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A Multilevel Developmental Contextual Approach To Substance Use and Addiction

Michael Windle, PhD[1]

[1]Department of Behavioral Sciences and Health Education, Emory University, 1518 Clifton Road NE, Room 520, Atlanta, Georgia 30322 mwindle@emory.edu

Abstract

Emerging technological advances in genetics and neuroscience have spawned innovative or elaborated conceptual models in the field of addiction science, as well as contributed to the mushrooming of new knowledge. By addictions, reference is made to chronic, often relapsing disorders typified by obsession, compulsion, or physical or psychological dependence. In this article it is proposed that a multilevel developmental contextual approach to substance use and addictions provides a useful framework for integrating existing studies across disciplines and serving as a generative guide to intriguing novel research questions. The multilevel developmental contextual approach emphasizes multiple factor influences on substance use and addiction, the conjoint influence of variables from different levels of analysis (e.g., genetic, biochemical, physiological, cognitive, social, neighborhood, societal), and dynamic, probabilistic behavior-outcome relations (i.e., the occurrence as well as the nature of expression of substance problems and addiction depend on a range of emerging, interactive factors that may vary across individuals and across time). The approach is illustrated with a long-term prospective study of predictors of binge drinking from adolescence to young adulthood and a description of the role of brain processes and mechanisms involved in the development and expression of alcohol use during adolescence.

Keywords

Addictions; Substance use; Dependence; Development; Longitudinal; Genetic

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"For every complex problem there is an answer that is clear, simple, and wrong."

--H.L. Mencken

In recent years we have witnessed significant changes in the life sciences, especially with regard to advances in genetics and neuroscience. For example, technological advances have enabled scientists to more directly study genes, gene processes, and gene products in a manner inaccessible to Darwin. Likewise, although still in the nascent stages of development, advances in neuroimaging technology have enabled the investigation of brain structure and function in a manner not available to prior generations of neuroscientists. The generation of new knowledge facilitated by these technological advances has contributed to new (or elaborated) conceptual models in the field of substance use and addiction science, including integrative, multilevel, biopsychosocial models. The multilevel developmental

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Michael Windle, Ph.D., is a Rollins Endowed Professor and Chair of the Department of Behavioral Sciences and Health Education in the Rollins School of Public Health. He conducts multiple longitudinal studies on risk and protective factors for a range of adolescent and adult health behaviors, including alcohol, tobacco, and other substance use, psychiatric and addictive disorders, violence and delinquency, risky sexual behaviors, suicide, and victimization. Dr. Windle received an NIH MERIT Award for his research on adolescent alcohol use and related problems.

contextual approach, presented subsequently, may be most sharply contrasted with a single-factor disease model that emphasizes singularity with regard to factor prominence (e.g., the "violence gene", the monoamine hypothesis of depression), reductionism to the biological level with regard to necessary and sufficient conditions to infer causality, and "hard" determinism (i.e., inevitability) with regard to ultimate disease manifestation or outcome.

By contrast, the multilevel developmental contextual approach emphasizes multiple factor influences on substance use and addiction, the conjoint influence of variables from different levels of analysis (e.g., genetic, biochemical, physiological, cognitive, social, neighborhood, societal), and dynamic, probabilistic behavior-outcome relations (i.e., the occurrence as well as the nature of expression of substance use problems and addiction depend on a range of emerging, interactive factors that may vary across individuals and across time). A further characteristic of the multilevel developmental contextual approach is the integral role of temporal factors and dynamic processes related to lifespan development, and to the importance of the timing of factors (e.g., pubertal onset, onset and duration of externalizing behaviors) that may influence alternative life course trajectories of substance use and addiction among individuals. Historically, this revision in conceptual approaches to substance use and addiction has yielded a shift from more linear, additive statistical models to interactive (multiplicative) and non-linear statistical models.

The objectives of this article are threefold. First, the basic tenets and fundamental concepts of a multilevel developmental contextual approach to substance use and addiction are provided within a dynamic diathesis-stress model. The dynamic diathesis-stress model integrates the perspectives of lifespan developmental psychology and the (univariate) diathesis-stress model of psychiatry. Second, two substantive illustrations to substance use guided by this model are provided, including (a) an application with data from a long-term (22-year) prospective study of predictors of substance use and mental health disorders from adolescence to early middle-adulthood; and (b) a description of the potential roles of brain processes and mechanisms involved in the development and expression of substance use and addiction across the lifespan. Third, some implications of the dynamic contextual model are discussed in relation to some prominent issues in the field of substance use and addiction science.

Heterogeneity and the Dynamic Diathesis-Stress Model of Developmental Psychopathology

A prototypic model that influenced early genetic research on alcoholism and other substance use and mental health disorders stemmed from successes in medical genetics, such as that with phenylketonuria (PKU). PKU is a single gene disorder that is inherited as an autosomal-recessive trait in accord with Mendel's law of segregation; untreated, PKU can cause mental retardation. PKU is an inherited error of metabolism disorder, yielding the organism unable to metabolize phenylalanine, a common amino acid found in many foods. However, treatment for PKU, based on the identification of this single gene disorder, is straightforward and involves strict dietary control of the patient's intake of phenylalanine (Scriver & Crow, 1980). Adherence to the dietary controls by pregnant mothers virtually eliminates the risk for PKU in their offspring.

While this prototypic, single gene disorder approach was useful in the case of PKU and some other medical disorders (e.g., Tay-Sachs disease, muscular dystrophy syndrome), and continues to be of value for the investigation of some rare medical conditions, its usefulness for more complicated phenotypes such as substance use and mental health disorders is likely to be quite limited. For these phenotypes, genetic heterogeneity appears to be the rule rather than the exception. More specifically, for these common phenotypes, a number of genetic

and nongenetic factors may independently cause the disorder (Tsuang, Faraone, & Lyons, 1993). Thus, for example, the phenotype of alcohol disorders as measured via standard clinical diagnostic criteria is not likely to reflect a unitary underlying (disease) mechanism. Goldman (1995) stated that "Alcoholism is an umbrella diagnosis for overlapping pathologies caused by multifactorial genetic and environmental sources of variation" (p. 829).

As researchers and practitioners move away from single factor (e.g., "the alcohol gene") causal models to more elaborated and complicated multifactor causal models, it is useful to have a conceptual framework to organize the existing literature, to provide direction for research questions, and to evaluate the impact of measured components of a system in a study within a more comprehensive system of interrelationships. Figure 1 provides one such framework that attempts to integrate conceptual models from two research orientations -- the lifespan or life course developmental approach, and the diathesis-stress psychiatric epidemiology model. Lifespan behavioral scientists (Baltes, 1987; Bronfenbrenner, 1977; Lerner, 1982) have proposed that human development is best understood as a dynamic (i.e., patterned, time changing) process that is influenced by a range of multilevel contextual factors. These multilevel (i.e., biogenetic, psychological, sociocultural) factors may vary in influence across the lifespan, and are influenced by the active, self-selective behaviors of the individual within the constraints and facilitative opportunity structures afforded by environments. Consequently, human behavior is embedded, or nested, within a wide range of proximal (e.g., family, school or work settings) and distal (e.g., sociohistorical events such as wars, historical trends in the availability of substances, or major technological advances such as the computer revolution) contextual events that influence variability in individual growth trajectories.

The diathesis-stress model has been a prominent conceptual orientation for research in psychiatric epidemiology for a number of years. The model suggests that mental illness results from the two distinct components of diathesis and stress. *Diathesis* refers to constitutional (e.g., temperament) and genetically inherited characteristics that increase a person's vulnerability, or risk, to a (specific) disorder; *stress* refers to environmental events (e.g., death of a significant other, work or parental role stress, neighborhood disorganization) that impact the mental health and daily functioning of people. According to the diathesis-stress model, in order to understand the etiology of mental health and substance use disorders, we must consider the relational structure between these two relatively independent components. For instance, relatively low levels of stress may precipitate the onset of a disorder for an individual with a high vulnerability to a disorder (due to a family history of the disorder and a difficult temperament). By contrast, relatively high levels of stress would need to be encountered to precipitate an episode of a disorder for an individual with a low vulnerability for a disorder. Thus, the diathesis-stress model attempts to account for variability in the occurrence, onset, and time course of substance use and mental health disorders via the postulation of interactive (dynamic) relations between diathesis and stress processes.

The dynamic diathesis-stress model of developmental psychopathology attempts to integrate lifespan and diathesis-stress perspectives by: (a) recognizing that human development reflects multivariate, dynamic (i.e., patterned, time-ordered change) processes; (b) incorporating a multilevel, contextual factor orientation; and (c) emphasizing person (diathesis) and environmental (stress) processes that are salient to understanding timing and duration issues surrounding the expression of substance use and mental health disorders. Hence, while retaining the fundamental person-environment relationship described by the more static, traditional diathesis-stress model, this expanded dynamic contextual model formulation also recognizes that: (a) risk factors beyond those that are constitutional in

origin (i.e., genetic), such as family and peer factors, impact the onset and time course of disorders; (b) diathesis and stress factors influence one another across time in a bidirectional (rather than unidirectional) fashion; and (c) interrelationships among diathesis and stress factors vary across the lifespan in terms of strength and duration.

For a more concrete illustration, Figure 1 provides a schema for utilizing this model to characterize risk for the offspring of alcoholic parents (or children of alcoholics, COAs). Prevalence estimates for the occurrence of an alcohol disorder among COAs in the United States have ranged from four-to-nine times relative to non-COAs (Russell, 1990). However, despite this substantively significant increase in risk among COAs, it is nevertheless also true that the simple majority (more than 50%) of COAs do not become alcoholics (Sher, 1991; Windle & Searles, 1990). Furthermore, among the total population of alcoholics, a large percentage of alcoholics are from families negative for history of alcoholism. It is this kind of heterogeneity in alcohol outcomes that necessitates the consideration of more complex, dynamic person-environment process models. That is, if genetic influences were the sole, or primary, cause of alcoholism, then one may anticipate that virtually all COAs would become alcoholics, and few, if any, non-COAs would become alcoholics. We know that this is inconsistent with the empirical literature. Furthermore, COAs are at risk for a range of psychological problems (not just alcoholism), suggesting that a single factor (e.g., a single gene) cannot adequately account for these diverse outcomes.

The boxes displayed in Figure 1 provide domains of identifiable risk factors that are associated with the expression of alcohol disorders. The domains and associated exemplars (listed within each of the boxes) are not viewed as exhaustive of potential factors, but rather as illustrative (for more extensive reviews of the COA literature, see Sher, 1991; Windle & Searles, 1990). According to the model, vulnerability (diathesis) is conferred on the offspring of COAs through several possible mechanisms. With reference to parental factors, assortative mating (i.e., alcoholics marrying alcoholics) (Hall, Hesselbrock, & Stabenau, 1983) may increase risk in two ways. First, vulnerability may be increased by a heightened genetic predisposition toward alcoholism by the joint (genetic) lineages of paternal and maternal sides of the family. Second, vulnerability may be increased via unpredictability and inconsistency of parenting in households in which both parents are frequently inebriated. Thus, assortative mating for alcoholism may increase the diathesis (person vulnerability) and the (environmental) stress level for COAs. Similar “dual level” complications may also occur by selective mating practices by alcoholics and partners who exhibit other psychiatric disorders or chronic patterns of criminal offending.

Although assortative mating may increase the risk of an alcohol disorder among offspring (Hall et al., 1983), two important research questions remain. Do all offspring from this mating pattern eventually develop an alcohol disorder, and what variables mediate the relationship between the parental pairing and child outcomes? It is clear that the answer to the first question is no -- not all offspring from the parental pairing of alcoholics become an alcoholic. This adds even more importance to the second question, because it suggests that the mediation processes reflecting life course patterns of development vary across individuals from the same family (e.g., some sibs, or twin members, will develop an alcohol disorder, whereas others will not). In addition, even though two sibs from the same family both develop an alcohol disorder, they each may do so through different mechanisms (e.g., one through an early onset, antisocial behavior pathway, and the other through a later onset, cumulative pathway) (Zucker, 2006).

Some of the possible person (diathesis) and environmental (stress) variables that may contribute to variation in outcome for COAs (from alcoholic parents or an alcoholic parent) are provided in the second column of Figure 1. The family history of alcoholism risk may be

manifest through a range of biological variables, including deficits in working memory associated with a reduced amplitude P300 response (Begleiter, Porjesz, & Kissin, 1984), differential sensitivity and tolerance to ethanol (Schuckit, 1994), or lower levels of monoamine oxidase (MAO) (Devor, Cloninger, Huffman, & Tabakoff, 1993). Similarly, alcoholism risk may be expressed with regard to a range of temperament and cognitive factors, including a difficult temperament (Blackson, Tarter, Loeber, Ammerman, & Windle, 1996; Tubman & Windle, 1995), early onset positive alcohol expectancies (Miller, Smith, & Goldman, 1990), or low intellectual functioning and school performance (Werner, 1986). Finally, features of the family environment (e.g., financial strain, high marital conflict) and extra-familial environment (e.g., deviant peers) may increase risk for alcoholism among COAs. Obviously, such familial and extra-familial risk factors are not unique to COAs; the model presupposes that these factors occur more frequently, at higher intensity and perhaps in more destructible forms (e.g., “explosive”, violent parenting, persistent or severe marital conflict), or at higher levels among COAs, thereby increasing risk. Note that these familial and extra-familial risk factors are associated vulnerabilities of family history of alcoholism and do not reflect constitutional differences in origin.

According to the dynamic diathesis-stress model, it is probable that several of the mediational factors enumerated above contribute to the development of an alcohol disorder. Further, these factors (e.g., temperament, intelligence, parenting deficits) influence and are influenced by environmental contextual variables such as characteristics of the neighborhood (e.g., levels of violent crime, number of bars and liquor stores, amount of drinking by people in the streets), school and family climate variables (e.g., level of safety and support), peer groups (e.g., level of alcohol and drug use), and media influences (e.g., positive portrayals of alcohol use by mass media) . Because human development is intrinsically transactional by nature (i.e., involves the mutual exchange of information and material from the surrounding physical and social environment), the arrows between some of the person (diathesis) and environment (stressors) boxes reflect bidirectional influences (also see Lerner, 1982). For example, children with a difficult temperament often contribute significantly to higher levels of interpersonal conflict with significant others, including parents, teachers, and peers (Blackson et al., 1996; Dunn, 1980). Across time, such a difficult temperamental style may restrict friendship choices (e.g., to other more aggressive or deviant children) and increase risk for personal victimization. The findings of Rutter (1987) indicated that children with a difficult temperament were more likely than their sibs to be the target of parental criticism and hostility. Findings by Keough (1986) also indicated that even when children were matched on level of intellectual performance, teachers rated children with a difficult temperament as lower with regard to academic functioning than those without a difficult temperament.

In summary, the diathesis-stress model of developmental psychopathology suggests that multiple factors and their time-ordered, dynamic, and bidirectional person-environment relations need to be considered to account for variability in outcomes associated with being the offspring of an alcoholic parent. For a more focused discussion on developmental transitions and the impact of timing of developmental events (e.g., pubertal onset) on alcohol use during early-to-mid-adolescence, please see Windle, Spear, Fuligni, et al. (2008).

Illustration of Addressing Heterogeneity of Growth with Lives Across Time Study

The dynamic diathesis-stress model described previously poses a number of challenges to investigators who seek to examine the multiple pathways toward or away from substance use disorders. That is, if a starting point for the study of the phenomenon of interest is that:

(1) heterogeneity is the norm for the behavior/disorder of interest; (2) multiple factors impact the behavior/disorder; and (3) influences are reciprocal and dynamic in nature across time, then there are implications for sampling, research design, measurement, and statistical modeling that need to be considered to optimally address important research questions. We have used the dynamic diathesis-stress model to guide our scientific thinking and practice in a community-based longitudinal study referred to as Lives Across Time: A Prospective Study of Adolescent and Adult Development (LAT), which has been ongoing since 1988 and has been funded since its inception by the National Institute on Alcohol Abuse and Alcoholism. The initial sample consisted of over 1200 adolescents (mean age=15.6 yrs.) and their primary caregivers but across time the sample increased because it was populated both with mothers and fathers, as well as the spouses of the initial adolescents when they married in young adulthood (for more details about the LAT, see Windle, Mun, & Windle, 2005). An important focus of the LAT is to identify salient prospective risk and protective factors for the development of substance abuse and mental health disorders among adolescents as they transition to young adulthood.

For purposes of this illustration, I chose to present data from a study of predictors of latent growth curve trajectories of heavy (binge) drinking identified via a latent class growth model (Windle et al., 2005). Repeated measures (longitudinal) data produce a line or trajectory (straight or curved) for each individual that describes their individual scores across time; this across time trajectory reflects intraindividual change. For example, if there were four times points and alcohol consumption increased by one drink at each time point, this would indicate a linear increase in change across time. Because not everyone begins at the same level for any attribute measured (e.g., substance use) or changes in exactly the same way, there are individual differences in the intraindividual change. The general notion behind growth mixture distribution models, of which the latent class growth model is one type, is that there may be substantial variation in these individual differences in intraindividual change that may be captured by growth parameters (e.g., intercepts, slopes) that may reflect distinct, sub-population differences of growth patterns rather than simply variation about a common curve (or set of parameters associated with the single growth curve). That is, latent growth mixture models are able to utilize variation in growth parameters (e.g., initial level, shape, and rate of growth) to facilitate the identification of distinct but unobserved subgroups within a population.

We used a latent class growth model with multi-wave data from the LAT to model trajectories of heavy drinking (HD) from ages 16-25, and then identified adolescent predictors that distinguished the identified trajectory groups (Windle et al., 2005). Because males and females manifest different patterns of alcohol use and related problems, we conducted analyses separately by sex group, though we will focus only on males in this illustration. Briefly, four trajectories were identified: non-HD stable group; (2) moderate-HD stable group; (3) high-HD stable group; and (4) very high HD group (see Figure 2). From ages 19-22, the very high HD group averaged consuming 6 or more alcoholic beverages on 9 or more days in the last month relative, for example, to the moderate-HD stable group that averaged consuming 6 alcoholic beverages on one day in the last month. Comparisons among the four trajectory groups were made with regard to adolescent predictors from several domains, including values and beliefs, interpersonal functioning, and substance use and other problem behaviors. Different adolescent predictors were associated with these distinctive trajectories suggesting different developmental processes contributed to these differential, long-term patterns of heavy drinking. For example, for the very high HD group, the distinctive pattern included lower school grades, lower religious commitment, lower task orientation, more stressful life events, an earlier onset on alcohol use, and higher levels of adolescent delinquent behavior.

The propose of this illustration is to indicate that there are longitudinal quantitative methods that enable one to address heterogeneity issues with regard to substance use phenotypes (in this instance heavy drinking), to incorporate multiple factor influences that may differ for subpopulations, and to capture a more dynamic process narrative of individual development than that afforded by aggregated, whole sample approaches that treat intraindividual variation as an error term.

Studying Substance Use and Brain Processes from a Developmental Contextual Perspective

As presented and described in Figure 1, different features of brain functioning are integrally involved in multiple processes related to substance use and disorders across the lifespan. Focusing on alcohol as an example, the majority of neuroscience research on alcohol use and alcohol disorders has focused on adults (e.g., identifying structural or functional deficits and pathologies), though there is a burgeoning literature that has focused on children and adolescents, often using positive family history high-risk designs (DeBellis et al., 2000; Hill, 2004; Tapert & Schweinsburg, 2005; White & Swartzwelder, 2005). In general, there have been some consistencies reported in the child and adolescent literature that suggest that higher alcohol use (in community samples) and/or higher risk status (e.g., family history positive for alcoholism) is associated with poorer neuropsychological test performance, differences in psychophysiological parameters (e.g., reduced amplitude P3 responses to visual and auditory tasks), and structural and functional differences in neuroimaging studies. For example, DeBellis et al. reported that alcohol-dependent adolescents had a significantly smaller hippocampal volume relative to a sex- and age-controlled comparison group. The hippocampus is integrally involved in learning and memory and a smaller volume may contribute to the reduced functioning of these critically important cognitive activities. Using a high risk sample of multiplex alcohol dependent families, Hill et al. (2001; 2007) reported differences in the amygdala and cerebellar volume among high-risk offspring with minimal alcohol exposure, thereby suggesting that such differences preceded alcohol exposure. Glahn, Lovallo, and Fox (2007) reported that a behaviorally disinhibited temperament among family history positive (for alcoholism) young adults displayed amygdalar hyporesponsiveness and a failure to avoid risky decisions, and hypothesized that these conditions may increase a person's liability for alcohol abuse.

Nevertheless, as has been described in reviews of the extant literature (Tapert & Schweinsburg, 2005; White & Swartzwelder, 2005), there have been a quite limited number of neuroimaging studies conducted with children and adolescents regarding alcohol dose-response relationships, and even fewer with longitudinal data. Given the lack of a strong theoretical or empirical data base within the neuroimaging literature to guide the optimal selection of measurement protocols, tasks, or regions of interest for the children and adolescents with regard to alcohol intake, my colleagues and I are using the developmental contextual approach to guide some of our decisions to address a research question about the potential effect(s) of alcohol (or other substance) use exposure on brain development and functioning (e.g., related to risky decision-making, working memory). The ability to address this research question would be greatly enhanced by using a longitudinal design; this would enable one to systematically examine how exposure to alcohol and variation in the timing, dose, and duration of use, are associated with changes in critical structural and functional areas of the developing brain, and how other contextual influences (e.g., hormonal, family, peer, neighborhood) may impact or moderate these influences on substance-related behavioral consequences.

It is important in such a prospective study to begin data collection at ages preceding the probable time-periods of high dose exposure to alcohol via drinking. In addition to the onset

and escalation of alcohol use during early adolescence, there are also neurodevelopmental changes in brain structure and function at the neural level. The age period of adolescence is characterized by particularly robust alterations in secondary and tertiary expanses of the cerebral cortex, encompassing components of the temporal, parietal, and prefrontal cortices, as well as alterations in key subcortical structures within the medial temporal lobe (Giedd, Castellanos et al. 1997; Giedd, Blumenthal et al. 1999; Gogtay, Giedd et al. 2004; Sowell, Thompson et al. 2004; Toga and Thompson 2003). Moreover, functional connectivity is likely to change during this period, based on gradual increases in the white -to-gray-matter ratio. These changes are likely to reflect an increase in myelin – i.e., the white insulating sheathing that surrounds some axonal processes of neurons connecting spatially disparate brain regions – coupled with the pruning of dendritic processes in cell body (gray matter) regions (De Bellis, Keshavan et al., 2001). Such changes in connectivity are likely to contribute to maturation of neurocognitive processes that depend upon functioning within distributed neural circuits. At a neural systems level, changes in structural connectivity are likely to be reflected in changes in the degree to which specific brain regions become engaged during specific cognitive tasks.

Given these normative developmental changes in brain structure and function across adolescence, a research design must be employed that would enable disentangling brain changes associated with normative development from that associated with alcohol exposure. A possible design to achieve this would be to repeatedly scan adolescents who vary in their levels of alcohol use across several years with experimental tasks that would assess domains of critical importance (e.g., working memory, decision-making). This proposed research in in progress, but does demonstrate how the dynamic developmental contextual model may be used to sharpen research questions by impacting design and sampling features.

Implications of dynamic diathesis-stress model and heterogeneity issues for substance use and addiction

So how does the dynamic diathesis-stress model and the inclusion of developmental contextual influences impact the study of substance use and addictions? First, I should note that because of its multiple meanings by different investigators I have tended to avoid the use of the word “addiction” in my research and have used more specific, measurable phenotypes related to onset, levels of use, problems, symptoms, etc. Therefore, the study of cardinal symptoms of dependence, such as loss of control, craving, tolerance, and physical dependence may be operationalized, measured, and incorporated in a dynamic diathesis-stress model to facilitate the study of common and specific precursors, correlates, and consequences of these phenotypes, along with multi-level contextual influences across time. The resulting identified causal pathways are thereby linked to more time-ordered trajectories of specific phenotypes, intermediate phenotypes, or endophenoypes (i. e., a biomarker for a behavioral symptom that has a genetic connection) with empirical referents.

Second, the dynamic diathesis-stress model orients one towards a multiple gene, multifactorial, mulitlevel formulation with a focus on mechanisms and processes that explain the dynamic conditions under which the targeted phenomena (e.g., intermediate phenotypes and endophenotypes) of interest are manifested rather than toward a generic descriptor (e.g., the addictive personality). Third, the value of a more comprehensive and encompassing substance use and disorder model is that it enables a perspective on the brain as pivotally involved in regulatory processes that include both multilevel, dynamic genetic and environmental factors that impact mechanisms and processes over time related to key time-related parameters (e.g., initiation, escalation, maintenance, termination, relapse) of substance involvement.

Fourth, this perspective provides a context for brain processes and mechanisms in interaction with other environmental features (including varying levels of exposure to substances) that enable the expression of multiple input and output features, capabilities for learning and plasticity, and processes such as redundancy, substitution, and compensation to adapt to injuries and other disruptions. It has been proposed that addiction is a brain disorder characterized by neuroadaptation to substances that serve to regulate (e.g., up- and down-regulation of neurotransmitters) and strengthen relationships between specific substances (e.g., nicotine, cocaine) and specific collaborative brain systems (e.g., the reward system). Assuming that this characterization is accurate, of which there is some evidence for some substances (e.g., nicotine) and far less for others, the question still arises as to whether this biological unit explanation of addiction (or dependence) is necessary and sufficient. From the multilevel developmental contextual model perspective, this seems highly unlikely in providing a comprehensive explanation to the phenomena of interest, or to facilitate the identification of multiple targets for different interventions.

And fifth, from a public health perspective, a focus solely on addiction (or dependence) may cloak the multiple mortality and morbidity outcomes associated with substance use and abuse that is common to a much larger segment of the population. For example, a limited number of adolescents meet criteria for substance dependence or addiction, but the societal costs for these non-addictive substance use behaviors are enormous. For example, alcohol use is associated with the three highest causes of mortality among adolescents--injury, suicide, and homicide, as well as with multiple causes of morbidity (Windle, 1999). The proposed model facilitates inquiry into time-related factors contributing to multiple substances, multiple substance use phenotypes (e.g., craving, loss of control, driving under the influence) and endophenotypes (e.g., cortical arousal indicators such the P3 response), and multiple significant time parameters related to the initiation, escalation, maintenance, termination, and relapse of substance use.

Summary

The move away from simple, single-cause explanations of substance use disorders has been precipitated by the increasing recognition of the dynamic (patterned, time-ordered change), multifactorial, and heterogenous nature of the phenomenon under investigation. This recognition is not unique to the study of substance use disorders, but rather is also being confronted by investigators of a range of mental disorders (e.g., Alzheimer's disease, schizophrenia, depressive illness) and chronic diseases (e.g., diabetes, cardiovascular disease). This article attempted to highlight the complexity involved in confronting issues associated with this more current multivariate, dynamic, heterogenous group orientation, and provided a conceptual model to organize existing research and to provide future research directions. It is unlikely that any single study can incorporate the measurement of all of the potential variables identified in the conceptual model (see Figure 1); however, it may be useful to identify what factors are, and are not, being accounted for in a given study, and how this enhances or constrains the significance of the findings. It is also hopefully evident in the figure that the interrelations among these variables may (and in most instances do) change across the course of development (Windle et al., 2008). By development, reference is made both to ontogeny and time-ordered changes associated with the progressions (e.g., onset, escalation, maintenance, termination, relapse) of substance use disorders. This more dynamic formulation attempts to acknowledge the complexity of causal relations involved in substance use disorders by addressing the heterogeneity directly and providing a framework for organizing and integrating research findings. This seems to be a more promising pathway to the future rather than, to paraphrase Mencken, “clear and simple solutions that are wrong”.

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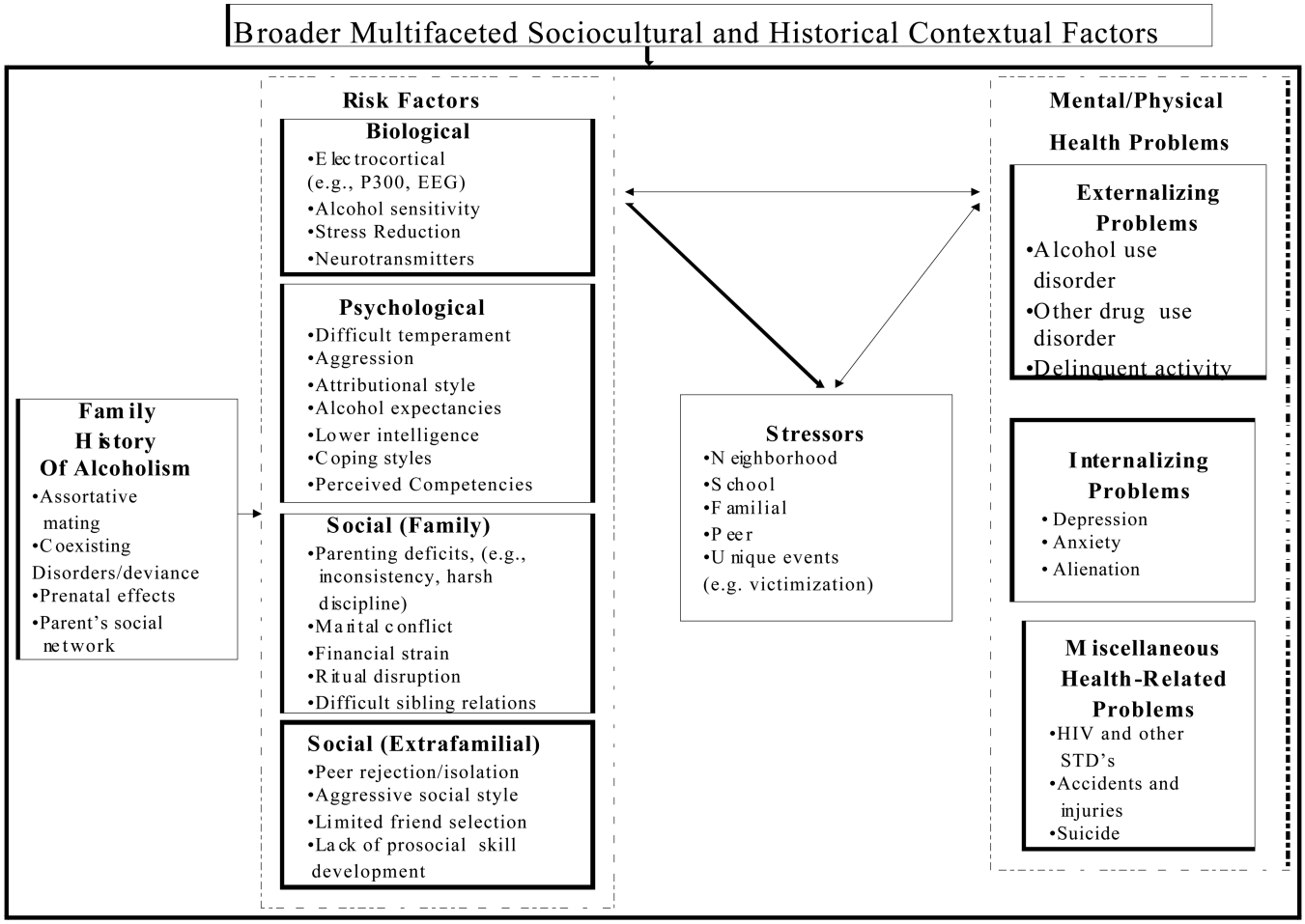

Figure 1.
Dynamic diathesis-stress model for children of alcoholics

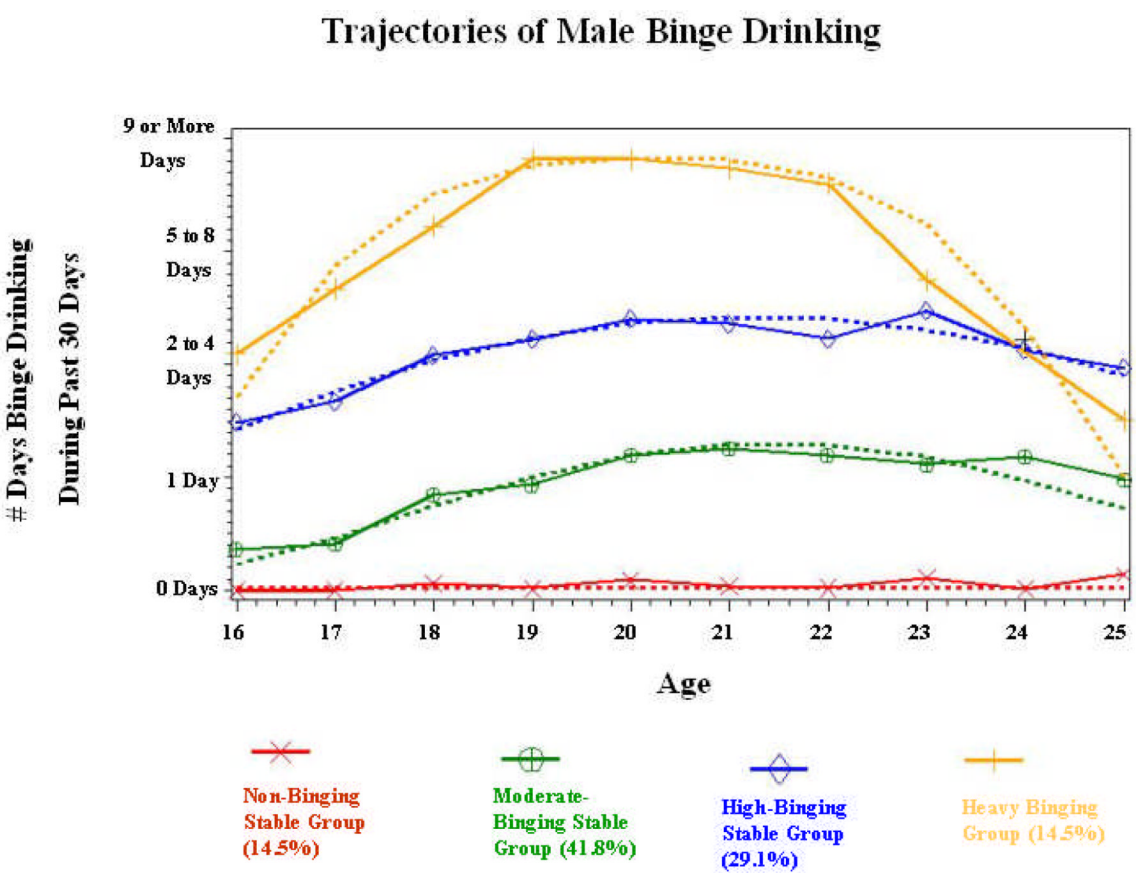

Figure 2.
Male heavy (binge) drinking trajectories