Chapter 2

The Etiology of Addiction

A Contemporary Biopsychosocial Approach

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A successful addiction model must synthesize pharmacological, experiential, cultural, situational, and personality components in a fluid and seamless description of addictive motivation. It must account for why a drug is more addictive in one society than another, addictive for one individual and not another, and addictive for the same individual at one time and not another. The model must make sense out of the essentially similar behavior that takes place with all compulsive involvements. In addition, the model must adequately describe the cycle of increasing yet dysfunctional reliance on an involvement until the involvement overwhelms other reinforcements available to the individual.

[1]

Introduction

The goal of the current chapter is to review contemporary perspectives on the etiology, or the causes, of addictive disorders. As illustrated by the epigraph above, this is no small task because of the complexity of these conditions and because the study of addiction is the focus of multiple disciplines using highly divergent perspectives. Furthermore, these different perspectives have not generated a single accepted account for why a person develops an addiction, but a number of empirically-grounded theoretical approaches that broadly fall into three domains—biological determinants, psychological determinants, and social determinants. These are collectively referred to as the biopsychosocial model of addiction, and the chapter will successively address these three domains, starting with neurobiological and genetic models, subsequently reviewing psychological theories, and then surveying social and societal influences. Finally, the chapter concludes with reflections on the progress and future priorities in understanding the causes of addiction.

Given the wide scope of this chapter, the emphasis will be on breadth over depth, and on theory over individual empirical studies. A fully comprehensive account of the etiology of addiction in each of these areas is beyond the scope of the chapter and incompatible with the clinical orientation of this volume. This raises the question of what the appropriate role of theory should be in the treatment of addiction. Scientific theories represent the abstracted relations among a wide array of empirical observations and, optimally, theory and treatment represent two sides of the same coin, the former describing the devel-

opment of the condition and the latter seeking to reverse-engineer the acquired dysfunction. Thus, a premise of the chapter is that a foundation in the causal models of addiction provides a scientifically-minded clinician with a framework for approaching treatment. Theories don't provide a simple answer to why a given patient developed their presenting problem, but go deeper than symptoms to articulate the important processes and mechanisms that are putatively operative. Moreover, as the theories discussed below are grounded in empirical observation, theoretically-informed treatment is one key aspect of evidence-based treatment.

Biological Models of Addiction

Neurobiological Models of Addiction

Major progress has been made in understanding the effects of addictive drugs in the brain, leading to a number of influential neurobiological models. One of the earliest theories that shaped neurobiological perspectives was the *psychostimulant theory of addiction* [2], which identified a neurobiological common denominator across drugs of addictive potential via increases in dopamine release in the medial forebrain bundle, a neuronal tract within the mesolimbic dopamine pathway. Dopaminergic activation in this region was putatively responsible for subjective reward and for motivating behavior for survival and reproduction [3, 4]. Thus, mesocortical dopaminergic activity was theorized to be the common basis for the pleasure associated with drug effects and addiction potential across diverse pharmacological compounds. In terms of etiology, the principal mechanism was the sheer magnitude of dopaminergic stimulation produced compared to natural reinforcers. In contrast, subsequent theories specifically focused both on how drugs affected the brain acutely and how repeated administration gave rise to long-standing or potentially permanent brain changes, termed neuroadaptations, that cemented high levels of drug motivation.

Among more recent models, one of the most influential is the *incentive sensitization theory* [5, 6]. Again, incentive sensitization suggests that activation of mesolimbic dopamine substrates is critical to the development of the motivational and appetitive properties; however, incentive sensitization shifted the focus away from drug reward and parsed the role of dopamine more finely. Specifically, rather than mediating either the hedonic impact of the reward (i.e., its pleasure, how much it is liked) or rewarding learning, dopamine was hypothesized to subserve the incentive salience of the reward (i.e., its motivational value, how much it is wanted). Over time, via neuroadaptative changes that result from acute overstimulation of dopamine neurotransmission, sensitization of the incentive salience attribution is hypothesized to take place via associative (Pavlovian) conditioning, creating a chronic state of wanting (also called craving). Furthermore, the processes of wanting and liking are hypothesized to be dissociable, meaning that an individual sensitizes to the motivational

salience of the drug without necessarily increasing how much the person likes the drug. The liking process in turn is thought to be subserved by endogenous opioids in the ventral tegmental area. In terms of behavioral consequences, incentive sensitization is hypothesized to give rise to attentional bias toward drug stimuli and high levels of craving [7].

An alternative formulation, the *cellular learning model of addiction*, makes the case that addiction should be more broadly considered a disorder of learning and memory [8, 9]. From this perspective, sensitization of dopamine neurotransmission is one part of the neurobiology of addiction, but the subsequent downstream learning processes are even more important. Specifically, this account proposes that potent psychoactive drug effects contribute to synaptic plasticity that leads to long-term increases in the salience of drug rewards and, by comparison, decreases in the salience of alternative rewards [8, 9]. This is hypothesized to take place by way of drug-induced remodeling of neuronal dendrites, axons, and synapses, either via up- or down-regulation of gene expression or expression-based effects that lead to morphological synaptic changes. Supporting this thesis, addictive drugs have been robustly found to induce alterations in gene expression associated with synaptic plasticity, including inducing ΔFosB, a relatively long-lasting transcription factor that increases sensitivity to the rewarding and locomotor stimulant effects of addictive drugs [10, 11]. Thus, the highly potent psychoactive effects of addictive drugs are theorized to become deeply instantiated in the brain via potent effects on circuitry for learning new events and remembering important ones from the past.

Other neurobiological theories contrast with the preceding models that emphasize the drug acquiring very high rewarding salience. One dominant line of inquiry has pursued addiction as a series of transitions from voluntary use to habitual use to, ultimately, compulsive use of alcohol and other drugs [12, 13]. The neurobiological substrates responsible for these changes are theorized to be a transition from processing in the ventral striatum, which is responsible for subjectively rewarding drug effects subserving goal directed behavior, to the dorsal striatum, which is responsible for motor and habit learning. This neuroadaptive change is theorized to be a transition from deliberative action-outcome instrumental learning to reflexive stimulus-response learning, such that drug-seeking ultimately becomes increasingly automatic and outside of voluntary control. A substantial body of preclinical research supports this shift [14]. The *ventral-to-dorsal striatum account* is not necessarily incompatible with incentive sensitization, but it certainly emphasizes automaticity in behavior over increasing subjective drug motivation.

The *allostatic model of addiction* [15–17] shares a parallel with the ventral-to-dorsal striatum model to the extent that it emphasizes stages in addiction characterizing the initial heavy use of alcohol and drugs for its rewarding properties followed by chronic and uncontrolled use that is no longer driven by reward-seeking. Specifically, addiction is theorized to progress through three stages: (1) binge use/intoxication; (2) withdrawal/negative affect; and (3) preoccupation/anticipation (craving). These stages map on to progressive

neuroadaptive changes in the striatum, extended amygdala, hippocampus, and orbitofrontal cortex. Furthermore, the development of addiction is characterized as an aberrant homeostatic, or allostatic, process that involves changes in reward and stress circuits following persistent exposure to addictive drugs. This model is one of the few that explicitly integrates the neurobiology of the acute rewarding effects of drugs with mechanisms related to negative reinforcement associated with withdrawal and stress (e.g., corticotrophin-releasing factor, neuropeptide Y). One of the primary advantages of this model is that it integrates a wide array of findings on molecular, cellular, and neuronal changes that are associated with the pathophysiology of addiction. However, evidence from this model is drawn primarily from studies of alcohol, as opposed to other drugs of abuse.

Finally, although most of the preceding models have emphasized neuroadaptive changes in subcortical circuitry, it is worth noting that there are also contemporary neurobiological models that focus on deficits and acquired changes in prefrontal cortex functioning. In particular, neuroimaging studies and preclinical models have revealed dysregulation in subunits of the prefrontal cortex responsible for inhibitory control and reactivity to stimuli signaling drug availability [18–20]. Thus, addiction can be understood as resulting from both pathological adaptations within motivational systems and higher-level prefrontal systems.

Genetic Influences on Addiction

A limitation to most of the preceding models is that they typically describe addiction as a general process, not in relation to individual risk. In reality, addiction develops in only a minority of individuals who experiment with addictive drugs [21] and understanding which individuals are most vulnerable has important implications for both prevention and treatment. In biological models of addiction, the question of individual vulnerability largely pertains to genetic influences and genetic variation conferring etiological risk is well established. For example, there is an extensive literature using twin and adoption designs to ascertain the aggregate heritability of addictive disorders, generally suggesting 40–60% heritability [22, 23]. More recently, substantial heritability has also been identified using genomic complex trait analysis, a novel technique that generates estimates using variation in common single nucleotide polymorphisms (SNPs) across the genome [24, 25].

These studies make it clear that genetic variation is an important influence on the development of addiction, but the mechanisms by which this influence is conferred have been elusive. Candidate gene studies have generated mixed findings and atheoretical genome-wide association studies have generally not identified significant loci. However, two notable exceptions are robust evidence that variation in a locus responsible for alcohol pharmacokinetics is a protective factor against alcohol use disorder, and that variation putatively related to nicotine pharmacodynamics is a risk factor for nicotine dependence. In the first case, the *ALHD2* gene is responsible for aldehyde dehydrogenase activity, a key enzyme for breaking down acetaldehyde resulting from alcohol metabolism, and the

A allele of an SNP (rs671) within *ALDH2* results in substantially lower enzymatic activity. As a result, if A allele carriers drink alcohol, they experience an acetaldehyde buildup and a number of unpleasant symptoms, including flushing, nausea, headache, and tachycardia. The A allele is relatively common in Asian populations and effectively makes carriers "allergic" to alcohol, exerting a powerful protective effect against alcohol use disorder [26]. In the second case, a number of large-scale studies have convincingly implicated variants on chromosome 15 with nicotine dependence. This region contains the α5-α3-β4 nicotinic receptor gene cluster, and nicotinic cholinergic receptors are key sites of action for nicotine. In particular, a locus in the α5 nicotinic receptor subunit gene (*CHRNA5*), rs16969968, has been associated with significantly increased risk for developing nicotine dependence and smoking-related diseases, such as lung cancer and chronic obstructive pulmonary disease [27].

These findings represent two success stories in understanding addiction genetics, illustrating the ways that genetic variation may influence the pharmacokinetics and pharmacodynamics of drug effects to influence addiction risk. However, it is also clear that major gaps in knowledge remain and that progress in addiction genetics has been slower than anticipated, even after the development of sophisticated genome-wide techniques. In general, there is little evidence for one major "addiction gene" or a small number of highly influential loci. Instead, the current perspective is that it is likely that hundreds or thousands of variants contribute small magnitude effects to affect risk.

Difficulty in identifying genetic influences on addiction may also be a function of the heterogeneity of the clinical phenotype, given the many permutation symptoms that may be present. To address this, there is increasing interest in identifying narrower, more discrete behavioral phenotypes that are putatively more closely related to specific neurobiological processes and genetic variation in particular [28, 29]. These characteristics are also called intermediate phenotypes or endophenotypes, and are predicted both to increase power to detect specific genes underlying the risk for a given disorder and to inform mechanisms of risk or protection.

Psychological Models of Addiction

A Reinforcement-Based Approach

One of the earliest psychological theories of addictive behavior that is still actively pursued to this day is an operant learning approach. With foundations in early learning theory [30, 31], this approach theorizes that substance use is fundamentally a form of instrumental learning, meaning the behavior is primarily determined by its consequences and, more specifically, the reinforcing properties of the drug [32–34]. This comprises both positive reinforcement (i.e., effects provided by the drug that strengthen motivation), such as stimulation, social enhancement, orosensory, or gustatory properties; and negative reinforcement (i.e., states removed by the drug that strengthen motivation), such as the

alleviation of anxiety, depression, other psychiatric symptoms, or withdrawal symptoms. Importantly, these different forms of positive and negative reinforcement are not mutually exclusive, operating concurrently, and in the context of punishing drug consequences and the presence (or absence) of alternative reinforcers. In broad strokes, this approach proposes that a drug's positively and negatively reinforcing properties, its punishing properties, the opportunity for alternative reinforcers, and the timing of the aforementioned jointly determine the reinforcing value of the drug, the final common pathway to use. These processes are theorized to be the proximal mechanisms by which other known risk factors (e.g., genetic and environmental vulnerabilities) contribute to substance use, and individual differences in each domain are responsible for differences in vulnerability across individuals.

Considerable evidence supports this approach, starting with data from early residential studies revealing that drug consumption could be studied experimentally and fundamentally conformed behavioral principles [35, 36]. Subsequently, human laboratory studies convincingly demonstrated that drug consumption conformed to key predictions from operant theory in terms of sensitivity to increases in response cost and the presence of alternative reinforcers [37–39].

More recently, a reinforcement-based model of addiction has been extended using behavioral economics, which integrates psychological and economic principles to understand decision-making and consumption behavior. This is a natural extension, following from recognition that operant behavior in complex environments with multiple options and different costs and benefits is essentially a behavioral microeconomy and that decision-making is a critical final common pathway to consumption behavior. Integrating economic concepts into addiction research also provides powerful tools for quantifying reinforcing value. One form of behavioral economic decision-making that has been extensively examined in relation to addiction is preference for smaller immediate rewards compared to larger delayed rewards. This is considered a behavioral economic index of impulsivity and is discussed below with other measures of impulsivity. In addition, purchase tasks that assess estimated drug consumption at escalating levels of price have been used to efficiently measure the reinforcing value of drugs, which is significantly associated with substance misuse and has been found to predict treatment response. An alternative measure characterizes substance-related reinforcement compared to non-drug alternative reinforcement, a measure of disproportionate reliance on drug-related reinforcement, and has also been linked to level of drug involvement [40–44]. Finally, a reinforcement-based approach has given rise to treatments that either seek to develop mutually exclusive alternative reinforcers to compete with drug use or directly reinforce elements of treatment, which are among some of the best supported treatments [45, 46].

Variability in Acute Drug Effects

A related perspective emphasizes on the importance of variation in the drug's subjective effects as a determinant of use and misuse. This has most extensively

been investigated in relation to alcohol, but clearly has relevance to other drugs also. Early theories of alcohol effects predicted that individuals primarily drink alcohol because of its ability to reduce tension, the so-called tension reduction hypothesis. However, the evidence that a direct, consistent effect of alcohol is to alleviate tension is weak [47, 48]. Subsequently, it has become clear that alcohol's direct effects are best understood as having both stimulant and sedative properties, with the former predominating during the ascending limb of the blood–alcohol curve and the latter predominating during the descending limb [49, 50]. In addition, attenuated response to alcohol has been identified as a risk factor for lifelong alcohol misuse [51, 52], and a recent meta-analysis revealed consistent evidence that the risk factor of having a positive family history of alcohol use disorder is conferred by attenuated alcohol effects [53]. However, it is notable that other studies have prospectively linked augmented stimulant effects to greater alcohol problems while greater levels of sedative effects are protective against the development of an alcohol use disorder [54, 55], thus suggesting that important aspects of this relationship remain insufficiently understood.

Cognitive Processes

The preceding theories reflect proximal properties of substances, but cognitive models emphasize the intervening role of mental or information processing mechanisms. One dominant cognitive model emphasizes the importance of expectancies in determining addictive behavior. Expectancies refer to cognitive templates that reflect the memorial residues from previous experiences and exist to anticipate experiences and facilitate behavior. Expectancies reflect bidirectional relationships in which experiences stamp imprints into the brain's memory systems, and these imprints preemptively generate responses, effectively creating self-fulfilling behavioral prophecies. Expectancies are believed to be partially responsible for placebo effects, to medications in general [56] and to addictive drugs [57]. Furthermore, expectancy inventories on expectancies reveal the multifarious beliefs that individuals hold about drug effects [58]. For example, a wide variety of alcohol expectancies have been characterized, including global positive effects, sexual enhancement, social facilitation, assertiveness, relaxation/tension reduction, and interpersonal power [58], and expectancies have been significantly associated with substance use cross-sectionally and longitudinally [59–61]. Importantly, expectancies do not necessarily reflect direct pharmacological actions of alcohol so much as the individual's aggregated construal of alcohol's effects, resulting from the complex intersection of pharmacology, accurate and inaccurate attributions in ambiguous social and interpersonal contexts, and the background context sociocultural messages, norms, and advertising. For example, as noted above, alcohol may not have direct anxiolytic effects, but a person may attribute tension reduction properties to drinking beer because it is consumed as part of an after-work routine or because the brand markets it in that capacity.

Related cognitive determinants are motives for substance use, the pattern of reasons that a person reports for why he or she uses the drug. Like expectancies, motives are typically assessed using self-report assessments and validated measures have revealed distinct patterns of motives. For example, most drugs are used for social, enhancement, and coping motives [62–65]. However, differences are also present across drugs. For example, pain management is important for opioid users [64, 66]; sensory expansion is a distinct motivational domain for marijuana [65]; and social conformity represents a subfactor for young adult drinkers [67]. Facets of motivation have been robustly associated with levels of substance use and clinical severity, with coping motives exhibiting particularly robust associations [64, 67]. A larger array of motives have been identified for smoking, 13 in total (see Chapter 5). Of these, tolerance, craving, loss of control, and automaticity have been identified as the primary dependence motives, and are most robustly associated with nicotine dependence [68].

Within a cognitive framework, expectancies and motives can be thought of as explicit reflective cognitive processes, or declarative "top-down" processes in which the individual reports introspectively available cognitions about the drug. An important complement to those mechanisms are implicit automatic cognitive processes, or unconscious "bottom-up" processes that reflect the salience and weighting of drugs within a person's cognitive network. Implicit cognition can be measured in a variety of different ways, but the common theme is using behavioral tasks that embed drug-related information and use behavioral performance, often interference, to reveal how salient drug information is within the person's cognitive network. Level of cognitive bias on these measures has been significantly associated with level of substance misuse [69] and has also been found to be predictive of treatment response [70, 71]. Indeed, implicit cognition has given rise to novel adjunctive retraining treatments to degrade these acquired associations [72, 73]. Implicit and explicit measures of cognition are weakly associated, with some shared variance but both independently predicting substance involvement [74].

Personality Factors

The notion of an "addictive personality" has also elicited considerable interest as a psychological determinant of addiction, but has also been controversial [75], and there is weak evidence for any singular pattern of personality characteristics that is commonly present in addiction [76]. On the other hand, there is evidence that some normative personality traits are consistently associated with addictive behavior, including positive links with neuroticism and negative links with conscientiousness and agreeableness [77–80]. However, the most robust link between characterological traits and addiction is present for associations with measures of impulsivity, broadly defined as capacity for self-control of arising impulses. Importantly, impulsivity is measured in a variety of different ways and it is increasingly understood to be a multidimensional psychological trait. Self-reported impulsive personality traits on questionnaires reveal a number of

different facets. For example, the UPPS-P impulsive behavior scale comprises five subscales, including positive and negative urgency (i.e., proneness to act out during positive and negative mood states), premeditation (lack of) (i.e., level of deliberation or forethought), perseverance (lack of) (i.e., level of persistence or follow-through), and sensation seeking (i.e., preference for stimulating, exciting, or novel experiences). Of these, all of the traits have been linked to substance use, but positive and negative urgency are particularly related to clinical severity [81]. A second multidimensional measure of self-reported impulsive personality traits is the Barratt Impulsiveness Scale, which has also been robustly linked to addictive disorders and other externalizing behavior [82]. Beyond self-report, behavioral tasks can be used to measure orientation to immediate versus delayed reward (also referred to as delay discounting or delay of gratification), and capacity to inhibit prepotent motor responses (also referred to as response inhibition). In both cases, higher levels of impulsive responding have been linked to addictive disorders [83, 84]. However, it is notable that although the associations within the three domains of personality traits, delay discounting, and response inhibition are generally moderate to large, correlations across domains are generally small to negligible [85–87], suggesting they are distinct from one another.

Developmental Psychopathology

The last important psychological perspective is that of developmental psychopathology, an approach that seeks to understand psychiatric conditions as maladaptive deviations from normative human development. This perspective broadens the etiological lens to recognize influences prior to active drug use, such as prenatal influences and adverse childhood events [88, 89], and across the lifespan. In particular, a critical developmental window in the development of addiction is from adolescence to young adulthood, approximately 13–25. This is a broad window, but within it the vast majority of individuals will initiate their first exposures to addictive drugs and sizable proportions will progress to regular use and clinically significant misuse. For example, alcohol consumption peaks during emerging adulthood and is the most significant source of morbidity and mortality for this cohort [90, 91]. Furthermore, in the later phase of that time window, many individuals will naturally reduce consumption or stop using altogether, referred to as "maturing out" of drug use. In this way, it is not dissimilar to other forms of experimentation and role exploration that are present in adolescence, behaviors that are believed to be evolutionarily adaptive for developing autonomy, social status, and mate selection [92]. However, drug use during adolescence and young adulthood can also interfere with important developmental goals, such as educational attainment, career development, long-term relationships, and having a family [93–95], setting the stage for potentially lifelong problems. Notably, successful maturing out of substance use has been found to be a function of role transitions in terms of work, marriage, and parenthood [96–98]. Thus, there appear to be developmentally limited and

lifetime persistent forms of substance use and substance use disorder [99], subtypes that are not unlike other externalizing behavior [100].[1] Taken together, converging data suggest that this developmental window is similar to an ethological "critical period," setting the stage for healthy and unhealthy substance use across the lifespan [101–103]. Furthermore, the preceding psychological mechanisms can also be understood within a developmental framework, with changes in expectancies, motives, and facets of impulsivity also predicting healthy and unhealthy changes in substance use during adolescence and young adulthood [104–108].

A final note pertaining to developmental psychopathology is that the perspective has been substantially enhanced by a deeper understanding of neurocognitive development. For example, the development of prefrontal cortex is gradual and protracted across adolescence and into young adulthood [109, 110]. Unfortunately, as a result, the developing brain appears to be more susceptible to neurotoxic effects of substance use [111, 112]. Furthermore, at least in preclinical models, adolescents appear to be more sensitive to reinforcing drug effects and less sensitive to the punishing effects [113]. Thus, adolescence and young adulthood represent a developmental window characterized by a surge in substance use during a period of neurocognitive vulnerability, with potential ramifications across the life span.

Social Models of Addiction

Social Networks

The importance of social factors in addiction is readily apparent from the observation that substance use is very commonly a social activity and the proverb that "birds of a feather flock together." Furthermore, there is a large empirical literature supporting this perspective. For example, social enhancement features prominently in measures of expectancies and motives [58, 62–65] and estimated substance use among close social affiliates is highly correlated with personal use [114, 115]. The importance of social influences can also be seen in clinical research. For example, in large randomized controlled trials, changes in the alcohol-related composition of the important individuals in a person's life have been found to predict treatment response, irrespective of experimental condition [116, 117]. Positive changes in social networks have been found to be mechanisms of the positive effects of Alcoholics Anonymous [118]. Furthermore, an intervention specifically developed to create a more positive social network has been shown to significantly increase behavioral and attitudinal support for not drinking and to significantly decrease drinking itself [119, 120].

The critical influence of a person's social ecology has been even more clearly revealed via social network analysis (SNA), a family of methodologies for quantitatively characterizing the structure of relationships among people [121–123]. There are broadly two SNA approaches, *egocentric* and *sociocentric*. Egocentric SNA refers to a person's self-reported social network (i.e., the

network from the perspective of that individual, referred to as the "ego"). Sociocentric SNA refers to the objective social network (i.e., each person rates their relationship with each other person, such that the network is a latent property of cross-ratings). The advantage of egocentric SNA is that it provides the ego's perspective on the important people in their lives, whereas the advantage of sociocentric SNA is that it characterizes an objective network of individuals. A number of studies have examined social network dynamics relating to addictive behavior and have generated a number of important insights. For example, in early adolescents, individuals who are central to their social networks are more likely to use alcohol [124] and have been found to have more influence on their friends' alcohol use [125]. In addition, there is evidence for what are referred to as *selection dynamics* (e.g., drinkers seeking out other drinkers) and *influence dynamics* (i.e., the presence of drinkers in a network inducing more drinking), and these dynamics vary across adolescence [126–130]. Similarly, in adults, drinkers have been found to cluster together and social network characteristics predict changes in drinking over time [131–133], with parallel findings for other addictive disorders [115, 124, 129, 134].

Collectively, a social network perspective proposes that individuals self-select into networks of social relationships that are populated with people exhibiting similar levels of substance use (or lack thereof). For individuals with addiction, these networks are theorized to have a self-perpetuating influence on their members over time, including impeding behavior change in treatment. Thus, for some individuals, treatment may not just require abstaining or reducing alcohol, tobacco, cocaine, or heroin, but giving up important interpersonal relationships too. Here again, there is a maladaptive cycle in which social network influences recursively maintain the addictive behavior.

Classes of Social Influence and Mechanisms

It is important to recognize that not all members in social networks are of equal importance and the level of influence varies across the life span. In the critical period of adolescence and young adulthood, parental influences and peer influences are particularly powerful. A number of different parental influences have been identified. Arguably, the most important influence is parental substance use [135, 136], which can model the behavior, communicate perceived approval, and increase availability. In addition, parenting style is an important factor. Authoritative parenting is protective against substance use [137, 138], but the reverse is true for harsh parenting and parental hostility [139–141]. As parent–child connectedness and parental support are also negatively related to substance use [137, 138], it appears that both structure and warmth are important protective influences. Peer influences on substance use can be divided into three broad domains: overt offers, reflecting direct requests to use; modeling, reflecting passive social influence by familiar or unfamiliar peers; and social norms, reflecting the overestimation of typical behavior within a cohort [142]. All three domains are influential to varying extents [143–146]. In addition, in the case of

social norms, social media campaigns have been undertaken to modify widespread overestimates, albeit with mixed evidence of efficacy [147].

Although parental and peer influences are most relevant to adolescents and young adults, dyadic influences, or significant others, are a potent social influence throughout adulthood. This is particularly an issue because individuals who use substances are more likely to be in a relationship together [148, 149], referred to as assortative mating, leading to dual-addiction couples. Like parental substance use, substance use among significant others provides a form of modeling, communicates approval, and provides access to substances [150]. However, addiction in couples is also associated with additional adverse patterns and consequences, such as intimate partner violence and poor parenting [150]. Thus, addiction among both members of a dyad represents a particularly deep embedding of the condition within a social network.

Sociocultural Influences

Finally, social influences on addiction include higher-order factors within society and culture, such as religion, economic conditions, and public policy. Religion is highly influential in overall population levels of substance use [151, 152] and, in terms of public policy, levels of taxation have major impacts on tobacco and alcohol consumption [153, 154]. Related to taxation, there is robust evidence that minimum pricing for alcohol reduces consumption [155, 156] and reduces negative consequences from drinking [157]. Other regulatory public policy influences include legal age of consumption, private versus state monopoly markets, law enforcement, density of outlets, and the availability of drink specials/"happy hours" [158]. Of course, economic and policy influences largely only pertain to legal addictive drugs or gambling because illicit drugs are unregulated. However, access to evidence-based prevention and treatments, and costs of care, are also important sociocultural factors that affect treatment for all forms of addiction [159–161]. In each of the preceding cases, these represent ways that a geographic area can have a favorable or unfavorable sociocultural climate toward the development and treatment of addiction.

Conclusions

If the goal of scientific theory is "to carve nature at its joints," then by extension, in clinical science, the goal of treatment is to intervene upon the dysfunction that is present in each of the resulting parts. A contemporary biopsychosocial approach carves addiction into three major sections and then further subdivides in a number of different ways. What emerges across these multifarious accounts is that there is no simple or singular answer to the question of why people develop addiction. Contemporary neurobiological theories of addiction offer incisive insights into addiction, emphasizing that psychoactive drugs use evolutionarily novel levels of stimulation to subvert, or even hijack, ancient brain systems that are responsible for adaptive motivation, learning, and executive control.

Psychologically, elevations in the reinforcing value of drug effects, maladaptive explicit and implicit cognitive processing, and deficits in self-regulatory capacities all contribute to persistent drug use, influences that are superimposed upon a developmental backdrop. Finally, social factors play a critical role, from family members and friends to extended social networks and a person's broader sociocultural context. A common theme in these accounts is the presence of recursive etiological processes, or feedforward processes that, once initiated and sufficiently engaged, are theorized to become self-sustaining and exacerbating. In other words, across theoretical accounts, there is convergence that addiction is a disorder of "vicious cycles," or patterns of maladaptive overconsumption that over time become increasingly difficult to change.

The array of perspectives reveals both strengths and weaknesses in the science of addiction. The contemporary approach provides a rich multidimensional perspective, spanning levels of analysis and addressing the complexity of the condition. However, rather than reflecting true synthesis across levels of analysis, a biopsychosocial approach still predominantly reflects discrete perspectives within each of these three domains. Furthermore, theoretical perspectives typically do not extend across disciplinary boundaries. Biological, psychological, and social approaches tend to be siloed away from each other, especially as methodological and disciplinary differences get larger. For example, there are no links between preclinical animal models, human developmental psychopathology, and tax policy. In this way, the field is akin to the parable about "the blind men and the elephant"—researchers in many different areas of the field are correctly identifying important aspects of a large complex problem, but no holistic theoretical viewpoint provides an overall framework.

Importantly, however, a merging of perspectives is increasingly taking place. Neuroimaging is increasingly permitting insights from preclinical models to be investigated directly in human participants affected by addiction. Genetic variables are being woven into psychological and social frameworks, and reciprocally behavioral and social measures are serving as novel phenotypes for genetic dissection or as moderators of genetic influences. Novel medications are targeting promising neural pathways from preclinical research and providing innovative mechanisms of action. These will be the advances that permit more comprehensive accounts of addiction to be developed, ones that more satisfactorily rise to the challenge of the epigraph at the chapter's start. Furthermore, even in its current incarnation, the contemporary biopsychosocial approach nonetheless provides a wealth of etiological processes and mechanisms for clinicians to consider in treating patients, making it an indispensable perspective in evidence-based treatment of addiction.

Note

1. Beyond a binary distinction, it is worth noting that a wide variety of theoretically and empirically derived addiction subtypes or trajectory profiles have been identified, but that a comprehensive review of these denominations is beyond the scope of the chapter.

References

1. Peele S, Alexander BK (1998) Theories of addiction. In: Peele S, editor. *The meaning of addiction: an unconventional view*. San Francisco (CA): Jossey-Bass.
2. Wise RA, Bozarth MA. A psychomotor stimulant theory of addiction. *Psychol Rev*. 1987;94:469–492.
3. Nesse RM, Berridge KC. Psychoactive drug use in evolutionary perspective. *Science*. 1997;278:63–66.
4. Kelley AE, Berridge KC. The neuroscience of natural rewards: relevance to addictive drugs. *J Neurosci*. 2002;22:3306–3311. doi:20026361.
5. Robinson TE, Berridge KC. The neural basis of drug craving: an incentive-sensitization theory of addiction. *Brain Res Brain Res Rev*. 1993;18:247–291.
6. Robinson TE, Berridge KC. Incentive-sensitization and addiction. *Addiction*. 2001;96:103–114. doi:10.1080/09652140020016996.
7. Robinson TE, Berridge KC. Review. The incentive sensitization theory of addiction: some current issues. *Philos Trans R Soc Lond B Biol Sci*. 2008;363: 3137–3146. doi:10.1098/rstb.2008.0093.
8. Hyman SE Addiction: a disease of learning and memory. *Am J Psychiatry*. 2005; 162:1414–1422. doi:10.1176/appi.ajp.162.8.1414.
9. Hyman SE, Malenka RC, Nestler EJ. Neural mechanisms of addiction: the role of reward-related learning and memory. *Annu Rev Neurosci*. 2006;29:565–598. doi:10.1146/annurev.neuro.29.051605.113009.
10. Kelz MB, Chen J, Carlezon WA, et al. Expression of the transcription factor deltaFosB in the brain controls sensitivity to cocaine. *Nature*. 1999;401:272–276. doi:10.1038/45790.
11. Colby CR, Whisler K, Steffen C, et al. Striatal cell type-specific overexpression of DeltaFosB enhances incentive for cocaine. *J Neurosci*. 2003;23:2488–2493.
12. Robbins TW, Everitt BJ. Drug addiction: bad habits add up. *Nature*. 1999;398: 567–570. doi:10.1038/19208.
13. Everitt BJ, Robbins TW. Neural systems of reinforcement for drug addiction: from actions to habits to compulsion. *Nat Neurosci*. 2005;8:1481–1489. doi:10. 1038/nn1579.
14. Everitt BJ, Robbins TW. From the ventral to the dorsal striatum: devolving views of their roles in drug addiction. *Neurosci Biobehav Rev*. 2013;37:1946–1954. doi:10.1016/j.neubiorev.2013.02.010.
15. Koob GF, Le Moal M. Drug addiction, dysregulation of reward, and allostasis. *Neuropsychopharmacology*. 2001;24:97–129. doi:S0893-133X(00)00195-0 [pii] 10. 1016/S0893-133X(00)00195-0.
16. Koob GF, Le Moal M. Addiction and the brain antireward system. *Annu Rev Psychol*. 2008;59:29–53. doi:10.1146/annurev.psych.59.103006.093548.
17. Koob GF, Volkow ND. Neurocircuitry of addiction. *Neuropsychopharmacology*. 2010;35:217–238. doi:npp2009110 [pii] 10.1038/npp.2009.110.
18. Kalivas PW, Volkow ND. The neural basis of addiction: a pathology of motivation and choice. *Am J Psychiatry*. 2005;162:1403–1413. doi:10.1176/appi.ajp.162.8. 1403.
19. Goldstein RZ, Volkow ND. Drug addiction and its underlying neurobiological basis: neuroimaging evidence for the involvement of the frontal cortex. *Am J Psychiatry*. 2002;159:1642–1652. doi:10.1176/appi.ajp.159.10.1642.

20. McClure SM, Bickel WK. A dual-systems perspective on addiction: contributions from neuroimaging and cognitive training. *Ann N Y Acad Sci*. 2014;1327:62–78. doi: 10.1111/nyas.12561.
21. Grant BF, Dawson DA, Moss HB. Disaggregating the burden of substance dependence in the United States. *Alcohol Clin Exp Res*. 2011;35:387–388. doi:10.1111/j.1530-0277.2011.01433.x.
22. Goldman D, Oroszi G, Ducci F. The genetics of addictions: uncovering the genes. *Nat Rev Genet*. 2005;6:521–532. doi:nrg1635 [pii] 10.1038/nrg1635.
23. Agrawal A, Lynskey MT. Are there genetic influences on addiction: evidence from family, adoption and twin studies. *Addiction*. 2008;103:1069–1081. doi:10.1111/j.1360-0443.2008.02213.x.
24. Palmer RHC, McGeary JE, Heath AC, et al. Shared additive genetic influences on DSM-IV criteria for alcohol dependence in subjects of European ancestry. *Addiction*. 2015;110:1922–1931. doi:10.1111/add.13070.
25. Bidwell LC, Palmer RHC, Brick L, et al. Genome-wide single nucleotide polymorphism heritability of nicotine dependence as a multidimensional phenotype. *Psychol Med*. 2016;1–11. doi:10.1017/S0033291716000453.
26. Luczak SE, Glatt SJ, Wall TL. Meta-analyses of ALDH2 and ADH1B with alcohol dependence in Asians. *Psychol Bull*. 2006;132:607–621. doi:10.1037/0033-2909.132.4.607.
27. Bierut LJ. Convergence of genetic findings for nicotine dependence and smoking related diseases with chromosome 15q24-25. *Trends Pharmacol Sci*. 2009. doi:S0165-6147(09)00168-0 [pii] 10.1016/j.tips.2009.10.004.
28. Gottesman II, Gould TD. The endophenotype concept in psychiatry: etymology and strategic intentions. *Am J Psychiatry*. 2003;160:636–645.
29. MacKillop J, Munafò MR. *Genetic influences on addiction: an intermediate phenotype approach*. Cambridge (MA): MIT Press; 2013.
30. Thorndike EL. *Animal intelligence*. New Brunswick (NJ): Transaction Publishers; 2011.
31. Skinner BF. *The behavior of organisms: an experimental analysis*. Acton (MA): Copley Publishing Group; 1966.
32. Bigelow GE. An operant behavioral perspective on alcohol abuse and dependence. In: Heather N, Peters TJ, Stockwell T, editors. *International handbook of alcohol dependence and problems*. Chichester (UK): John Wiley & Sons; 2001:299–315.
33. Higgins ST, Heil SH, Lussier JP. Clinical implications of reinforcement as a determinant of substance use disorders. *Annu Rev Psychol*. 2004;55:431–461. doi:10.1146/annurev.psych.55.090902.142033.
34. Bickel WK, Johnson MW, Koffarnus MN, et al. The behavioral economics of substance use disorders: reinforcement pathologies and their repair. *Annu Rev Clin Psychol*. 2014;10:641–677. doi:10.1146/annurev-clinpsy-032813-153724.
35. Mello NK, Mendelson JH. Operant analysis of drinking patterns of chronic alcoholics. *Nature*. 1965;206:43–46.
36. Mendelson JH, Mello NK. Experimental analysis of drinking behavior of chronic alcoholics. *Ann N Y Acad Sci*. 1966; 133:828–845.
37. Bigelow G. An operant behavioral analysis of alcohol abuse and dependence. In: Heather N, Peters TJ, Stockwell T, editors. *International handbook of alcohol dependence and problems*. Chichester (UK): John Wiley & Sons; 2001:299–315.
38. Budney AJ, Higgins ST, Hughes JR, Bickel WK. The scientific/clinical response to the cocaine epidemic: a MEDLINE search of the literature. *Drug Alcohol Depend*. 1992;30:143–149. doi:0376-8716(92)90019-9 [pii].

39. Jones JD, Comer SD. A review of human drug self-administration procedures. *Behav Pharmacol*. 2013;24:384–395. doi:10.1097/FBP.0b013e3283641c3d.
40. Correia CJ, Simons J, Carey KB, Borsari BE. Predicting drug use: application of behavioral theories of choice. *Addict Behav*. 1998;23:705–709. doi:S0306-4603(98)00027-6 [pii].
41. Correia CJ, Carey KB, Borsari B. Measuring substance-free and substance-related reinforcement in the natural environment. *Psychol Addict Behav*. 2002;16:28–34.
42. MacKillop J, Murphy JG. A behavioral economic measure of demand for alcohol predicts brief intervention outcomes. *Drug Alcohol Depend*. 2007;89:227–233. doi:S0376-8716(07)00022-1 [pii] 10.1016/j.drugalcdep.2007.01.002.
43. Murphy JG, Correia CJ, Colby SM, Vuchinich RE. Using behavioral theories of choice to predict drinking outcomes following a brief intervention. *Exp Clin Psychopharmacol*. 2005;13:93–101. doi:2005-05782-002 [pii] 10.1037/1064-1297.13.2.93.
44. Murphy JG, MacKillop J, Skidmore JR, Pederson AA. Reliability and validity of a demand curve measure of alcohol reinforcement. *Exp Clin Psychopharmacol*. 2009;17:396–404. doi:2009-23091-004 [pii] 10.1037/a0017684.
45. Stitzer M, Petry N. Contingency management for treatment of substance abuse. *Annu Rev Clin Psychol*. 2006;2:411–434. doi:10.1146/annurev.clinpsy.2.022305.095219.
46. Meyers RJ, Smith JE, Lash DN. The community reinforcement approach. *Recent Dev Alcohol*. 2003;16:183–195.
47. Cappell H, Herman CP. Alcohol and tension reduction: a review. *Q J Stud Alcohol*. 1972;33:33–64.
48. Greeley J, Oei T. Alcohol and tension reduction. In: Leonard KE, Blane HT, editors. Psychological theories of drinking and alcoholism. 2nd ed. New York: Guilford Press; 1999:14–53.
49. Martin CS, Earleywine M, Musty RE, et al. Development and validation of the Biphasic Alcohol Effects Scale. *Alcohol Clin Exp Res*. 1993;17:140–146.
50. Ray LA, MacKillop J, Leventhal A, Hutchison KE. Catching the alcohol buzz: an examination of the latent factor structure of subjective intoxication. *Alcohol Clin Exp Res*. 2009;33:2154–2161. doi:10.1111/j.1530-0277.2009.01053.x.
51. Schuckit MA. A longitudinal study of children of alcoholics. *Recent Dev Alcohol*. 1991;9:5–19.
52. Schuckit MA. Biological, psychological and environmental predictors of the alcoholism risk: a longitudinal study. *J Stud Alcohol*. 1998;59:485–494.
53. Quinn PD, Fromme K. Subjective response to alcohol challenge: a quantitative review. *Alcohol Clin Exp Res*. 2011. doi:10.1111/j.1530-0277.2011.01521.x.
54. King AC, de Wit H, McNamara PJ, Cao D. Rewarding, stimulant, and sedative alcohol responses and relationship to future binge drinking. *Arch Gen Psychiatry*. 2011;68:389–399. doi:10.1001/archgenpsychiatry.2011.26.
55. Hendershot CS, Wardell JD, McPhee MD, Ramchandani VA. A prospective study of genetic factors, human laboratory phenotypes, and heavy drinking in late adolescence. *Addict Biol*. 2016. doi:10.1111/adb.12397.
56. Stewart-Williams S, Podd J. The placebo effect: dissolving the expectancy versus conditioning debate. *Psychol Bull*. 2004;130:324–340. doi:10.1037/0033-2909.130.2.324.
57. Metrik J, Rohsenow DJ. Understanding the role of substance expectancies in addiction. In: MacKillop J, de Wit H, editors. *The Wiley-Blackwell handbook of addiction psychopharmacology*. Chichester: John Wiley & Sons; 2013:459–488.

58. Brown SA, Christiansen BA, Goldman MS. The Alcohol Expectancy Questionnaire: an instrument for the assessment of adolescent and adult alcohol expectancies. *J Stud Alcohol*. 1987;48:483–491.
59. Darkes J, Greenbaum PE, Goldman MS. Alcohol expectancy mediation of biopsychosocial risk: complex patterns of mediation. *Exp Clin Psychopharmacol*. 2004;12:27–38. doi:10.1037/1064-1297.12.1.27 2004-10475-007 [pii].
60. Smith GT, Goldman MS, Greenbaum PE, Christiansen BA. Expectancy for social facilitation from drinking: the divergent paths of high-expectancy and low-expectancy adolescents. *J Abnorm Psychol*. 1995;104:32–40.
61. Christiansen BA, Smith GT, Roehling PV, Goldman MS. Using alcohol expectancies to predict adolescent drinking behavior after one year. *J Consult Clin Psychol*. 1989;57:93–99.
62. Cooper ML, Frone MR, Russell M, Mudar P. Drinking to regulate positive and negative emotions: a motivational model of alcohol use. *J Pers Soc Psychol*. 1995;69:990–1005.
63. Ward LC, Kersh BC, Shanks D. Psychometric assessment of motives for using cocaine in men with substance use disorders. *Psychol Rep*. 1997;80:189–190. doi:10.2466/pr0.1997.80.1.189.
64. Jones RE, Spradlin A, Robinson RJ, Tragesser SL. Development and validation of the opioid prescription medication motives questionnaire: a four-factor model of reasons for use. *Psychol Addict Behav*. 2014;28:1290–1296. doi:10.1037/a0037783.
65. Simons J, Correia CJ, Carey KB. A comparison of motives for marijuana and alcohol use among experienced users. *Addict Behav*. 2000;25:153–160.
66. Barth KS, Maria MM-S, Lawson K, et al. Pain and motives for use among non-treatment seeking individuals with prescription opioid dependence. *Am J Addict*. 2013;22:486–491. doi:10.1111/j.1521-0391.2013.12038.x.
67. Kuntsche E, Knibbe R, Gmel G, Engels R. Why do young people drink? A review of drinking motives. *Clin Psychol Rev*. 2005;25:841–861. doi:10.1016/j.cpr.2005.06.002.
68. Piasecki TM, Piper ME, Baker TB. Tobacco dependence: insights from investigations of self-reported smoking motives. *Curr Dir Psychol Sci*. 2010;19:395–401. doi:10.1177/0963721410389460.
69. Rooke SE, Hine DW, Thorsteinsson EB. Implicit cognition and substance use: a meta-analysis. *Addict Behav*. 2008;33:1314–1328. doi:10.1016/j.addbeh.2008.06.009.
70. Kahler CW, Daughters SB, Leventhal AM, et al. Implicit associations between smoking and social consequences among smokers in cessation treatment. *Behav Res Ther*. 2007;45:2066–2077. doi:10.1016/j.brat.2007.03.004.
71. Carpenter KM, Martinez D, Vadhan NP, et al. Measures of attentional bias and relational responding are associated with behavioral treatment outcome for cocaine dependence. *Am J Drug Alcohol Abuse*. 2012;38:146–154. doi:10.3109/00952990.2011.643986.
72. Wiers RW, Eberl C, Rinck M, et al. Retraining automatic action tendencies changes alcoholic patients' approach bias for alcohol and improves treatment outcome. *Psychol Sci*. 2011;22:490–497. doi:10.1177/0956797611400615.
73. Attwood AS, O'Sullivan H, Leonards U, et al. Attentional bias training and cue reactivity in cigarette smokers. *Addiction*. 2008;103:1875–1882. doi:10.1111/j.1360-0443.2008.02335.x.

74. Reich RR, Below MC, Goldman MS. Explicit and implicit measures of expectancy and related alcohol cognitions: a meta-analytic comparison. *Psychol Addict Behav*. 2010;24:13–25. doi:10.1037/a0016556.
75. Nathan PE. The addictive personality is the behavior of the addict. *J Consult Clin Psychol*. 1988;56:183–188.
76. Sher KJ, Trull TJ. Personality and disinhibitory psychopathology: alcoholism and antisocial personality disorder. *J Abnorm Psychol*. 1994;103:92–102.
77. Malouff JM, Thorsteinsson EB, Rooke SE, Schutte NS. Alcohol involvement and the five-factor model of personality: a meta-analysis. *J Drug Educ*. 2007;37: 277–294.
78. Malouff JM, Thorsteinsson EB, Schutte NS. The five-factor model of personality and smoking: a meta-analysis. *J Drug Educ*. 2006;36:47–58.
79. Kotov R, Gamez W, Schmidt F, Watson D. Linking "big" personality traits to anxiety, depressive, and substance use disorders: a meta-analysis. *Psychol Bull*. 2010;136:768–821. doi:10.1037/a0020327.
80. Maclaren VV, Fugelsang JA, Harrigan KA, Dixon MJ. The personality of pathological gamblers: a meta-analysis. *Clin Psychol Rev*. 2011;31:1057–1067. doi:10.1016/j.cpr.2011.02.002.
81. Coskunpinar A, Dir AL, Cyders MA. Multidimensionality in impulsivity and alcohol use: a meta-analysis using the UPPS model of impulsivity. *Alcohol Clin Exp Res*. 2013;37:1441–1450. doi:10.1111/acer.12131.
82. Stanford MS, Mathias CW, Dougherty DM, et al. Fifty years of the Barratt Impulsiveness Scale: an update and review. *Pers Individ Dif*. 2009;47:385–395.
83. MacKillop J, Amlung M, Few L, et al. Delayed reward discounting and addictive behavior: a meta-analysis. *Psychopharmacology (Berl)*. 2011;216:305–321. doi:10. 1007/s00213-011-2229-0.
84. Smith JL, Mattick RP, Jamadar SD, Iredale JM. Deficits in behavioural inhibition in substance abuse and addiction: a meta-analysis. *Drug Alcohol Depend*. 2014;145: 1–33. doi:10.1016/j.drugalcdep.2014.08.009.
85. Stahl C, Voss A, Schmitz F, et al. Behavioral components of impulsivity. *J Exp Psychol Gen*. 2014;143:850–886. doi:10.1037/a0033981.
86. MacKillop J, Miller JD, Fortune E, et al. Multidimensional examination of impulsivity in relation to disordered gambling. *Exp Clin Psychopharmacol*. 2014; 22:176–185. doi:10.1037/a0035874.
87. Cyders MA, Coskunpinar A. Measurement of constructs using self-report and behavioral lab tasks: is there overlap in nomothetic span and construct representation for impulsivity? *Clin Psychol Rev*. 2011;31:965–982. doi:10.1016/ j.cpr.2011.06.001.
88. Konijnenberg C. Methodological issues in assessing the impact of prenatal drug exposure. *Subst Abuse*. 2015;9:39–44. doi:10.4137/SART.S23544.
89. Enoch MA. The role of early life stress as a predictor for alcohol and drug dependence. *Psychopharmacology (Berl)*. 2011;214:17–31. doi:10.1007/s00213-010-1916-6.
90. Hingson RW, Zha W, Weitzman ER. Magnitude of and trends in alcohol-related mortality and morbidity among U.S. college students ages 18–24, 1998–2005. *J Stud Alcohol Drugs Suppl*. 2009:12–20.
91. Schulenberg JE, Maggs JL. A developmental perspective on alcohol use and heavy drinking during adolescence and the transition to young adulthood. *J Stud Alcohol Suppl*. 2002:54–70.

92. Ellis BJ, Del Giudice M, Dishion TJ, et al. The evolutionary basis of risky adolescent behavior: implications for science, policy, and practice. *Dev Psychol*. 2012;48:598–623. doi:10.1037/a0026220.
93. Bachman JG, Wadsworth KN, O'Malley PM, et al. *The decline of substance use in young adulthood: changes in social activities, role, and beliefs*. Mahwah (NJ): Erlbaum; 2002.
94. Gotham HJ, Sher KJ, Wood PK. Alcohol involvement and developmental task completion during young adulthood. *J Stud Alcohol*. 2003;64:32–42.
95. Wood MD, Sher KJ, McGowan AK. Collegiate alcohol involvement and role attainment in early adulthood: findings from a prospective high-risk study. *J Stud Alcohol*. 2000;61:278–289.
96. Lee MR, Chassin L, MacKinnon DP. Role transitions and young adult maturing out of heavy drinking: evidence for larger effects of marriage among more severe premarriage problem drinkers. *Alcohol Clin Exp Res*. 2015. doi:10.1111/acer.12715.
97. Lee MR, Chassin L, Villalta IK. Maturing out of alcohol involvement: transitions in latent drinking statuses from late adolescence to adulthood. *Dev Psychopathol*. 2013;25:1137–1153. doi:10.1017/S0954579413000424.
98. Dawson DA, Grant BF, Stinson FS, Chou PS. Maturing out of alcohol dependence: the impact of transitional life events. *J Stud Alcohol*. 2006;67:195–203.
99. Zucker RA. The four alcoholisms: a developmental account of the etiologic process. *Nebr Symp Motiv*. 1986;34:27–83.
100. Moffitt TE. Adolescence-limited and life-course-persistent antisocial behavior: a developmental taxonomy. *Psychol Rev*. 1993;100:674–701.
101. Chartier KG, Caetano R. Trends in alcohol services utilization from 1991–1992 to 2001–2002: ethnic group differences in the U.S. population. *Alcohol Clin Exp Res*. 2011;35:1485–1497. doi:10.1111/j.1530-0277.2011.01485.x.
102. Chartier KG, Caetano R. Ethnicity and health disparities in alcohol research. *Alcohol Res Heal*. 2010;33:152–160.
103. Jackson CA, Henderson M, Frank JW, Haw SJ. An overview of prevention of multiple risk behaviour in adolescence and young adulthood. *J Public Heal*. 2012;34(Suppl 1):i31–i40. doi:10.1093/pubmed/fdr113.
104. Littlefield AK, Verges A, McCarthy DM, Sher KJ. Interactions between self-reported alcohol outcome expectancies and cognitive functioning in the prediction of alcohol use and associated problems: a further examination. *Psychol Addict Behav*. 2011;25:542–546. doi:10.1037/a0022090.
105. Littlefield AK, Sher KJ, Wood PK. Do changes in drinking motives mediate the relation between personality change and "maturing out" of problem drinking? *J Abnorm Psychol*. 2010;119:93–105. doi:10.1037/a0017512.
106. Patrick ME, Wray-Lake L, Finlay AK, Maggs JL. The long arm of expectancies: adolescent alcohol expectancies predict adult alcohol use. *Alcohol Alcohol*. 2010;45:17–24. doi:10.1093/alcalc/agp066.
107. Quinn PD, Harden KP. Differential changes in impulsivity and sensation seeking and the escalation of substance use from adolescence to early adulthood. *Dev Psychopathol*. 2013;25:223–239. doi:10.1017/S0954579412000284.
108. Littlefield AK, Sher KJ, Wood PK. Is "maturing out" of problematic alcohol involvement related to personality change? *J Abnorm Psychol*. 2009;118:360–374. doi:10.1037/a0015125.
109. Paus T. Mapping brain maturation and cognitive development during adolescence. *Trends Cogn Sci*. 2005;9:60–68. doi:10.1016/j.tics.2004.12.008.

110. Casey BJ. Beyond simple models of self-control to circuit-based accounts of adolescent behavior. *Annu Rev Psychol*. 2015;66:295–319. doi:10.1146/annurev-psych-010814-015156.
111. Jacobus J, Tapert SF. Neurotoxic effects of alcohol in adolescence. *Annu Rev Clin Psychol*. 2013;9:703–721. doi:10.1146/annurev-clinpsy-050212-185610.
112. Jacobus J, Tapert SF. Effects of cannabis on the adolescent brain. *Curr Pharm Des*. 2014;20:2186–2193.
113. Spear LP, Varlinskaya EI. Sensitivity to ethanol and other hedonic stimuli in an animal model of adolescence: implications for prevention science? *Dev Psychobiol*. 2010;52:236–243. doi:10.1002/dev.20457.
114. MacKillop J, Acker JD, Bollinger J, et al. The Brief Alcohol Social Density Assessment (BASDA): convergent, criterion-related and incremental validity. *J Stud Alcohol Drugs*. 2013;74(5):810–15.
115. Fortune EE, MacKillop J, Miller JD, et al. Social density of gambling and its association with gambling problems: an initial investigation. *J Gambl Stud*. 2012. doi:10.1007/s10899-012-9303-3.
116. Stout RL, Kelly JF, Magill M, Pagano ME. Association between social influences and drinking outcomes across three years. *J Stud Alcohol Drugs*. 2012;73:489–497.
117. Longabaugh R, Wirtz PW, Zywiak WH, O'Malley SS. Network support as a prognostic indicator of drinking outcomes: the COMBINE study. *J Stud Alcohol Drugs*. 2010;71:837–846.
118. Kelly JF, Stout RL, Magill M, Tonigan JS. The role of Alcoholics Anonymous in mobilizing adaptive social network changes: a prospective lagged mediational analysis. *Drug Alcohol Depend*. 2011;114:119–126. doi:10.1016/j.drugalcdep.2010.09.009.
119. Litt MD, Kadden RM, Kabela-Cormier E, Petry N. Changing network support for drinking: initial findings from the network support project. *J Consult Clin Psychol*. 2007;75:542–555. doi:2007-11558-004 [pii] 10.1037/0022-006X.75.4.542.
120. Litt MD, Kadden RM, Kabela-Cormier E, Petry NM. Changing network support for drinking: network support project 2-year follow-up. *J Consult Clin Psychol*. 2009;77:229–242. doi:2009-03774-004 [pii] 10.1037/a0015252.
121. Borgatti SP, Mehra A, Brass DJ, Labianca G. Network analysis in the social sciences. *Science*. 2009;323:892–895. doi:10.1126/science.1165821.
122. Rosenquist JN. Lessons from social network analyses for behavioral medicine. *Curr Opin Psychiatry*. 2011;24:139–143. doi:10.1097/YCO.0b013e3283438061.
123. Burt RS, Kilduff M, Tasselli S. Social network analysis: foundations and frontiers on advantage. *Annu Rev Psychol*. 2013;64:527–547. doi:10.1146/annurev-psych-113011-143828.
124. Ennett ST, Bauman KE, Hussong A, et al. The peer context of adolescent substance use: findings from social network analysis. *J Res Adolesc*. 2006;16:159–186. doi:10.1111/j.1532-7795.2006.00127.x.
125. Crosnoe R, Needham B. Holism, contextual variability, and the study of friendships in adolescent development. *Child Dev*. 2004;75:264–279.
126. Mundt MP. The impact of peer social networks on adolescent alcohol use initiation. *Acad Pediatr*. 2011;11:414–421. doi:10.1016/j.acap.2011.05.005.
127. Mundt MP, Mercken L, Zakletskaia L. Peer selection and influence effects on adolescent alcohol use: a stochastic actor-based model. *BMC Pediatr*. 2012;12:115. doi:10.1186/1471-2431-12-115.

128. Fujimoto K, Valente TW. Decomposing the components of friendship and friends' influence on adolescent drinking and smoking. *J Adolesc Health*. 2012;51:136–143. doi:10.1016/j.jadohealth.2011.11.013.
129. Fujimoto K, Valente TW. Social network influences on adolescent substance use: disentangling structural equivalence from cohesion. *Soc Sci Med*. 2012;74: 1952–1960. doi:10.1016/j.socscimed.2012.02.009.
130. Cruz JE, Emery RE, Turkheimer E. Peer network drinking predicts increased alcohol use from adolescence to early adulthood after controlling for genetic and shared environmental selection. *Dev Psychol*. 2012;48:1390–1402. doi:10.1037/a0027515.
131. Rosenquist JN, Murabito J, Fowler JH, Christakis NA. The spread of alcohol consumption behavior in a large social network. *Ann Intern Med*. 2010;152: 426–433. doi:10.7326/0003-4819-152-7-201004060-00007.
132. Bullers S, Cooper ML, Russell M. Social network drinking and adult alcohol involvement: a longitudinal exploration of the direction of influence. *Addict Behav*. 2001;26:181–199.
133. Lau-Barraco C, Braitman AL, Leonard KE, Padilla M. Drinking buddies and their prospective influence on alcohol outcomes: alcohol expectancies as a mediator. *Psychol Addict Behav*. 2012;26:747–758. doi:10.1037/a0028909.
134. Meisel MK, Clifton AD, MacKillop J, et al. Egocentric social network analysis of pathological gambling. *Addiction*. 2013;108:584–591. doi:10.1111/add.12014.
135. Grant BF. The impact of a family history of alcoholism on the relationship between age at onset of alcohol use and DSM-IV alcohol dependence: results from the National Longitudinal Alcohol Epidemiologic Survey. *Alcohol Health Res World*. 1998;22:144–147.
136. Den Exter Blokland EAW, Engels RCME, Hale WW, et al. Lifetime parental smoking history and cessation and early adolescent smoking behavior. *Prev Med (Baltim)*. 2004;38:359–368. doi:10.1016/j.ypmed.2003.11.008.
137. Ryan SM, Jorm AF, Lubman DI. Parenting factors associated with reduced adolescent alcohol use: a systematic review of longitudinal studies. *Aust N Z J Psychiatry*. 2010;44:774–783. doi:10.1080/00048674.2010.501759.
138. Resnick MD, Bearman PS, Blum RW, et al. Protecting adolescents from harm: findings from the National Longitudinal Study on Adolescent Health. *JAMA*. 1997;278:823–832.
139. Johnson V, Pandina RJ. Effects of the family environment on adolescent substance use, delinquency, and coping styles. *Am J Drug Alcohol Abuse*. 1991;17:71–88.
140. Lamis DA, Malone PS, Lansford JE, Lochman JE. Maternal depressive symptoms as a predictor of alcohol use onset and heavy episodic drinking in youths. *J Consult Clin Psychol*. 2012;80:887–896. doi:10.1037/a0028959.
141. Bailey JA, Hill KG, Oesterle S, Hawkins JD. Parenting practices and problem behavior across three generations: monitoring, harsh discipline, and drug use in the intergenerational transmission of externalizing behavior. *Dev Psychol*. 2009;45:1214–1226. doi:10.1037/a0016129.
142. Borsari B, Carey KB. Peer influences on college drinking: a review of the research. *J Subst Abus*. 2001;13:391–424.
143. Jaccard J, Blanton H, Dodge T. Peer influences on risk behavior: an analysis of the effects of a close friend. *Dev Psychol*. 2005;41:135–147. doi:10.1037/0012-1649.41.1.135.

144. Graham JW, Marks G, Hansen WB. Social influence processes affecting adolescent substance use. *J Appl Psychol*. 1991;76:291–298.
145. Perkins HW, Meilman PW, Leichliter JS, et al. Misperceptions of the norms for the frequency of alcohol and other drug use on college campuses. *J Am Coll Health*. 1999;47:253–258. doi:10.1080/07448489909595656.
146. Wolfson S. Students' estimates of the prevalence of drug use: evidence for a false consensus effect. *Psychol Addict Behav*. 2000;14:295–298.
147. Lewis MA, Neighbors C. Social norms approaches using descriptive drinking norms education: a review of the research on personalized normative feedback. *J Am Coll Health*. 2006;54:213–218. doi:10.3200/JACH.54.4.213-218.
148. Agrawal A, Heath AC, Grant JD, et al. Assortative mating for cigarette smoking and for alcohol consumption in female Australian twins and their spouses. *Behav Genet*. 2006;36:553–566. doi:10.1007/s10519-006-9081-8.
149. Grant JD, Heath AC, Bucholz KK, et al. Spousal concordance for alcohol dependence: evidence for assortative mating or spousal interaction effects? *Alcohol Clin Exp Res*. 2007;31:717–728. doi:10.1111/j.1530-0277.2007.00356.x.
150. Leonard KE, Eiden RD. Marital and family processes in the context of alcohol use and alcohol disorders. *Annu Rev Clin Psychol*. 2007;3:285–310. doi:10.1146/annurev.clinpsy.3.022806.091424.
151. AlMarri TSK, Oei TPS. Alcohol and substance use in the Arabian Gulf region: a review. *Int J Psychol*. 2009;44:222–233. doi:10.1080/00207590801888752.
152. Roberts SCM. Macro-level gender equality and alcohol consumption: a multilevel analysis across U.S. States. *Soc Sci Med*. 2012;75:60–68. doi:10.1016/j.socscimed.2012.02.017.
153. Chaloupka FJ, Yurekli A, Fong GT. Tobacco taxes as a tobacco control strategy. *Tob Control*. 2012;21:172–180. doi:10.1136/tobaccocontrol-2011-050417.
154. Wagenaar AC, Salois MJ, Komro KA. Effects of beverage alcohol price and tax levels on drinking: a meta-analysis of 1003 estimates from 112 studies. *Addiction*. 2009;104:179–190. doi:10.1111/j.1360-0443.2008.02438.x.
155. Stockwell T, Auld MC, Zhao J, Martin G. Does minimum pricing reduce alcohol consumption? The experience of a Canadian province. *Addiction*. 2012;107:912–920. doi:10.1111/j.1360-0443.2011.03763.x.
156. Stockwell T, Zhao J, Giesbrecht N, et al. The raising of minimum alcohol prices in Saskatchewan, Canada: impacts on consumption and implications for public health. *Am J Public Health*. 2012;102:e103–e110. doi:10.2105/AJPH.2012.301094.
157. Stockwell T, Zhao J, Marzell M, et al. Relationships between minimum alcohol pricing and crime during the partial privatization of a Canadian government alcohol monopoly. *J Stud Alcohol Drugs*. 2015;76:628–634.
158. Treno AJ, Marzell M, Gruenewald PJ, Holder H. A review of alcohol and other drug control policy research. *J Stud Alcohol Drugs*. 2014;75(Suppl 1):98–107.
159. Bridging the Gap between Practice and Research: Forging Partnerships with Community-Based Drug and Alcohol Treatment—PubMed—NCBI. Available from: www.ncbi.nlm.nih.gov/pubmed/25101381.
160. Oliva EM, Maisel NC, Gordon AJ, Harris AHS. Barriers to use of pharmacotherapy for addiction disorders and how to overcome them. *Curr Psychiatry Rep*. 2011;13:374–381. doi:10.1007/s11920-011-0222-2.
161. Carroll KM. Lost in translation? Moving contingency management and cognitive behavioral therapy into clinical practice. *Ann N Y Acad Sci*. 2014;1327:94–111. doi:10.1111/nyas.12501.