized children may be at increased risk of substance abuse later in life); Martin H. Teicher & Jacqueline A. Samson, *Childhood Maltreatment and Psychopathology: A Case for Ecophenotypic Variants As Clinically and Neurobiologically Distinct Subtypes*, 170 AM. J. PSYCHIATRY 1114, 1119 (2013) ("Physical maltreatment appears to be a particularly salient risk factor for the development of substance abuse and progression to injection drug use."). *See generally* Andrea L. Stone et al., *Review of Risk and Protective Factors of Substance Use and Problem Use in Emerging Adulthood*, 37 ADDICTIVE BEHAVS. 747 (2012) (describing the risk factors for substance abuse, including stressful life events and transition periods).

[58] Piazza & Deroche-Gamonet, *supra* note 2, at 406.

[59] Ball et al., *supra* note 22, at 1, 8; *see also* Volkow & Morales, *supra* note 10, at 716 ("[L]ow levels of D2R in striatum may mediate the risk for compulsive drug taking in part by impairing PFC regions that inhibit prepotent responses and enable flexibility of behavioral choices as a function of changing environments.").

[60] *See e.g.* Emily B. Falk et al., *From Neural Responses to Population Behavior: Neural Focus Group Predicts Population-Level Media Effects,* 23 PSYCHOL. SCI. 439, 443 (2012) (finding that ventromedial scans of the PFC were more effective than subject self-reporting in gauging their likely behavior).

after controlling for self-reported intentions and efficacy, which are traditional measures of behavior change.[61] Furthermore, strengthening the PFC could help prevent the onset of addiction because during backward-shifting of conditioned reinforcers, drugs activate the same neurobiological mechanisms as the normal learning process for appetitive stimuli.[62] One way to do this would be through mindfulness training, which increases activation in the frontal lobe, involved in emotion, memory, initiating thinking, reasoning, and judgement, as well as behavior, movement, and speaking.[63]

Health-seeking skills also include beliefs such as self-efficacy, self-esteem,[64] a sense of meaning and purpose, and a growth mindset, which are crucial and widely-studied factors in neural resilience and overall well-being.[65] Identifying, developing, and applying character strengths contributes to mental well-being,[66] improves assertiveness and self-control, and reduces bad conduct.[67] A growth mindset was correlated with decreased mental health problems[68] and increased empowerment and self-esteem.[69] Positive beliefs in one's abilities predicted actively coping with adversity, planning, processing one's emotions, and leveraging social support.[70] The brain structures that support this self-referential processing (mPFC, PCC, inferior parietal lobe) structurally and functionally benefit from

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[61] Emily B. Falk et al., *Neural Activity During Health Messaging Predicts Reductions in Smoking Above and Beyond Self-Report*, 30 HEALTH PSYCHOL. 177, 182 (2011).

[62] Piazza & Deroche-Gamonet, *supra* note 2, at 387, 401.

[63] Zohreh Doborieh et al., *Spiking Neural Network Modelling Approach Reveals How Mindfulness Training Rewires the Brain*, 9 SCI. REP., Apr. 23, 2019, at 1, 1, 7 (2019).

[64] *See* Reivich & Seligman, *supra* note 39, at 25 ("There are a number of evidence-based protective factors that contribute to resilience: optimism, effective problem solving, faith, sense of meaning, self-efficacy, flexibility, impulse control, empathy, close relationships, and spirituality.").

[65] Guang Zeng et al., *Effect of Growth Mindset on School Engagement and Psychological Well-Being of Chinese Primary and Middle School Students: The Mediating Role of Resilience,* 7 FRONTIERS PSYCHOL., Nov. 29, 2016, at 1, 2.

[66] MARTIN E. P. SELIGMAN, FLOURISH: A VISIONARY NEW UNDERSTANDING OF HAPPINESS AND WELL-BEING 85 (2011); Reivich & Seligman, *supra* note 39, at 25, 29.

[67] J.J. Cutuli et al., *Preventing Co-Occurring Depression Symptoms in Adolescents with Conduct Problems*: *The Penn Resiliency Program*, 1094 ANNALS N.Y. ACAD. SCI. 282, 285 (2006).

[68] *See* Jessica L. Schleider et al., *Implicit Theories and Youth Mental Health Problems: A Random-Effects Meta-Analysis,* 35 CLINICAL PSYCHOL. REV. 1, 1 (2015) (finding, as a result of a meta-analysis, that youths who believe that personal characteristics are fixed tend to have more mental health problems).

[69] Fenneke Verberg et al., *Mindset and Perseverance of Adolescents with Intellectual Disabilities: Associations with Empowerment, Mental Health Problems, and Self-Esteem,* 91 RES. DEVELOPMENTAL DISABILITIES 1, 8 (2019).

[70] Julie Doron et al., *Coping with Examinations: Exploring Relationships Between Students' Coping Strategies, Implicit Theories of Ability, and Perceived Control*, 79 BRIT. J. EDUC. PSYCHOL. 515, 520 (2009).

mindfulness meditation.[71] Experienced meditators exhibit increased functional connectivity between the PCC, dorsal anterior cingulate cortex (ACC), and dorsolateral (dl)PFC during rest and mindfulness meditation, suggesting increased conflict monitoring and cognitive control,[72] as well as an immediate, sustained, enhancement in resilience.[73]

Regarding health values and goals, the ability to evaluate one's own health goals and the agency to choose better ones is critical. At the loss-of-control stage of addiction, the NAcc and mPFC lose synaptic plasticity; as their ability to select appropriate goal-directed behaviors is impaired, behavior crystalizes around one goal, leading to extreme perseverance.[74] The dopaminergic corticostriatal neurons, which are involved in cognitive control processes, are targeted by drug use;[75] their dysfunction has been associated with relapse.[76] The dorsal striatum and putamen permit afferent information into the PFC, contributing to informational processing of motivational stimuli (e.g. cravings, emotional memories, stressful situations, drug-related cues) and either goal crystallization or goal change.[77]

In terms of self-management and self-governance, ability to cope with unique individual vulnerabilities (e.g. genetic predispositions, low sensitivity to dopamine, social risk, adolescence, transition periods[78]) is critical. Root causes of drug addiction are often unrelated to the drug problem itself,[79] and effective

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[71] Hölzel et al., *Mindfulness*, *supra* note 22, at 546-47.

[72] Judson A. Brewer et al., *Meditation Experience is Associated with Differences in Default Mode Network Activity and Connectivity,* 108 PROC. NAT'L ACAD. SCI. U.S. 20254, 20255 (2011); Seoyeon Kwak et al., *The Immediate and Sustained Positive Effects of Meditation on Resilience Are Mediated by Changes in the Resting Brain,* FRONTIERS HUM. NEUROSCIENCE, Mar. 26, 2019, at 1, 6.

[73] Hölzel et al., *Mindfulness*, *supra* note 22, at 539.

[74] Piazza & Deroche-Gamonet, *supra* note 2, at 387, 407.

[75] *See generally* Liana Fattore & Marco Diana, *Drug Addiction: An Affective-Cognitive Disorder in Need of a Cure,* 65 NEUROSCIENCE BIOBEHAVIORAL REVS. 341, 351 (2016) ("Structure and functioning of dopamine neurons is incontestably affected by virtually all drugs of abuse, and synaptic plasticity of dopaminergic cells in the ventral striatum and prefrontal cortex has been widely described.").

[76] *See* Judson A. Brewer al., *Pretreatment Brain Activation During Stroop Task is Associated with Outcomes in Cocaine-Dependent Patients,* 64 BIOLOGICAL PSYCHIATRY 998, 1001 (2008) (finding that increased activity in corticostriatal brain regions is related to resisting stress-related stimuli associated with relapses).

[77] Piazza & Deroche-Gamonet, *supra* note 2, at 389.

[78] *See generally* Palmer & McGeary, *supra* note 6 (describing models of drug addiction in teens and young adults).

[79] *See e.g.*, Wiss, *supra* note 56, at 2-4 (exploring the "social and environmental factors" driving the opioid epidemic).

treatment addresses co-morbid mental disorders and non-drug related needs.[80] For example, stress contributes to addiction vulnerability, maintenance, and relapse.[81] Stress challenges the brain's ability to self-regulate, compromising PFC functioning and leaving the visual-sensory-based Situationally Accessible Memory (SAM) system vulnerable to addiction triggers;[82] furthermore, changes in corticotropin-releasing factor (CRF) compromise neurocircuitry.[83] Stress exposure releases dynorphin, which preferentially activates kappa opioid receptors (kOR) to increase the rewarding effects of drugs, and reciprocally activates CRF.[84] Reciprocal activation between CRF and orexin systems may additionally explain stress-induced relapse, as these drugs enhance the release of CRF, which promotes impulsivity and vulnerability to addiction, while increasing the neurotransmitter norepinephrine, which in turn is thought to interact with CRF to also increase the rewarding effects of drugs.[85]

Therefore, ability to manage external pressures from personal, social and professional situations, including societal forces such as the mass media and systemic oppression, is essential. A growth mindset and perceived control are linked to faster stress recovery, [86] and decreased PTSD symptoms, depression, substance use, and self-injurious motivations.[87] A growth mindset enhances resilience and protects against stress.[88] The mPFC and HPA axis can be inoculated against stress through experience with moderate stressors and behavioral strategies of exposure and reconsolidation; the mPFC and amygdala also benefit from active avoidance strategies that help to reduce fear and facilitate general active coping.[89] The brain regions implicated in extinguishing conditioned fear responses and its retention are the vmPFC, amygdala, and hippocampus; the vmPFC and hippocampus cooperatively

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[80] *See generally* Kelly & Daley, *supra* note 14 (discussing effective treatment of those with substance abuse disorders and other mental health disorders).
[81] Ouzir & Errami, *supra* note 2222.
[82] Holly Matto, *A Bio-Behavioral Model of Addiction Treatment: Applying Dual Representation Theory to Craving Management and Relapse Prevention*, 40 SUBSTANCE USE MISUSE 529, 532 (2005).
[83] Wiss, *supra* note 56, at 3.
[84] Ouzir & Errami, *supra* note 2222, at 62.
[85] *Id.* at 61-62; O. Levran et al., *Stress-Related Genes and Heroin Addiction: A Role for a Functional FKBP5 Haplotype*, 45 PSYCHONEUROENDOCRINOLOGY 67, 68-9 (2014).
[86] Jessica L. Schleider & John R. Weisz, *Reducing Risk for Anxiety and Depression in Adolescents: Effects of a Single-Session Intervention Teaching that Personality Can Change*, 87 BEHAV. RES. THERAPY 170, 178 (2016).
[87] Hans S. Schroder et al., *Growth Mindset of Anxiety Buffers the Link Between Stressful Life Events and Psychological Distress and Coping Strategies*, 110 PERSONALITY INDIVIDUAL DIFFERENCES 23, 23 (2017).
[88] Zeng et al., *supra* note 6565, at 2, 6.
[89] Tabibnia & Radecki, *supra* note 30, at 62-64.

inhibit fear, perhaps by down-regulating the amygdala to suppress fear, and vmPFC activation and thickness is important in successful extinction recall.[90] These regions are functionally and structurally strengthened through mindfulness practice: increasing activation and grey matter concentration in the vmPFC and hippocampus.[91]

The positive counterpart of coping with vulnerabilities and decreasing sensitivity to stressors is the ability to live a good life, attain pleasure, maintain a sense of meaning and purpose, and improve negative emotions without using substances. The mesolimbic dopamine system mediates natural rewards and the effects of drugs,[92] which are significantly higher than natural rewards and do not habituate like natural reinforcers.[93] Studies suggest that addiction prevention programs should strengthen young people's abilities, develop their developmental assets, and promote life satisfaction.[94] Furthermore, replacement activities and habits that naturally create pleasurable feelings of reward, such as prosocial motivation, vicarious experience of others' rewards,[95] and exercise obviate the need for dopamine that may initiate substance use.[96]

The ability to build and enjoy social relationships and connection is a critical resource in generating mental rewards that preclude pleasure-seeking through drugs. Experiences like laughter, pride in accomplishment, great joy, a feeling of belonging, meaning, and life purpose that contribute to well-being are amplified through positive relationships.[97] Social support and connection are reliable ways to feel better[98] that are correlated with physical

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[90] Britta K. Hölzel et al., *Could Meditation Modulate the Neurobiology of Learning Not to Fear?, in* POSITIVE NEUROSCIENCE 175, 178-79 (Joshua D. Greene, India Morrison & Martin E.P. Seligman eds., 2016); Hölzel et al., *Mindfulness*, *supr*a note 22, at 543, 546.
[91] Hölzel et al., *supra* note 90, at 180; Hölzel et al., *supra* note 22, at 546-47.
[92] Bickel et al., *supra* note 55, at 7.
[93] Piazza & Deroche-Gamonet, *supra* note 2, at 401.
[94] Shek et al., *supra* note 31, at 2.
[95] *See* Jamil Zaki & Jason P. Mitchell, *Prosociality as a Form of Reward Seeking, in* POSITIVE NEUROSCIENCE, *supra* note 90, at 57, 62 ("[P]eople may experience reward based on prosocial *outcomes*, such as the vicarious joy one experiences while watching others receive prizes or display positive emotion." (emphasis added)).
[96] *See* Richard A. Dienstbier, *Arousal and Physiological Toughness: Implications for Mental and Physical Health,* 96 PSYCHOL. REV. 84, 84 (1989) ("Physical fitness through regular aerobic exercise is particularly important as a possible means for self-regulated [psychological] toughening," which "corresponds with positive performance in even complex tasks, with emotional stability, and with immune system enhancement"). Physical exercise is widely recognized as effective in combatting medical diseases and stress, while enhancing mood and cognition. Tabibnia & Radecki, *supra* note 30, at 67.
[97] Celia Menéndez-Hernández et al., *Evaluation of the Addiction Prevention Program "Entre Todos,"* 2 M.L.S. EDUC. RES. 7, 11 (2018); Shek et al., *supra* note 31, at 3.
[98] SELIGMAN, *supra* note 66, at 206.

health, psychological well-being, and longevity; they impact the amygdala, mPFC, and HPA axis activation.[99] Conversely, social isolation is associated with increased cognitive decline and risk of mortality.[100] Abilities for social encounters and dealing with stress are significantly influenced by attachment style, developed through personal history and childhood experiences,[101] with poor attachment being linked to substance abuse.[102] For example, infant-maternal social connection activates dorsal striatal activity in the infant's reward circuit; however, neglect or abuse during the first three months decreases the rewards associated with familiar relationships and thus relatively increases the rewards of impulsivity, novelty, and drugs.[103] Insecure attachment was additionally linked to interpersonal stress, leading to increased cortisol production, HPA axis and amygdala activation, behavioral disinhibition,[104] and decreased PFC regulation of the amygdala.[105]

Creative thinking and mental agility are additional essential capabilities for avoiding the onset of addiction. Onset of addiction depends on corticostriatal neuroplasticity[106] while addiction is characterized by a loss of synaptic plasticity in the NAcc and PFC;[107] adolescent abuse of alcohol is associated with hippocampal neurodegeneration.[108] Young people who believed personal traits are fixed experienced more self-regulatory distress.[109] Conversely, flexible,

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[99] Tabibnia & Radecki, *supra* note 3030, at 67.

[100] Laura Fratiglioni et al., *An Active and Socially Integrated Lifestyle in Late Life Might Protect Against Dementia*, 3 THE LANCET NEUROLOGY 343, 343 (2004).

[101] Pascal Vrticka & Patrik Vuilleumier, *Neuroscience of Human Social Interactions and Adult Attachment Style*, 6 FRONTIERS HUM. NEUROSCIENCE 1, 1, 4, 6-8, 11 (2012).

[102] Chambers, *supra* note 3333, at 549.

[103] *Id*.

[104] Mayfield et al., *supra* note 5, at 276.

[105] *See* Chambers, *supra* note 33, at 555 ("[T]he HPA axis is activated during interpersonal stress [which is increased in insecurely attached individuals] through increased activation of the amygdala, as well as through the lack of inhibition by the PFC, leading to increased cortisol production . . . [which] further increases amygdala activation.").

[106] *See* Bickel et al., *supra* note 55, at 8 (explaining that the neurobehavioral transition from voluntary to compulsive drug use "depend[s] on the neuroplasticity in both cortical and striatal structures" and that drug-seeking and taking is characterized by prefrontal cortical control when drug use is voluntary).

[107] *See* Piazza & Deroche-Gamonet, *supra* note 2, at 394-96 (explaining that long-term depression of synaptic transmission (LTD, a measure of synaptic plasticity) appeared in the NAcc and PFC of rats that self-administered cocaine but not the control group of rats).

[108] *See* Morris et al., *supra* note 4, at 596, 604 (stating that prior research showed "[b]oth animal models and human studies show that the hippocampus and its associated functions are particularly impaired in adolescents with [alcohol use disorder]" and that they observed "cell death in the adolescent rat hippocampus following binge alcohol exposure" in their own study).

[109] *See* Schleider et al., *supra* note 68, at 1 ("Compared to youths who believe that personal traits are malleable, those who believe that personal traits are fixed experience more academic and self-regulatory distress.").

exploratory cognitive states enhance resilience by promoting adaptability and change, such as adopting a new strategy for problem solving.[110] Positive reappraisal (re-evaluating a situation to change its emotional impact) can increase positive emotion,[111] while plasticity (redirecting function towards better health) improves resilience.[112] Active cognitive reappraisal increases PFC activation and decreases amygdala activation.[113] Notably, dispositional mindfulness was correlated with reappraisal success and increased activation in the left and right dorsomedial (dm)PFC,[114] and experienced meditators exhibited greater cortical thickness and higher concentrations of grey matter in the right anterior insula and temporoparietal junction, crucial for regulating first-person perspective.[115]

Ability to manage (experience, distinguish, perceive) emotions[116] is a critical ability. Self-awareness involves the ability to identify thoughts, emotions, and behaviors, as well as patterns in each that are counterproductive.[117] Individuals may rely on immediate reinforcement from fatty food, drugs, or

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[110] *See* Hans L. Melo & Adam K. Anderson, *The Function of Positive Emotions in Exploration, in* POSITIVE NEUROSCIENCE, *supra* note 90, at 209, 219 (explaining that psychologists have recently hypothesized that emotional flexibility is the psychological mechanism behind resilience because "[r]esilient individuals might recover from distress by adapting flexibly to the changing demands of stressful events").

[111] *See* Kateri McRae & Iris B. Mauss, *Increasing Positive Emotion in Negative Contexts, in* POSITIVE NEUROSCIENCE, *supra* note 90, at 158, 162 ("[Positive Reappraisal] can be used to increase several aspects of emotional responding, including self-reported positive emotion, and sympathetic nervous system activation.").

[112] *See* Bruce S. McEwan*, In Pursuit of Resilience: Stress, Epigenetics, and Brain Plasticity*, 1373 ANNALS N.Y. ACAD. SCI. 56, 56 (2016) ("The healthy brain has a considerable capacity for resilience, based upon its ability to respond to interventions designed to open "windows of plasticity" and redirect its function toward better health.").

[113] *See* Christian E. Waugh et al., *Emotion Regulation Changes the Duration of the BOLD Response to Emotional Stimuli,* 11 SOC. COGNITIVE & AFFECTIVE NEUROSCIENCE 1550, 1555 (2016) (stating experimental results that showed decreased activation duration in the amygdala and "a significant lengthening of the response in dorsomedial and ventrolateral prefrontal cortices" when the experimental subject used positive and negative reappraisal techniques as opposed to no techniques).

[114] Hölzel et al., *Mindfulness, supra* note 22, at 544.

[115] *See id.* at 542 ("Two cross-sectional studies comparing the gray matter morphometry of the brains of experienced mediators and controls showed that mediators had greater cortical thickness . . . and greater gray matter concentration . . . in the right anterior insular . . . . 8 weeks of [mindfulness practice] led to increases in gray matter concentration in the temporoparietal junction.").

[116] Menéndez-Hernández et al., *supra* note 97, at 11; *see also* Shek et al., *supra* note 31, at 3 (explaining that poor emotional intelligence is connected to addiction behaviors).

[117] *See* Reivich & Seligman, *supra* note 39, at 27 (defining self-awareness as "identifying one's thoughts, emotions, and behaviors, and patterns in each that are counterproductive").

procrastination to distract themselves from or restabilize their emotions.[118] Drugs flood the dopamine system, fundamental in regulating the function of limbic systems that process emotions and stress, with extremely high and instantaneous dopamine; repetitive substance abuse activates reward pathways in an unusual way causing neurophysiological and neuroplastic changes that reinforce an addictive cycle.[119]

Regulating one's emotions through emotion disclosure, affect labeling, or cognitive reappraisal improves and reduces short-term and long-term stress (autonomic nervous system, ACC, amygdala) [120] while improving physical and psychological long-term well-being.[121] Strategies such as exposure therapy, cognitive restructuring, and psychoeducation may help PFC systems modulate emotion-generative systems;[122] a typical pattern is increased PFC activation and decreased amygdala activation, suggesting that PFC exerts an inhibitory top-down influence on the amygdala.[123] When individuals with cocaine

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[118] *See* Roy F. Baumeister & Todd F. Heatherton, *Self-Regulation Failure: An Overview*, 7 PSYCHOL. INQUIRY 1, 5 (1996) ("Unfortunately, some of the most compelling short-term stimuli are precisely the things that the person is otherwise trying to control (e.g., alcohol, sweet foods, or drugs)"); Bickel et al., *supra* note 78, at 20 ("[H]owever, this perspective also describes the key concepts in which individuals engage in short term reinforcers such as eating fattening food, taking drugs, or procrastinating in an attempt to distract them from or restabilize their emotions." (citations omitted)); *see also* Wiss, *supra* note 79, at 4 ("[O]pioid misuse may be a coping mechanism for unresolved emotional pain that cannot be easily addressed in other ways.").

[119] Koob & Le Moal, *supra* note 11; Koob & Le Moal, *supra* note 12; Volkow & Morales, *supra* note 10, at 712; *see also* Ouzir & Errami, *supra* note 22, at 60 ("[R]epeated substance abuse produces the activation of the reward pathways in the brain in an unusual way causing neurophysiological and neuroplastic changes.").

[120] *See* Tabibnia & Radecki, *supra* note 30 30, at 68-70 (explaining empirical studies that demonstrated emotion disclosure can improve long-term physical and psychological wellbeing and suggesting mechanisms for the improvement such as reduced use of prefrontal resources ("lower ACC-based error-related negativity") or reencoding implicit amygdala-based memory in explicit neocortex-based memory, affect labeling reduced autonomic arousal and amygdala activation, and that cognitive appraisal led to lower autonomic arousal and diminished amygdala response to aversive images).

[121] *Id.* at 68-69 (showing that emotional disclosure "can improve physical and psychological well-being in the long-term").

[122] *See* Patricia Ribeiro Porto et al., *Does Cognitive Behavioral Therapy Change the Brain? A Systematic Review of Neuroimaging in Anxiety Disorders*, 21 J. NEUROPSYCHIATRY & CLINICAL NEUROSCIENCE 114, 116-117 (2009) (finding that women with a phobia of spiders treated with exposure therapy and cognitive restructuring experienced no activation in the anterior cingulate cortex post-treatment).

[123] *See* Hölzel et al., *supra* note 22, at 543 ("A typical pattern detected when individuals deliberately regulate affective responses is increased activation within the PFC and decreased activation in the amygdala, suggesting that PFC projections to the amygdala exert an inhibitory top-down influence." (citations omitted)).

dependence employed these 'top-down' cognitive strategies for regulating negative emotions, researchers found increased lateral mPFC activation and decreased amygdala and orbitofrontal cortex (OFC) activation;[124] regulation of negative emotion recruits right lateral PFC and lateral OFC regions.[125] Neural effects of cognitive behavioral therapy for emotional regulation and fear extinction include: reduced activation of the dlPFC, hippocampus, amygdala, and temporal cortex, increased activity in the prefrontal, temporoparietal, occipital, PCC, and mPFC regions.[126] Higher dispositional mindfulness is associated with increased vmPFC, mPFC, and ventrolateral PFC activation, decreased amygdala activity, and greater amygdala inhibition by the PFC.[127]

Ability to manage behavior is also critical in addiction prevention.[128] Self-regulation involves "the ability to regulate impulses, thinking, emotions, and behaviors to achieve goals."[129] Dopamine acts on the corticostriatal neurons directly involved in estimating outcome values, planning actions, and motivation, disrupting the executive functions of the PFC such as decision-making, judgement, self-control, self-regulation, working memory,

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[124] *See* Bickel et al., *supra* note 78, at 20-21 ("[W]hen [individuals with cocaine dependence] employed 'top down' strategies for regulating negative emotions, such as reappraisal, researchers found increased lateral and medial prefrontal cortex activation, and concurrent decreased activation in the amygdala and orbitofrontal cortex.").

[125] *See* McRae & Mauss, *supra* note 135, at 163-164 (citing three studies which showed that "down-regulation of negative emotions recruits right lateral prefrontal cortex and lateral orbitofrontal cortex regions to a greater extent than up-regulation").

[126] *See* Ribeiro Porto et al., *supra* note 146, at 116 (citing studies that showed "significant activation of the dorsolateral prefrontal cortex and parahippocampal gyrus regions" after CBT was used to treat spider phobia, "[a] reduction of activities at the temporal lobe region [and] . . . [d]ecreased activity at the right amygdala, hippocampus, rhinal activity, and periamygdaloid" after CBT was used to treat social phobia, "a decrease in the activation of the frontal orbital cortex" after treatment for OCD, and an "increase of activity in the left hemisphere . . . in the prefrontal, temporoparietal and occipital regions" following treatment for panic disorder).

[127] As Creswell et al. observe,

> After controlling for multiple individual difference measures, dispositional mindfulness was associated with greater widespread prefrontal cortical activation, and reduced bilateral amygdala activity during affect labeling, compared with the gender labeling control task. Further, strong negative associations were found between areas of prefrontal cortex and right amygdala responses in participants high in mindfulness but not in participants low in mindfulness.

J. David Creswell et al., *Neural Correlates of Dispositional Mindfulness During Affect Labeling*, 69 PSYCHOSOMATIC MED. 560, 560 (2007).

[128] Menéndez-Hernández et al., *supra* note 97.

[129] Reivich & Seligman, *supra* note 39, at 27.

learning, and motivation;[130] this contributes to, for example, the failure of the frontal lobe system to regulate impulsive behavior of the limbic system.[131] The onset of addiction—wherein drug-seeking and drug use behavior transitions from voluntary to compulsive—is paralleled by a neurobiological transition from goal-directed PFC control to habit-learned dorsal striatal control.[132]

Practices that instill a sense of calm and routine may have outsized impacts on health and well-being; these include 'uni-tasking'[133] and 'keystone habits.'[134] Mindfulness practices improve executive function of the amygdala and PFC[135] and enhance self-regulation by inducing neuroplastic changes in the front-limbic network, ACC, insula, and temporoparietal junction.[136] The ACC enables executive attention by detecting conflicting streams of information processing and alerting cognitive control; experienced meditators exhibit greater rostral ACC activation and greater dorsal ACC cortical thickness.[137] Although using self-control can result in temporary depletion,[138] self-control is critical in addiction prevention[139] and long-term development can improve self-control.[140] Growth mindsets also facilitate better self-regulation and goal achievement.[141]

Managing behavior is bolstered by the ability to see and believe that a short-term pleasurable gain is not worth a lifetime of addiction and the ability to

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[130] Koob & Le Moal, *supra* note 12, at 98; Volkow & Morales, *supra* note 10; P. Deligkaris, *Job Burnout and Cognitive Functioning: A Systematic Review*, 28 WORK STRESS 107, 108-109 (2014).

[131] *Matto*, *supra* note 82, at 532; Chris R. Brewin, *A Cognitive Neuroscience Account of Posttraumatic Stress Disorder and Its Treatment,* 39 BEHAV. RES. THERAPY 373, 377 (2001); *see also* Ouzir & Errami, *supra* note 22, at 63 (noting the well-established connection between dopamine and risk-associated behaviors).

[132] Bickel et al., *supra* note 55, at 8.

[133] *See* Gayetri Devi, *The Calm Brain: The Neurology of Stress and Calm or 'How to Relax without Drugs'*, HUFFINGTON POST (Dec. 7, 2017), https://www.huffpost.com/entry/stress-tips_b_1600102 [https://perma.cc/X23V-AV3D] (describing the benefits of meditation and uni-tasking—focusing on one task exclusively—to reduce stress).

[134] *See* Kim Marshall & Dave Marshall, *Mini-Observations: A Keystone Habit*, SCHOOL ADMINISTRATOR, Dec. 2017, at 1, 26 (analyzing keystone habits, "a simple routine that has a surprisingly large impact on people's lives," in the context of schools).

[135] Tabibnia & Radecki, *supra* note 30, at 69.

[136] Hölzel et al., *supra* note 22, at 537, 540.

[137] *Id.* at 540.

[138] *See generally* Roy F. Baumeister et al., *Ego Depletion: Is the Active Self a Limited Resource?*, 74 J. PERSONALITY & SOC. PSYCHOL. 1252, 1263-64 (1998) (examining "ego depletion" through psychological study).

[139] *Id.* at 1252.

[140] *See* Bickel et al., *supra* note 55, at 5 ("[A]ddictive consumption tends to diminish as individuals age into early and middle adulthood; this is known as maturing out.").

[141] Zeng et al., *supra* note 65, at 5.

recognize true long-term health outcomes is essential.[142] Disrupted dopaminergic signaling into the PFC helps explain impulsivity,[143] which along with risk-taking and novelty-seeking is significantly involved in drug-seeking initiation, maintenance, and relapse.[144] Adolescence is a particularly vulnerable period due to increased pro-motivational dopamine and reduced inhibitory serotonin.[145] The OFC is likely also significant in this ability: OFC damage is correlated with impaired decision-making and disinhibition.[146] Individuals addicted to amphetamine were found to both take longer to make decisions, and to make sub-optimal decisions; the same processes activated the inferior and OFC in non-addicted individuals.[147] The ability to make healthy choices in the face of sociocultural pressure is also impactful in successfully managing behavior;[148] this includes assertiveness[149] and problem solving.[150] Social learning theories and family interaction models explain how peer and family drug-use, relationships, and values contribute to either protection against or risk for drug-use.[151] As protective factors, social relationships can decrease strength of conditioned stimuli and enhance motivation for non-drug behaviors.[152]

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[142] *See* Shek et al., *supra* note 31, at 5 (showing the importance of educating adolescents on the short and long term consequences of addiction). *But see* Ouzir & Errami, *supra* note 22 (noting that many addicts continue to use drugs despite knowing that they may be dangerous).
[143] Koob & Volkow, *supra* note 10; Volkow & Morales, *supra* note 10.
[144] Ouzir & Errami, *supra* note 22, at 63.
[145] *Id.*
[146] Aviv Weinstein & W. Miles Cox, *Cognitive Processing of Drug-Related Stimuli: The Role of Memory and Attention*, 20 J. PSYCHOPHARMACOLOGY 850, 856 (2006).
[147] *Id.*
[148] *See* Shek et al., *supra* note 31, at 3 (noting that adolescents who can stand up to peer pressure are less likely to use drugs or drink alcohol).
[149] SELIGMAN, *supra* note 66.
[150] *See* Reivich & Seligman, *supra* note 39, at 25 (discussing the role effective problem-solving plays in resilience).
[151] *See generally* Palmer & McGeary, *supra* note 6 (describing models of drug addiction in teens and young adults).
[152] *See generally, e.g.*, Greg J. Duncan et al., *Cleaning Up Their Act: The Effects of Marriage and Cohabitation on Licit and Illicit Drug Use*, 43 DEMOGRAPHY 691 (2006) (finding that "marriage does indeed cause reductions in risky behavior, particularly among men" but that "cohabitation effects are less consistent"); Jie Guo et al., *Childhood and Adolescent Predictors of Alcohol Abuse and Dependence in Young Adulthood*, 62 J. STUD. ALCOHOL 754 (2001) ("Strong bonding to school, close parental monitoring of children and clearly defined family rules for behavior, appropriate parental rewards for good behaviors, high level of refusal skills and strong belief in the moral order predicted a lower risk for alcohol abuse and dependence at age 21."); Reivich & Seligman, *supra* note 39 ("There are a number of evidence-based protective factors that contribute to resilience: optimism, effective problem solving, faith, sense of meaning, self-efficacy, flexibility, impulse control, empathy, close relationships.").

Ability to generate positive emotions (e.g. happiness, love) bolsters resilience, health, well-being, and growth in the face of adversity, while buffering against stress and psychological health problems such as depression and anxiety.[153] Behavioral strategies include exercise, which naturally releases dopamine, norepinephrine, and serotonin,[154] and is correlated with lower all-cause mortality and CVD.[155] Flow, the experience of full engagement in a surmountable challenge with immediate feedback, is inherently gratifying.[156] Cognitive strategies include realistic optimism, minimizing catastrophic thinking, and fighting back against counterproductive thoughts in real time.[157] Optimism is correlated with lower cardiovascular disease;[158] reduced conduct problems,[159] depression, anxiety, hopelessness;[160] increased well-being and health related behavior.[161] Positivity is associated with dopaminergic

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[153] McRae & Mauss, *supra* note 111. *See generally* SELIGMAN, *supra* note 66 (discussing "positive psychology").

[154] *See* Romain Meeusen & Kenny De Meirleir, *Exercise and Brain Neurotransmission*, 20 SPORTS MED. 160, 160-161 (1995) (suggesting that most neurotransmitters, including dopamine, norepinephrine and serotonin are produced during exercise).

[155] *See* Xuemei Sui et al., *Estimated Functional Capacity Predicts Mortality in Older Adults*, 55 J. AM. GERIATRIC SOC. 1940, 1940 (2007) ("[S]ubjects with high CRF [cardiovascular fitness] had notably lower mortality risk than those with low CRF from all causes (HR 5 0.59, 95% CI 5 0.47–0.74) and from CVD (HR 5 0.57, 95% CI 5 0.41–0.80)."); *see also* D. C. Lee et al., *Does Physical Activity Ameliorate the Health Hazards of Obesity?* BRIT. J. SPORTS MED. 49, 50 (2008) (surveying studies which show that "moderate to high fitness eliminates the elevated risk of all-cause, CVD, and cancer mortality associated with obesity").

[156] SELIGMAN, *supra* note 66, at 11, 24.

[157] Reivich & Seligman, *supra* note 39, at 27, 29.

[158] Laura D. Kubzansky et al., *Is the Glass Half Empty or Half Full? A Prospective Study of Optimism and Coronary Heart Disease in the Normative Aging Study,* 63 PSYCHOSOMATIC MED. 910, 913 (2001).

[159] *See* Cutuli et al., *supra* note 67 ("[T]he PRP intervention is generally beneficial to all participants, these findings suggest that it is especially efficacious in preventing depression symptoms in young adolescents who already express significant levels of conduct problems."); *see also* SELIGMAN, *supra* note 66, at 84.

[160] Jane E. Gillham et al., *Preventing Depression Among Early Adolescents in the Primary Care Setting: A Randomized Controlled Study of the Penn Resiliency Program*, 34 J. ABNORMAL CHILD PSYCHOL. 203 (2006); Steven M. Brunwasser et al., *A Meta-Analytic Review of the Penn Resiliency Program's Effect on Depressive Symptoms*, 77 J. CONSULTING & CLINICAL PSYCHOL. 1042 (2009).

[161] Yulan Yu & Jun Luo, *Dispositional Optimism and Well-Being in College Students: Self-Efficacy as a Mediator,* 46 SOC. BEHAV. & PERSONALITY 783 (2018); Krishna Kuman Mishra, *Optimism and Well-Being*, 29 INT'L SOC. SCI. J. 75 (2013); Kimberly R. Vacek, Laura D. Coyle & Elizabeth M. Vera, *Stress, Self-Esteem, Hope, Optimism, and Well-Being in Urban, Ethnic Minority Adolescents*, 38 J. MULTICULTURAL COUNSELING & DEV. 99 (2010); Helena Espirito Santo & Fernanda Daniel, *Optimism and Well-Being Among Institutionalized Older Adults*, 31 GEROPSYCHOLOGY 5 (2018).

'play' systems and further corresponds to the flexible, creative exploration of new possibilities, alternative approaches, and future coping strategies in the frontopolar (BA10) cortices.[162] Compassion training programs have led to increased activity in the right amygdala, increasing positive emotion (as opposed to decreasing negative emotion).[163] The benefits of positive emotions extend to expressing and cultivating gratitude, which decreases distress while improving physical and psychological well-being.[164] Pride and gratitude activate the mesolimbic and basal forebrain, as well as the hypothalamus, which is responsible for bodily functions and stress levels.[165] Gratitude synchronizes activation of the reward circuit and hypothalamus, boosting serotonin and brain stem dopamine production.[166]

B. External Capabilities

Social norms against substance use are a necessary external ability, because sociocultural context develops individuals' behavior, forms expectations of consequences, and influences lifestyle.[167] For example, Moroccan socio-religious norms prohibit drugs and alcohol out of recognition of their extreme adverse consequences.[168] Herd immunity exists in social norms, the social contagion of behavior,[169] and reduced drug availability and exposure.[170] Peer, parental, and community influences can either increase risk for or protection against drug use and addiction; parental supervision and poverty are

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[162] Melo & Anderson, *supra* note 110, at 210.
[163] K. Ashar et al., *supra* note 90, at 133; *see also* Waugh et al., *supra* note 113, at 1557 ("Although the amygdala exhibited decreased duration of activation regardless of reappraisal instruction type, it exhibited decreased height of activation only when participants were instructed to decrease their negative emotion, not when they were instructed to increase their positive emotion.").
[164] Reivich & Seligman, *supra* note 39, at 29; Tabibnia & Radecki, *supra* note 30, at 68.
[165] Roland Zahn et al., *The Neural Basis of Human Social Values: Evidence from Functional MRI*, 19 CEREBRAL CORTEX 276, 276 (2009); *see also* Randy A. Sansone & Lori A. Sansone, *Gratitude and Well Being: The Benefits of Appreciation*, 7 PSYCHIATRY 18, 21 (2010) (cataloguing research linking gratitude to increased overall well-being).
[166] Zahn et al., *supra* note 165, at 277.
[167] Ouzir & Errami, *supra* note 22, at 64.
[168] El Kazdouh et al., *supra* note 31, at 4, 9.
[169] *See* Michael J. Young et al., *Immune to Addiction: The Ethical Dimensions of Vaccines Against Substance Abuse,* 13 NAT. IMMUNOLOGY 521, 522 (2012) (arguing that "one person's behavior is very likely to influence the behavior of others, which suggests a more 'infectious' disease model for addictive behavior").
[170] *See* Jeremy Mennis et al., *Risky Substance Use Environments and Addiction: A New Frontier for Environmental Justice Research,* 13 INT. J. ENVIRON. RES. PUB. HEALTH 1, 4 (2016) (discussing the negative impact of neighborhood concentrated disadvantage on individuals).

external risk factors.[171] Individuals were more likely to develop healthy habits if their partners did concurrently.[172] Children whose families ate together developed better academic skills, emotional regulation, and confidence;[173] however, the emotional deprivation of institutionalized and adopted children was reflected in increased amygdala activation.[174] Neurobiologically, activity in the anterior vmPFC, part of the reward pathway, is correlated with pride and guilt[175] and responds more strongly to upholding prosocial norms than to personal gain while responding negatively to violating social norms for self-interest.[176]

Social networks and social capital are critical for achieving positive health outcomes including preventing addiction and aiding recovery. Social relationships and connection can directly improve mood, reduce stress, release pleasurable feelings that diminish the need for dopamine from drugs. The ability to build and enjoy social relationships and connection, and all the positive feelings that come with them, is a critical internal and external capability.[177] Social support, such as among military veterans or therapists and patients,[178] has a direct positive effect on stressors and HPA axis activity.[179] Social reward, non-social reward, and drug

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[171] *See* Joseph Biederman et al., *Patterns of Alcohol and Drug Use in Adolescents Can Be Predicted by Parental Substance Use Disorders*, 106 PEDIATRICS 792, 794 (2000) (demonstrating that "exposure to parental SUDs . . . predicted SUDs in offspring"); Karl G. Hill et al., *Family Influences on the Risk of Daily Smoking Initiation*, 37 J. ADOLESCENT HEALTH 202, 209 (2005) (showing "that family factors matter in predicting the onset of daily smoking in adolescence"); Laura Lander et al., *The Impact of Substance Use Disorders on Families and Children: From Theory to Practice*, 28 SOC. WORK PUB. HEALTH 194, 204 (2013) ("Individuals with SUDs cannot be understood and treated effectively without considering the impact on the whole family. Addictions researchers have confirmed the reciprocal relationship between the disease of addiction and the environment."); Leigh Ann Simmons et al., *Illicit Drug Use Among Women with Children in the United States: 2002–2003* 19 ANNALS EPIDEMIOLOGY 187, 191 (2009) ("These findings support other research that has shown older women are less likely to use illicit substances than younger women, and the social support of having a marital partner reduces the odds of using drugs and other substances as a coping strategy." (citations omitted)). *See generally* Judith S. Brook et al, *The Psychosocial Etiology of Adolescent Drug Use: A Family Interaction Model*, 116 GENETIC, SOC. & GEN. PSYCHOL. MONOGRAPHS 114 (1990) (proposing a framework for understanding these psychosocial elements of adolescent drug use).

[172] Sarah E. Jackson et al., *The Influence of Partner's Behavior on Health Behavior Change: The English Longitudinal Study of Ageing*, 175 AM. MED. ASSOC. 385, 391 (2015).

[173] Marshall & Marshall, *supra* note 134.

[174] Chambers, *supra* note 33, at 550.

[175] Zahn et al. *supra* note 167, at 277.

[176] Zaki & Mitchell, *supra* note 95, at 61-62.

[177] Reivich & Seligman, *supra* note 39, at 27; Menéndez-Hernández et al., *supra* note 97, at 9, 11; Zeng et al., *supra* note 65, at 1-2 .

[178] Chambers, *supra* note 33.

[179] Beate Ditzen & Markus Heinrichs, *Psychobiology of Social Support: The Social Dimension of Stress Buffering*, 32 RESTORATIVE NEUROLOGY & NEUROSCIENCE 149, 152 (2014).

addiction are all processed in the same reward circuit (basal ganglia, striatum);[180] anticipating positive social feedback activates the NAcc, putamen, and thalamus,[181] and highly socially-motivated behavior is attributed to striatal dopamine.[182] Social relationships provide positive social support, role modeling, and opportunities for positive choices and behaviors.

Transition periods in a person's life greatly increase their risk of drug use.[183] This includes divorce (first-[184] or second-hand experience[185]), unemployment,[186] moving,[187] and dropping out of school.[188] Stress can disrupt development in the PFC, reward system, hippocampus, and amygdala.[189] Chaotic homes, abuse, and ACEs[190] are risk factors for drug use and addiction,[191] and the body's stress

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[180] Sören Krach et al., *The Rewarding Nature of Social Interactions*, 4 FRONTIERS BEHAVIORAL NEUROSCIENCE, May 28, 2010, at 1, 1 (2010) ("[S]ocial reward is processed in the same subcortical network as non-social reward and drug addiction."); *see also* Yoni K. Ashar et al., *Toward a Neuroscience of Compassion*, *in* POSITIVE NEUROSCIENCE, *supra* note 90, at 125, 129.

[181] Ditzen & Heinrichs, *supra* note 179; Krach et al., *supra* note 180; *see also* Katja N. Spreckelmeyer et al., *Anticipation of Monetary and Social Reward Differently Activates Mesolimbic Brain Structures in Men and Women*, 4 SOC. COGNITIVE & AFFECTIVE NEUROSCIENCE 158, 162 (2009) ("Testing for a linear increase of activation in response to increasing levels of anticipated monetary or social rewards revealed significant activation of cortical structures constituting the reward system, specifically the putamen, bilateral NAcc, thalamus and precuneus." (citations omitted)).

[182] Krach et al., *supra* note 180.

[183] As Palmer and McGreary observe,

> Research has demonstrated that there are critical transition periods during childhood, adolescence, and young adulthood where the risk for drug use is elevated. These transition periods include: (1) the transition from the security of the family environment to the school environment (elementary school), (2) the progression from elementary school to middle/junior high school, (3) the advancement from middle/junior high school to high school, and, lastly, (4) leaving home to go to college, work, or live on their own.

Palmer & McGeary, *supra* note 6, at 5; Krohn et al., *supra* note 23.

[184] Andrea L. Stone et al., *Review of Risk and Protective Factors of Substance Use and Problem Use in Emerging Adulthood,* 37 ADDICTIVE BEHAVS. 747, 755 (2012).

[185] *Id*. at 770.

[186] *Id*. at 769.

[187] Krohn et al., *supra* note 23, at 90.

[188] *Id.* at 98-99.

[189] Martha J. Farah, *Socioeconomic Status and the Brain: Prospects for Neuroscience-Informed Policy,* 19 NATURE REVS. NEUROSCIENCE 428, 433 (2018).

[190] Dube et al., *supra* note 56.

[191] Najavits et al., *supra* note 21; Stone et al., *supra* note 184.

response releases norepinephrine and noradrenaline,[192] contributing to impulsivity, shrinking the PFC and increasing the size of the amygdala thus making the brain more receptive to stress[193] and impairing sociability.[194]

Group memberships in various communities, in schools and churches are important factors. Exposure to and availability of drugs is a major risk factor in adolescent drug use and addiction.[195] The PFC is not fully developed until the mid-twenties,[196] which severely limits adolescents' ability to evaluate the risks of drugs and resist peer pressure.[197] Community after-school organized activities[198]

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[192] Lívea Dornela Godoy et al., *A Comprehensive Overview on Stress Neurobiology: Basic Concepts and Clinical Implications*, 12 FRONTIERS BEHAV. NEUROSCIENCE, July 3, 2018, at 1, 3.

[193] Bruce S. McEwen et al., *Stress Effects on Neuronal Structure: Hippocampus, Amygdala, and Prefrontal Cortex*, 41 NEUROPSYCHOPHARMACOLOGY REVS. 3, 17 (2016); *see also* Craig A. McEwen & Bruce S. McEwen, *Social Structure, Adversity, Toxic Stress, and Intergenerational Poverty: An Early Childhood Model,* 43 ANN. REV. SOC. 445, 462 (2017) (describing the impact of social structures and relationships on children's' brain development).

[194] Michael A. van der Kooij et al., *Role for MMP-9 in Stress-Induced Downregulation of Nectin-3 in Hippocampal CA1 and Associated Behavioural Alterations,* 5 NAT. COMM. 1, 3 (2014).

[195] Judith S. Brook et al., *The Onset of Marijuana Use from Preadolescence and Early Adolescence to Young Adulthood*, 11 DEV. & PSYCHOPATHOLOGY 901, 911 (1999); Guo et al., *supra* note 152; Kenneth J. Sher & Patricia C. Rutledge, *Heavy Drinking Across the Transition to College: Predicting First-Semester Heavy Drinking from Precollege Variables*, 32 ADDICTIVE BEHAVS. 819, 824 (2007); Robert A. Zucker et al., *Early Developmental Processes and the Continuity of Risk for Underage Drinking and Problem Drinking*, 121 PEDIATRICS S252, S257 (2008).

[196] Chambers, *supra* note 33; Krohn et al., *supra* note 23.

[197] Koob & Volkow, *supra* note 10, at 226; Daniel Romer & Michael Hennessy, *A Biosocial-Affect Model of Adolescent Sensation Seeking: The Role of Affect Evaluation and Peer-Group Influence in Adolescent Drug Use*, 8 PREVENTION SCI. 89, 90 (2007); *see also* ALASKA DEP'T OF HEALTH AND SOC. SERVICES, DIV. BEHAV. HEALTH, RISK AND PROTECTIVE FACTORS FOR ADOLESCENT SUBSTANCE USE (AND OTHER PROBLEM BEHAVIOR) 3 (2011) (illustrating how peer pressure can both function as a risk factor for substance use and as a protective factor disincentivizing substance use).

[198] *Id.* at 12 (listing "students that participate in one or more organized activities outside of school," including "clubs, lessons, volunteering, or helping activities one or more times per week" as less likely to engage in adolescent substance use); NAT'L RES. COUNCIL, YOUTH DEVELOPMENT AND NEIGHBORHOOD INFLUENCES: CHALLENGES AND OPPORTUNITIES 14 (Rosemary Chalk & Deborah A. Philips eds., 1997); *see also* GABRIEL M. GARCIA, LORI PRICE, & NEELOUT TABATABAI, UNIV. ALASKA ANCHORAGE DEP'T HEALTH SERVS., ANCHORAGE YOUTH RISK BEHAVIORAL SURVEY RESULTS: 2003–2013 TRENDS AND CORRELATION ANALYSIS OF SELECTED RISK BEHAVIORS, BULLYING, MENTAL HEALTH CONDITIONS, AND PROTECTIVE FACTORS 68 (2014) (finding that students who participate in organized after school activities at least 1 day per week were 15.5% less likely to engage in binge drinking and 30.7% less likely to currently be using marijuana).

and access to exercise[199] have both helped reduce vulnerability to drug-seeking and addiction. Adolescents are more impulsive and more vulnerable to peer pressure, judgement and decision-making faculties are not fully developed until the mid-twenties. Thus, peers and friends focused on health and flourishing create positive group influences. Peers, parents, and communities can be either risk or protective factors in drug use and addiction. Positive group influences include limited exposure and availability, positive activities and examples, parental support, education, supervision, and pro-health and well-being development.

Material circumstances and the extent to which individuals and groups feel secure or insecure in their immediate and broader macrosocial environment matter for addiction prevention and recovery. Concentrated disadvantage or economic deprivation (low income, high unemployment, low educational attainment) characterize risky substance use environments.[200] Socioeconomic status (SES) modulates proximal factors such as health status and functioning, cognitive stimulation, stress, and social relationships that influence brain structure and activity; for example, higher SES has been linked to cortical thickness.[201] Lower SES means less access to resources and more constraints on choice and behavior; the significance of control to psychological well-being suggests that this increases neuropsychological vulnerability to drug use and addiction. Indeed, multiple studies have shown that adults living in lower SES environments benefit from emotional regulation in terms of reduced depressive symptoms.[202] A secure, safe, hopeful and supportive immediate and macrosocial environment with a sense of fairness, opportunity, inclusion and equity can reduce direct and indirect risk factors for drug use (e.g., stress). Moreover, healthy family relationships, loving and nurturing home environments; welcoming, supportive and diverse schools and communities and job and career development stability help prevent addiction and aid recovery.

Finally, utilization and access to health services and the degree to which the public health and health care systems are enabling or disabling is important for addiction prevention and recovery. Environmental barriers to substance use treatment, such as a lack of access to public transportation, affordable distance and travel time, as well as treatment settings that are socially, culturally, and linguistically exclusive, are characteristics of a risky substance use

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[199] *See* Mark A. Smith & Elizabeth G. Pitts, *Access to a Running Wheel Inhibits the Acquisition of Cocaine Self-Administration,* 100 PHARMACOLOGY BIOCHEMISTRY BEHAV. 237, 240 (2011) ("The main finding of this study is that access to a running wheel significantly decreases the rate of acquisition of cocaine self-administration in male rats responding in a free operant procedure.").

[200] Mennis et al., *supra* note 170, at 1, 4.

[201] Farah, *supra* note 189, at 430.

[202] Allison S. Troy et al., *Change the Things You Can: Emotion Regulation Is More Beneficial for People from Lower Than from Higher Socioeconomic Status*, 17 EMOTION 141, 141-42 (2017).

environment.[203] Co-morbid mental disorders and non-drug related needs are often root causes and auxiliary reinforcers of drug addiction; co-morbidity implies exponentially detrimental interactions between illnesses occurring simultaneously or subsequently. Health services address co-morbid mental processes and support positive neurobiological developments, particularly during windows of opportunity. Multiple studies suggest that even when experienced in doses as brief as 5 minutes or through pictures, nature improves emotions and attention-direction,[204] while reducing negative rumination and a host of physical diseases.[205] In addition to effects of behavioral norms and group cognition on addiction, epigenetics suggest that social influences can enhance genetic risk of addiction, as gene expression and function can be altered by drugs or stress in one's sociocultural environment.[206] Cognitive-affective theories and effective treatments support the importance of public belief and enhance trust in health systems. Public health and health care systems can prevent neurobiological transitions to addiction and provide early treatment for lifelong recovery. Knowledge of the dangers of drugs, dependence and addiction through effective public health and health care systems contribute to beliefs of self-efficacy, empowerment and ownership, and likely increase effective utilization of impactful services.

CONCLUSION

Society needs an operationalized framework to address the disease of addiction, which continues to exact a tragic cost on public health and individual well-being. In light of neuroscientific discoveries, understanding addiction as a chronic brain disease suggests that despite individual vulnerabilities, preventative internal and external capabilities can be developed to protect the brain against drug addiction. The health capability model embodies a paradigmatic shift towards the positive health and flourishing of people living amongst

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[203] Mennis et al., *supra* note 170, at 16-17.

[204] Calum Neill, Janelle Gerard & Katherine D. Arbuthnott, *Nature Contact and Mood Benefits: Contact Duration and Mood Type*, 14 J. POSITIVE PSYCHOL. 756, 760 (2019); *see also* Marc G. Berman, John Jonides & Stephen Kaplan, *The Cognitive Benefits of Interacting with Nature*, 19 PSYCHOL. SCI. 1207, 1211 (2008) (discussing "the restorative value of nature as a vehicle to improve cognitive functioning").

[205] *See e.g.*, Gregory N. Bratman et al., *Nature Experience Reduces Rumination and Subgenual Prefrontal Cortex Activation*, 112 PROC. NAT'L ACAD. SCI. 8567, 8568 (2015) (showing exposure to nature reduced rumination and decreased sgPFC activity); Caoimhe Twohig-Bennett & Andy Jones, *The Health Benefits of the Great Outdoors: A Systematic Review and Meta-Analysis of Greenspace Exposure and Health Outcomes*, 166 ENV'T. RES. 628, 629, 636 (showing exposure to nature reduced cardiovascular and all-cause mortality).

[206] Chambers, *supra* note 33, at 557-8; L. Bevilacqua & D. Goldman, *Genes and Addictions*, 85 CLINICAL PHARMACOLOGY & THERAPEUTICS 359, 359 (2009).

dynamic social systems, signifying an alternative view of treating addiction as a failure of individual and societal capabilities for health.

Mapping addiction to neuroscience and the health capability model reveals a number of abilities that are critical for preventing drug addiction and aiding recovery. Internally, these include: healthy habits, health knowledge of the effects of drugs and of individual vulnerabilities, executing strategies to avoid addiction, self-esteem, health agency in evaluating personal health goals, coping with individual vulnerabilities and external pressures, attaining natural and healthy rewards, social relationships, creativity, managing emotions and behavior, assessing long-term gains, resisting social pressure, motivation for non-drug behaviors, and generating positive emotions. Externally, these include: positive and healthy social norms, relationships, group membership influences; security in material circumstances and the social, political, and economic environment; and knowledge, access, and utilization of public health and health care systems.

Understanding the science of addiction strongly suggests that the most impactful and inclusive approach is prevention and recovery, especially the awareness of the extreme toxicity and danger of introducing substances into the brain. Adolescents in particular must have and use knowledge of the dangers of drugs, dependence, and addiction to stay safe. The addiction prevention capabilities set presents an empirically-informed approach to fundamentally addressing etiologies of addiction and determinants of health, working towards the eradication of addiction in society. Capabilities work by training the brain to recognize and combat causes of addiction. Capabilities promote optimal functioning in the individual and society. A bolder approach is needed to create the conditions for all people to reach their highest potential of human flourishing.

Figure 3. Addiction Prevention Capabilities Set

INTERNAL FACTORS	NEUROBIOLOGICAL EFFECTS
A. Health status and health functioning: healthy habits • Sleep, energy management (meditation, controlled breathing, progressive muscle relaxation), exercise • Nutrition, hydration, dietary restriction	Creates a resilient wellness that obviates the need to seek short-term pleasure • Improves negative emotions, cognitive function, neurogenesis; decreases sensitivity to stressors, strength of conditioned stimuli Neural systems impacted: lateral PFC, neocortex, mPFC-amygdala connectivity, amygdala, hippocampus, HPA and homeostasis, serotonin, BDNF
B. Health knowledge • Dangers of putting a toxic substance in your brain • Costs and benefits of drug exposure • Unique individual vulnerabilities	Individual vulnerabilities include: • Trauma, ACEs • Adolescence, transition periods, social risk • Family history/genetic predisposition, low sensitivity to DA
Belief that the effects of drugs are dangerous and irreversible	Change in attitudes and beliefs that led to drug abuse (e.g. entitlement; poor understanding of consequences) Cognitive affective theories: young people use drugs less believed to be harmful (despite cultural factors)
General knowledge of the limits of self-control	Drug tolerance: brain adapts to frequent and higher doses, functioning normally in presence of drugs and abnormally in absence • Neural adaptation supports relapse even after long-term drug abstinence

• Addiction is a chronic brain disease which disrupts the ability to execute free will, dependence may persist for entire life	• Addiction heavily influenced by environmental circumstances • Neural systems impacted: DA neurons in the ventral striatum and PFC
C. Health-seeking skills and beliefs, self-efficacy Ability to execute strategies to avoid addiction under changing circumstances • Conditioned stimuli act as secondary reinforcers (DA shifts backwards, rewards behaviors that predict drug use)	Individual and population behavior change more associated with activity in the mPFC than self-reported judgements, intentions, and efficacy Strengthened PFC circuits are able to exert control Improves cognitive control over desires and emotions, predict and avoid situations where risk for taking drugs is heightened • Mindfulness training increases frontal and occipitoparietal activation
Self-esteem • Belief in ability predicted coping, planning, emotional processing, seeking social support	Identifying, developing, and applying character strengths: • Improves mental well-being, assertiveness, self-control; reduces bad conduct Mindfulness meditation strengthens brain structures that support self-referential processing (mPFC, PCC, inferior parietal lobe) Growth mindset linked to higher levels of empowerment, self-esteem, resilience, well-being (lower levels of mental illness)
D. Health values and goals Ability to evaluate one's own health goals and choose better ones	As drug use proceeds, the NAcc and mPFC (important in selecting appropriate goal-directed behaviors) lose synaptic plasticity: • Dorsal striatum and putamen control the flow of information into the PFC and PCC for processing • Results in loss of control, behavioral crystallization around one goal, including great perseverance no matter the consequences
E. Self-governance and self-management and perceived self-governance and management to achieve health outcomes Ability to cope with individual vulnerabilities • Root causes of drug addiction often stem from issues unrelated to the drug problem itself • Drug abuse may be a coping mechanism for unresolved emotional pain that cannot be easily addressed	Stress contributes to addiction vulnerability, maintenance, and relapse • Stress-induced relapse: CRF reciprocally activates kappa opioid receptors (which increase the rewarding effects of drugs), orexin, norepinephrine, dynorphi • Drugs also enhance the release of CRF, which in turn contributes to impulsivity and vulnerability to addiction Effective drug treatment addresses co-morbid mental disorders and non-drug related needs
Ability to live a good life and attain pleasure without using substances • Exercise, prosocial motivation, vicarious experience of others' rewards can create natural pleasurable feelings	Increase in DA from drugs is higher and more convenient, does not rapidly habituate (mesolimbic DA system reinforces the effects of drugs, perpetuating an addictive cycle that triggers neurophysiological changes) • Addiction prevention should focus on drug use prevention: strengthening skills, developing abilities, and promoting life satisfaction
Ability to build and enjoy social relationships and connection • Increases longevity, physical/psychological health	Social connection and support • Increases joy, laughter, purpose, meaning, belonging, support, connection Neural systems impacted: amygdala, mPFC, HPA
Ability to manage external pressures from personal and professional situations • Mass media, systemic oppression	Self-regulating is challenging under stress (CRF compromises PFC and VAM processing, leaving the brain sensitive to triggers) • mPFC and HPA experience stress inoculation (with moderate stressors); cognitive strategies strengthen amygdala and mPFC • Meditation strengthens regions involved in sustained extinction of conditioned fear (vmPFC, amygdala, hippocampus)
Creative thinking, mental agility, neural plasticity • Redirect behavior towards better health • Adopt new strategies for problem solving • Positive reappraisal	Flexible, exploratory cognitive state increases positive emotion and resilience; promotes adaptability and change • Growth mindset and perceived control enhance resilience: protects against stress; promotes faster stress recovery; contributes to goal achievement, self-regulation, less self-regulatory distress Increases PFC activation, decreases amygdala and OFC activation
F. Effective health decision-making Ability to manage (experience, distinguish, perceive, regulate) emotions • Self-awareness of counterproductive patterns in thoughts, emotions, and behaviors • Short-term reinforcers (e.g. fattening food, drugs, procrastinating) may be used to distract or restabilize	Limbic system (dlPFC, vPFC, ACC, dmPFC; emotional processing, stress reaction), relies on DA that is disrupted by drugs Emotional regulation (emotion disclosure, affect labeling, cognitive reappraisal/restructuring, exposure therapy, psychoeducation) increases PFC activity, modulates and decreases limbic system activity • Improves long-term physical and psychological health, regulation of negative emotions and fear extinction (right lPFC, PCC, lateral OFC; reduced amygdala-hippocampus blood flow) • Reduces short- and long-term stress (autonomic nervous system, ACC, amygdala) • Mindfulness meditation activates dmPFC, vPFC; reduces amygdala activity
Ability to manage behavior • Self-regulation of impulses, thinking, emotions, and behaviors to achieve goals	DA system fundamental to PFC (executive function, self-control/regulation, memory, decision-making, judgement, learning) and corticostriatal neurons (value estimation, planning, motivation), disrupted by drugs; results in failures to regulate limbic system

	• Drug-seeking and use transition from PFC/ventral striatal (goal-directed) to dorsal striatal control (habitual, compulsive) • PFC and PCC activated when trying to modulate motivational stimuli (cravings, emotional memories, stressful situations, drug-related cues), dysfunction associated with relapse Inoculation: use of self-control may cause temporary depletion, but can be developed in the long-term Mindfulness meditation strengthens conflict monitoring and cognitive control, enhances self-regulation • Neural systems impacted: fronto-limbic network, temporoparietal junction, ACC, insula • Greater activity and thickness in the ACC, which enables executive attention by detecting conflicting streams of information processing and alerting cognitive control
Belief that short-term pleasurable gain is not worth a lifetime of addiction • Ability to recognize long-term health outcomes	Impulsivity, risk-taking, novelty-seeking: significantly involved in drug use initiation, maintenance, and relapse • During adolescence, pro-motivational DA increases and inhibitory serotonin decreases • Damage in OFC associated with impaired decision making, disinhibition • Disrupted dopaminergic signaling into the PFC leads to more impulsivity
Ability to make healthy choices despite social pressure • Assertiveness and problem-solving skills	Social learning theories (peer and family drug use) Family interaction models (values, parenting attitudes, relationships)
G. Intrinsic motivation to achieve health Enhanced motivation for non-drug behaviors • Backward-shifted DA motivates drug-seeking behavior	Exercise naturally releases DA, norepinephrine, and serotonin; lower all-cause mortality and cardiovascular disease Flow: experience of full engagement of one's skills in a challenging activity, goal-seeking with immediate feedback on progress is inherently rewarding
H. Positive expectations about achieving health outcomes Ability to generate positive emotions and realistic optimism, minimize catastrophic thinking and directly address counterproductive thoughts	Optimism, positive emotions (happiness, love): • Decreases cardiovascular disease, bad conduct, depression, anxiety, hopelessness • Increases resilience, well-being, health-related behavior; predicts better coping and outcomes after stress • Associated with dopaminergic 'play' systems, frontopolar cortices, exploration, flexibility, and creativity • Compassion training programs have led to enhanced neural activity in the right amygdala, which can increase positive emotion
Expressing and cultivating gratitude • Prayer, laughter	Gratitude activates reward pathways (brain stem produces DA), hypothalamus (increases serotonin) • Decreases distress; increases psychological and physical well-being
EXTERNAL FACTORS	NEUROBIOLOGICAL EFFECTS
A. Social norms Sociocultural context develops individuals' behavior, forms expectations of consequences, and influences lifestyle • In Morocco, drugs and alcohol are forbidden because of the adverse consequences	During self-agency, activity in the anterior vmPFC (part of the reward pathway) correlated with pride and guilt • Responds more strongly to prosocial norms than personal gain; responds negatively to self-serving, counter-normal choices • Herd immunity in social norms, social contagion of behavior, group think • Late 1970s - early 1990s, late 1990s: drug use declined in young adults due to changes in attitudes, beliefs, and peer norms against drug use
B. Social networks and social capital for achieving positive health outcomes Social relationships and connection can directly improve mood, reduce stress, release pleasurable feelings that diminish the need for DA from drugs	Social relationships provide positive social support, role modeling, and opportunities for positive choices and behaviors • Directly reduces stress (activity of the HPA axis) Social reward, non-social reward, and drug use activate the same reward pathway (DA in the basal ganglia) • Striatal DA (same as drug addiction) drives socially motivated behavior; NAcc, putamen, and thalamus activated when positive social feedback is anticipated
C. Group membership influences • Limited exposure and availability • Positive activities and examples • Parental support, education, supervision, and pro-health and well-being development	Judgment and decision-making faculties not fully developed until the mid-20s • Adolescents are more impulsive, more vulnerable to peer pressure, peers and friends focused on health and flourishing • Peers, parents, and communities can be either risk or protective factors in drug use and addiction
D. Material circumstances • Job security; income security; excellent learning environments; economic diversity • After-school activities reduce vulnerability to drug use • Investments in flourishing individuals and communities	Lower socioeconomic status means less access to resources, fewer choices, more external constraints on behaviors and decisions; concentrated disadvantage (poverty, low income, high unemployment, low educational attainment) is a risk factor for drug use • Control is a major component of psychological well-being • Epigenetics: social influences can alter both gene expression and function

E. Economic, political, and social security in immediate and broader macrosocial environment A secure, safe, hopeful, and supportive immediate and macrosocial environment with a sense of fairness, opportunity, inclusion and equity can reduce direct and indirect risk factors for drug us (e.g, stress) • Healthy family relationships, loving and nurturing home environments • Job and career development and stability • Welcoming, supportive and diverse schools and communitie	Stress response (SAM and HPA) system releases norepinephrine and noradrenaline, chronic stress impairs brain function: • Shrinks the PFC and increases the amygdala, increasing sensitivity to stress • Disrupts development of PFC, reward system, hippocampus, amygdala • Increases impulsivity; reduces sociability • Transition times are risk factors for drug use: divorce, loss of job, moving, changing schools, chaotic homes, abuse, ACEs
F. Utilization and access to health services Environmental barriers to treatment constitute a risk factor: • Public transportation; distance and travel time • Inclusive treatment settings (social, culture, language)	Co-morbid mental disorders and non-drug related needs are often root causes and auxiliary reinforcers of drug addiction • Co-morbidity implies exponentially detrimental interactions between illnesses occurring simultaneously or subsequently • Health services address co-morbid mental processes and support positive neurobiological developments, particularly during windows of opportunity
G. Enabling public health and health care systems Knowledge of the dangers of drugs, dependence, addiction • Empowerment and ownership • Trust in the system • Effective, impactful public health campaigns and messaging	Neural vmPFC activity tracks more closely to efficacy of public health messaging than self-judgements of campaign efficacy • Public health and health care systems can prevent neurobiological transitions to addiction and provide early treatment for lifelong recovery Cognitive-affective theories support the importance of public belief and trust in health systems • Effective systems contribute to beliefs of self-efficacy, empowerment and ownership, likely increase effective utilization of impactful services

Notes: PFC = prefrontal cortex (prefixes: m = medial, v = ventral, d = dorsal, l = lateral); HPA = hypothalamic-pituitary-adrenal axis; BDNF = brain-derived neurotrophic factor; ACEs = adverse childhood experiences; DA = dopamine; PCC = posterior cingulate cortex; NAcc = nucleus accumbens; CRF = corticotrophin-releasing factor; VAM = visual attention model; ACC = anterior cingulate cortex; OFC = orbitofrontal cortex; SAM = sympathetic adrenal medullary pathway