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Application of person-centered medicine in addiction

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Abstract

This article discusses human individuality within a lifespan developmental perspective. The practical application of an individual differences framework for diagnosis, prevention and treatment of addiction is described. A brief overview of the methods conducive to knowledge development within the rubric of person-centered medicine that are available to practitioners working in office and clinic settings concludes the discussion.

Keywords

Addiction; development; etiology; person-centered medicine; prevention; risk; treatment

Introduction

The overarching concept guiding research and practice in person-centered medicine is *human individuality*. Each person in the population is not only biologically and psychologically unique, but also transacts with a variety of ever-changing physical and social environments. Comprehensive understanding of the etiology and natural history of medical and psychiatric disorders requires, therefore, an idiographic (individual-focused) perspective. By extension, effective prevention and treatment necessitates approaches that tailor intervention tactics to the specific characteristics and circumstances of the individual. The philosophical foundation of the idiographic perspective is generally attributed to Immanuel Kant who emphasized the distinctiveness of each person with respect to subjective (phenomenological) experience [1]. The scientific foundation, as discussed shortly, emanates primarily from the discipline of genetics.

Juxtaposed against empirical inquiry directed at uncovering fundamental universal laws governing human biology and behavior, referred to as the *nomothetic perspective*, the idiographic perspective in medicine underlines the importance of biophysical processes as well as subjective phenomenological experience for accurate evaluation and effective intervention. The idiographic and nomothetic perspectives are, however, not orthogonal or

mutually exclusive, but rather are complementary. To illustrate, using a practical example, randomized trials in prevention and treatment research are designed to measure effectiveness of a novel intervention. The results and conclusions drawn are typically framed in terms of mean or average effects reflecting the overall sample, even though the magnitude of intervention response is highly variable between the individuals who constitute the sample. However, with major strides in genetic research, it is opportune to blend the nomothetic and idiographic approaches to ascertain the specific intervention tactic that is most likely to be beneficial for the particular individual. In this fashion, the nomothetic and idiographic approaches are integrally joined conceptually and methodologically for comprehensive and effective health service delivery. Indeed, this blending of the two perspectives is also warranted in public health policy and practice in which interventions are targeted at the entire population, even though most interventions are usually not equally effective for every person. For instance, fluoridation of drinking water reduces the incidence of dental caries in varying degree among children; hence, hardening teeth enamel does not render all individuals equally safe from cavities, the most prevalent infectious disease in children living in advanced nations. While it is recognized that certain diseases can be prevented with close to 100% effectiveness using universal population-wide intervention (e.g. smallpox vaccination), the nomothetic approach alone often does not suffice. Consequently, the practice of clinical as well as public health medicine, in which a “standard” or “best practice” approach is deployed, must contend with a proportion of individuals who respond suboptimally, if at all, to a particular intervention. Intervention effectiveness is, therefore, maximized by joining the nomothetic approach with the idiographic approach; that is, taking into account biopsychological individuality and the individual’s unique environmental circumstances.

The idiographic approach

The idiographic (individual-focused) approach is especially pertinent to research and practice involving polygenic disorders owing to the fact that multifactorial etiology requires an individualized targeted approach to prevention and treatment. These disorders result from complex genetic, environment and phenotype-environment interactions occurring throughout the lifespan. Risky behavior, which is strongly influenced by genetics and is a diathesis to addiction, is regulated with varying effectiveness by prevailing laws, societal norms and cultural mores. In effect, a facilitative environment is required for expression of the phenotypic characteristics comprising the liability (e.g. low self-control), manifestation of the prodrome (e.g. habitual substance use) and subsequently the affected condition (addiction). Furthermore, it should be noted that while extensive evidence indicates that genetically predisposed thrill seeking motivation is a strong risk factor for addiction, as shown in Figure 1 (Panel A) [2], the pattern of association averaged for a whole sample obscures large between-person as well as within-person variation as shown in Panel B. These data demonstrate the hazard of generalizing results to specific individuals from results depicting an average characteristic of a sample. The importance notwithstanding of knowing the characteristics of a sample, denoted usually by measures of central tendency (mean, median, mode), practitioners of person-centered medicine must additionally strive to account for the factors contributing to each individual’s uniqueness that bear on etiology, prevention and treatment.

Individuality: concepts, applications and research

The present discussion consists of three sections. First, the conceptual framework for understanding the origins of individuality is described within a lifespan perspective. Although the discussion focuses on addiction, the conceptual framework is also applicable to other polygenic medical and psychiatric disorders. Addiction, however, is a particularly

good exemplar because of its high prevalence in the population, chronic and relapsing natural history, complex etiology and manifold co-occurring mental and physical illnesses. The second section of this article describes an application of the individual differences conceptual framework for prevention. As will be seen, this perspective is amenable to objective quantitative measurement that links to prevention and treatment tailored to the unique characteristics and circumstances of the individual. The third and last section describes research opportunities for practitioners of person-centered medicine who are based in office and clinic settings. Importantly, sound empirical investigation can be conducted using inexpensive, readily available user-friendly technology. Accordingly, clinicians are well-positioned to advance the empirical knowledge base.

Origins of Individuality

Casual observation readily reveals recognizable, albeit usually subtle, physical differences between monozygotic (identical) twins. Thus, in cases of identical genotype, the environment influences the biological and psychological uniqueness of each individual throughout life. Differences between unrelated individuals are even greater owing to genetic as well as environmental uniqueness. Consider, for instance, the vast individual differences in intelligence, attitudes, values and personality. Similarly, biological characteristics such as liver injury indicators, height, muscle strength, testosterone concentration and brain weight are marked by large inter-individual heterogeneity. Because biological and psychological traits are featured by large phenotypic variability, it is essential to understand the basis of these individual differences in order to understand etiology of a disorder so as to implement prevention and treatment interventions that are specific to the characteristics and needs of the particular individual.

Figure 2 depicts how the genotype and the environment interact. The particular quality of these interactions accounts for the differences between individuals on all biopsychological characteristics. For example, whereas the specific value of a phenotype (e.g. pulse = 75; IQ = 103), arises from the interplay of genes and environment, the relative contribution of genes, shared environment and unique environment are different between individuals. A first task, therefore, of the practitioner having a person-centered medicine perspective involves disaggregating the relative contribution of genetic and environmental influences on the a) predisposing vulnerability, b) prodrome and c) clinical phenotype. Upon completion of this task, it is feasible to select an empirically validated or devise a novel intervention that is effective for ameliorating the disturbance.

Applying the model shown in Figure 2 is, however, a daunting challenge because many genes, in conjunction with manifold facets of the environment, produce within the person a large array of both risk-enhancing and risk-attenuating biopsychological phenotypes. For instance, a person can have both high intelligence and low self-control. Accordingly, a risk-attenuating phenotype can offset risk due to the presence of risk-enhancing phenotypes. Addiction, for instance, is associated with many childhood phenotypes, including poor self-control, low executive cognitive capacities, mild ataxia, emotional dysregulation, suboptimal attention capacities, behavioral hyperactivity and thrill seeking [3,4]. The presence of offsetting risk-reducing phenotypes, such as traditional values and a belief that drugs are dangerous, can lower the risk for addiction. Accordingly, risk-enhancing and risk-attenuating phenotypes in combination determine the overall risk for addiction.

Further complicating assessment of addiction etiology, certain biopsychological phenotypes that are salient to risk, bias the individual to seek out particular types of environments. Thrill seeking individuals, for example, are more prone to seek out military combat, adventure and gambling. When exposed to combat, a tropical environment, or a casino, a subset respectively experience emotional disruption such as post-traumatic stress disorder (PTSD),

succumb to malaria and develop a gambling addiction. Similarly, thrill seeking is associated with risk for selection of a social milieu and friendships which potentiate the probability of developing addiction. In addition, specific aspects of the environment have a particularly strong influence on individuals having certain phenotypes. For example, a submissive or unassertive individual is more likely to accept a drug offer, thereby triggering habitual use and ultimately addiction. Elucidating etiology thus requires understanding the complex reciprocal interactions between phenotypes and facets of the environment that are independently and conjointly related to risk.

In addition, it is important to be cognizant that a liability-enhancing phenotype may be a “trait” depicting a dispositional characteristic of the individual (e.g. generalized physiological arousal) or expressed only in specific circumstances (e.g. arousal in response to a particular stimulus). Some disease-promoting phenotypes are manifest during the natural diurnal cycle (e.g. sleep apnea) or other cycle (e.g. premenstrual cycle), while others are evinced during an intentionally altered physiological state (e.g. violence while under the influence of alcohol). Pharmacotherapy is based on the assumption that modifying the internal milieu alone is sufficient to reduce severity of the phenotypes to within normal range comprising the prodrome or clinical disorder.

Addiction, like most chronic medical and psychiatric disorders, is strongly heritable [5,6]. Hence, children of addicted parents, even if reared by “normal” parents, have elevated risk of also developing addiction [7]. Indeed, a child’s risk of developing addiction covaries with the number of first-degree addicted relatives. Thus, biopsychological characteristics during childhood and adolescence that have a heritable basis and are related to risk for the disorder, should comprise a main intervention target. With respect to addiction, many studies have shown that the characteristics comprising risk are broadly encompassed within a multi-dimensional trait reflecting psychological self-regulation [4]. Low self-regulation (or dysregulation) is variously manifest as externalizing behavior, poor self-control, hyperactivity, aggressivity, low adherence to societal rules and conflict with adult authority [8,9]. However, because at least half the population of children who are at high genetic risk do not succumb to addiction, environmental factors also must be taken into account for both understanding etiology and planning effective intervention. It is well-known, for example, that the environment strongly influences the emergence of prodromal phenotypes, specifically anti-social behavior and substance use. Many reports have recorded that a dysfunctional family, economically disadvantaged neighborhood and peers who do not adhere to societal norms and laws also amplify the individual’s risk for addiction. Hence, understanding the etiology of addiction (as well as related disorders) at the individual level, in fashion that informs intervention, requires a systematic evaluation of the severity of the salient biopsychological characteristics constituting the liability in conjunction with determination of the relative influence of heritability, shared environment and unique environment on expression of these characteristics. Family history of addiction, quality of family interactions and neighborhood socioeconomic status are, for example, routinely evaluated as salient indicators of the genetic, shared environment and unique environment contribution to the individual’s risk for addiction [9].

It is also important to recognize that addiction, similar to many other psychiatric and medical disorders that are first manifest during adolescence or young adulthood, is a developmental outcome. Accordingly, elucidating etiology at the individual level is integrally connected to understanding the person’s developmental history. For example, exposure to addictive substances during fetal development is associated with earlier age onset of substance consumption. Addiction evinced during adolescence is usually presaged by childhood conduct problems and anti-sociality compared to addiction which emerges in middle or late adulthood. In early childhood, temperament disturbances are more likely to be

present [4]. A strong body of evidence has also accumulated showing that early onset puberty amplifies risk for substance abuse. Hence, it is essential to fully understand the developmental history so that the origins of the phenotypes comprising the predisposing liability and subsequently the clinical features of the disorder, are coherently portrayed to depict the etiological trajectory. A review of this literature can be found in Tarter et al. [4]. However, the point to be made at this juncture is that etiology in person-centered medicine requires explanation that encompasses the entire life narrative and, therefore, must be comprehended within the framework of a trajectory. Significantly, understanding the etiological trajectory has the vicarious benefit of consolidating the patient-practitioner relationship.

Figure 3 displays a model for elucidating the developmental patterning of phenotype-environment interactions comprising the etiological trajectory. As can be seen, the trajectory curve in this hypothetical example results in a disorder. The variety of possible pathways is, however, *infinite*. Beginning at conception, the individual's liability is quantifiable by phenotypes depicted as $V_1, V_2 \dots V_N$ [10,11]. Consistent with the principle of behavioral epigenesis, the aggregate of all phenotypes, the resultant phenotype (R), has a forward influencing effect on the individual's trajectory culminating ultimately in either a healthy socially adjusted outcome or a clinical disorder. This measured severity of overall liability is a vector owing to the fact that it is a quantity that has both magnitude and direction. Disaggregating the Resultant Vector affords the opportunity to devise an intervention plan that is tailored to the specific needs of the individual taking into account both individual characteristics and environmental circumstances. For example, a person having liability for depression is at heightened risk following an adverse event (e.g. death of spouse) or catastrophe (e.g. earthquake), as well as prevailing adverse circumstance (e.g. high crime neighborhood). Hence, the trajectory may progress in normative fashion until deflected by an environmental factor toward an adverse outcome. Similarly, a person having high liability (e.g. poor self-control) can have a good outcome in an environment that buffers risk. Much research has shown, for example, that social support attenuates risk for psychiatric disorder. Thus, mapping the trajectory leading to a disorder involves: a) specifying the array of risk-enhancing and risk-attenuating phenotypes as best as possible from conception onward; b) identifying the salient social and physical contextual factors during this period which enhance or diminish severity of the liability & c) clarifying the dynamic interactions between phenotypes and environmental influences leading to the prodrome and the disorder. Notably, the etiological trajectory can be more or less linear since childhood, resulting in either a good outcome or a disorder. Alternatively, it can suddenly change direction for the worse following an unpredictable adverse event (e.g. rape) or quickly change for the better following a positive event (e.g. marriage to a protective spouse). Indeed, the main assumption supporting foster home placement is that a secure family environment orients the developmental trajectory of high risk children toward a positive outcome.

Figure 4 illustrates how a single temperament trait, behavior activity level, interacts with the environment during ontogeny leading to attention deficit hyperactivity disorder (ADHD) and subsequently conduct disorder that commonly presages substance use leading to addiction. The increasingly larger circles reflect the individual's growing psychological repertoire (single temperament trait culminates in conduct disorder) and their progressive darkening reflects strengthening of the psychological disposition during ontogeny. Thus, beginning with a primary temperament trait, complex patterns of maladaptive behavior emerge that ultimately manifest as a psychiatric disorder. While this framework has been shown to be heuristic for delineating the etiology of addiction [12], it is also appropriate for delineating etiology of other medical and psychiatric disorders.

Several theoretical and empirical reviews [4,10,11] have advanced a developmental perspective of addiction etiology. A cardinal liability phenotype is low adherence to health promoting behavior. Health promoting behavior, ordinarily inculcated in early childhood as part of daily routine (e.g. nutritious diet, brushing teeth, regular sleep-wake cycle, hygiene), consolidates attitudes that thwart impulses to initiate self-injurious behaviors (smoking, alcohol use, drug use, risky sex). A healthy outcome is, however, contingent on sustained parental investment in the child. Parents in their role as mentors and caregivers inculcate values, reinforce behaviors and provide the oversight needed to promote their child's healthy development. Hence, whereas person-centered medicine emphasizes biopsychological individuality, the environment is an equally important influence on lifespan development. In an important program of research, it has been shown, for example, that practical advice provided by nurses during home visitations helps socioeconomically disadvantaged mothers improve their child's rearing environment, thereby lowering the child's probability of developing addiction and related problems [13]. In effect, person-centered medicine is also environment-centered medicine.

From science to practice

Many daunting challenges confront clinicians having a person-centered practice orientation. For instance, assessment of the patient is labor intensive and requires a wide breadth of expertise. The intervention (prevention or treatment) plan must be designed to address the specific needs of the individual taking into account chronological age and developmental stage in relation to the person's unique pattern of biopsychological strengths and liabilities and environmental circumstances. Accordingly, prognosis following an intervention is closely linked to the quality of the evaluation. The ensuing discussion succinctly describes a schema for conducting assessment of risk for disorders that have a multifactorial etiology. Although this schema has to date been applied only to addiction, it is also a heuristic strategy for assessment that informs prevention and treatment of other medical and psychiatric disorders.

Risk for a disorder can be partitioned into two components: transmissible and non-transmissible. Transmissible risk refers to inter-generational influence, whereas non-transmissible risk reflects the influence of environmental factors and acquired behaviors [14]. As shown in Figure 5, these two components of risk for addiction can be configured in a Cartesian coordinate system. In this manner, the sources and magnitude of risk are known. To illustrate the centrality of individuality in the practice of person-centered medicine, it can be seen in Figure 5 that there is vast heterogeneity in the youth population with respect to severity of transmissible and non-transmissible risk for addiction.

The framework depicted in Figure 5 guides efficient screening for disorder and has direct ramifications for maximizing intervention effectiveness. For instance, the probability of developing addiction to cannabis has been shown linearly to increase following first use only among youths who are at high transmissible risk [15]. Because initial exposure has a more deleterious consequence in high risk youths, it is crucial, therefore, expeditiously to identify vulnerable youths so that interventions can be implemented that are targeted to the predisposing biopsychological characteristics and environmental circumstances. In this fashion, resistance to alcohol and drug consumption is inculcated.

Documenting the relative contribution of transmissible and non-transmissible risk also has important prognostic utility. Significantly, the individual's location in a particular quadrant predicts marijuana use frequency up to nine years later. As shown in Figure 6, individuals scoring low on both transmissible and non-transmissible risk at age 10–12 have, as expected, the lowest frequency of marijuana consumption at age 19 while those scoring high on both dimensions have the highest frequency of consumption. Furthermore, the Cartesian

framework is informative for estimating the probability of other problems. Figure 7 illustrates that severity of violence at age 19 is greatest among youths who at ages 10–12 had conjoint high transmissible and non-transmissible risk whereas the lowest violence is observed in youths scoring low on both transmissible and non-transmissible risk. As with marijuana, youths located in the other two quadrants are not notably different from each other. In effect, elevated transmissible risk accompanied by low transmissible risk and *vice versa* are associated with intermediate magnitude of risk for marijuana use and violence and both aspects of risk contribute equally to the outcomes.

The Cartesian framework does not, however, depict the profile of risk-enhancing and risk-attenuating factors contributing to transmissible and non-transmissible risk. Once severity on the transmissible and non-transmissible dimensions is determined, additional assessment is required to delineate the individual's particular array of strengths and liabilities. In the field of addiction, several efficient and cost-effective instruments for measuring the specific components of risk have been developed. For instance, the revised *Drug Use Screening Inventory* (DUSI-R) [16] measures 18 problem areas and takes about 20 minutes to complete. It can be administered on the Web in over a dozen languages to quantify and profile severity of medical, behavioral, social and psychiatric problems. The *Assessment of Liability and EXposure to Substance use and Antisocial behavior* (ALEXSA) [17] is another instrument administered by computer. One of its main advantages is that it does not require an ability to read and thus is useful for profiling strengths and liabilities in young children [18].

The clinician is a scientist in person-centered medicine

Ready access to powerful computers and user-friendly software affords the opportunity for practitioners to execute sophisticated clinic and office-based research projects. Research conducted on small samples and single cases enables practitioners to test hypotheses regarding intervention effectiveness. Among the various paradigms, the *intermittent baseline design* is straightforward and rigorous. In this paradigm, the participant's clinical status (e.g. depression, addiction, memory capacity, ambulation, etc.) is initially measured a randomly selected number of times (preferably in equidistant intervals such as once per day) for a period of time termed the baseline phase. The treatment phase ensues during which the clinical condition continues to be measured using the same schedule as the baseline period. Randomization of the number of baseline observations eliminates potential spurious effects from unknown or alternative sources (much like randomization in clinical trials) [19,20]. The main analytic procedures are *time series analysis* [21], *trajectory analysis* [22], *state-space modeling* [23] and *systems dynamics models* [24]. These analytic strategies enable detecting changes attributable to a particular treatment, changes over time associated with the treatment and interactions between the treatment and the person's characteristics. In situations where the treatment can ethically be temporarily withdrawn and then re-introduced, improvement evinced only during the intervention provides convincing evidence of the treatment's effectiveness.

Conclusion

Inexpensive, objective and efficient tools are available to guide research pertaining to etiology, prevention and treatment within the conceptual framework of person-centered medicine. One exciting research opportunity in person-centered medicine involves developing and validating tools that are useful for profiling the configuration of biopsychological phenotypes and environmental influences pertinent to risk for and measurement of severity of medical and psychiatric disorders. Based on the individual-specific profile, interventions can be implemented that are targeted to each person's

predisposing assets and liabilities, prodrome characteristics and the clinical disorder. These interventions respectively constitute primary, secondary and tertiary prevention.

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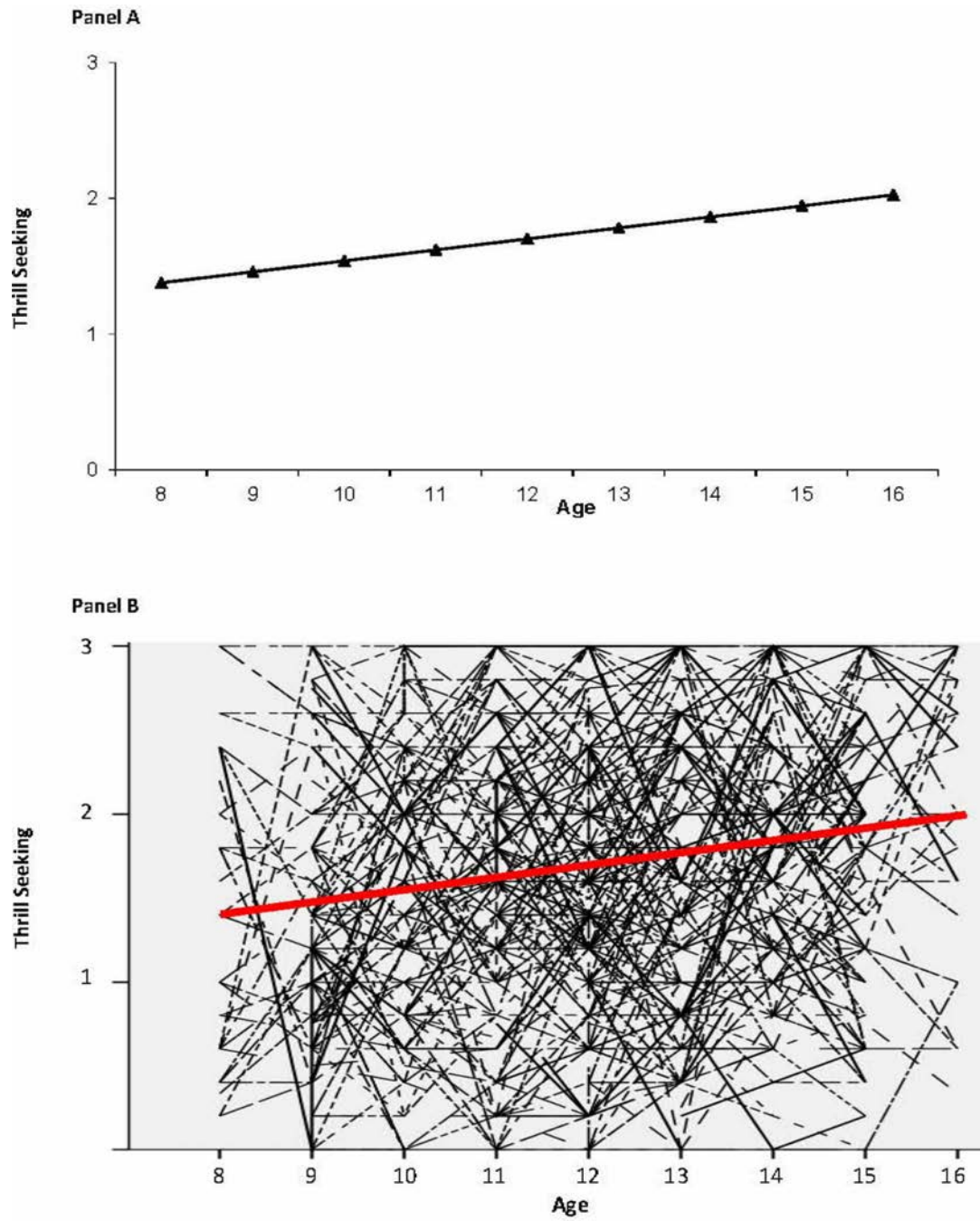


Figure 1.
Developmental change in thrill seeking in 1,147 youths.

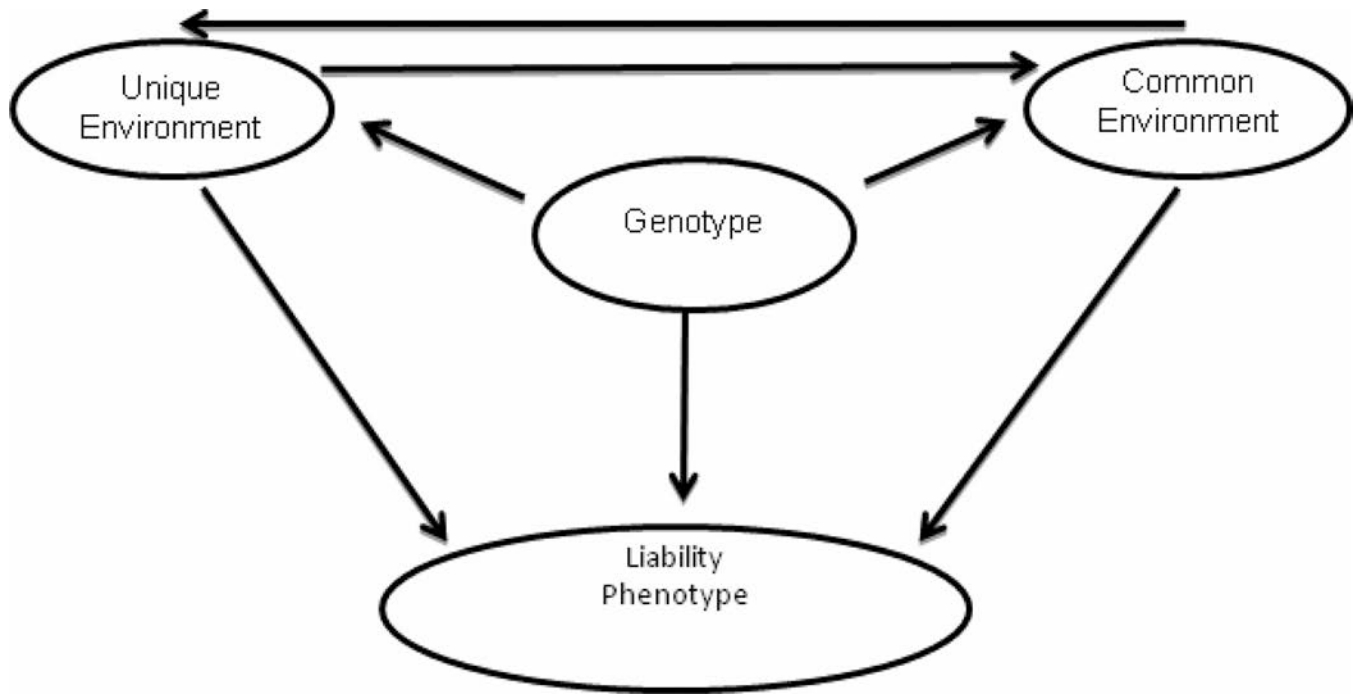


Figure 2. Determinants of human individuality in health and disease.

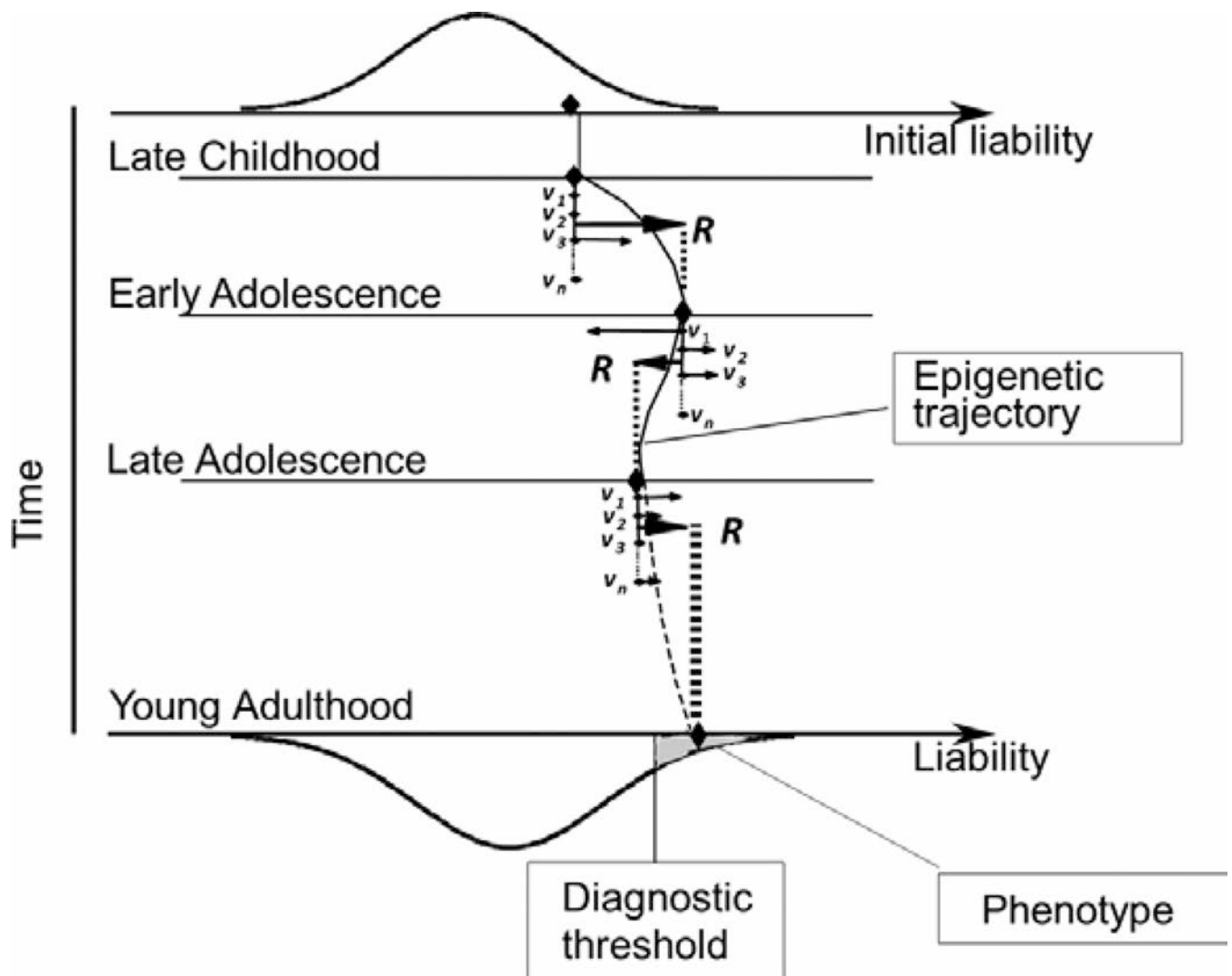


Figure 3. Developmental patterning to healthy and disease (shaded area) outcomes. (Adapted from Vanyukov et al., 2003b) [11].

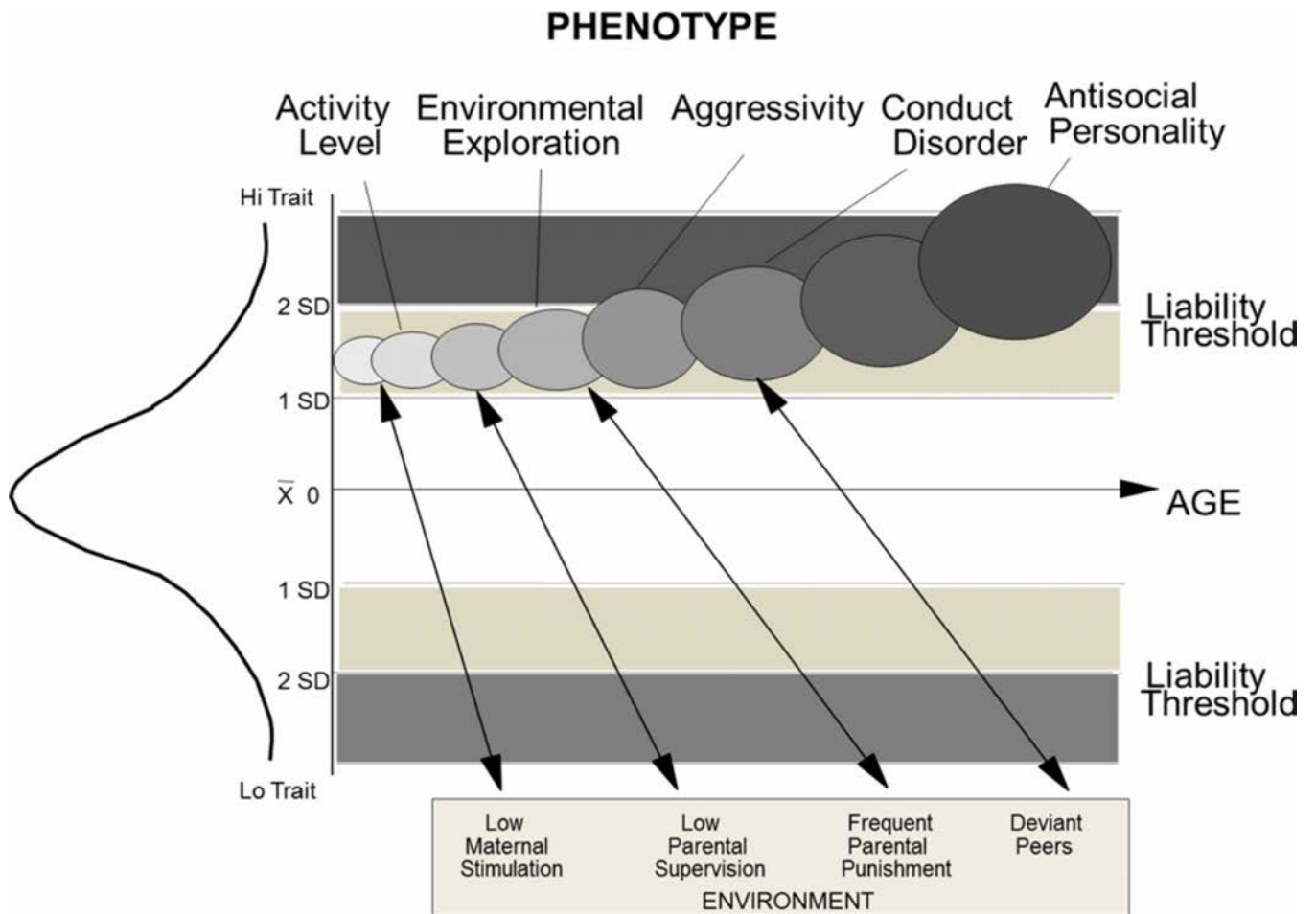


Figure 4. Person-environment interactions during development producing increasingly complex and stable phenotypes (Adapted from Tarter and Vanyukov, 1994) [12].

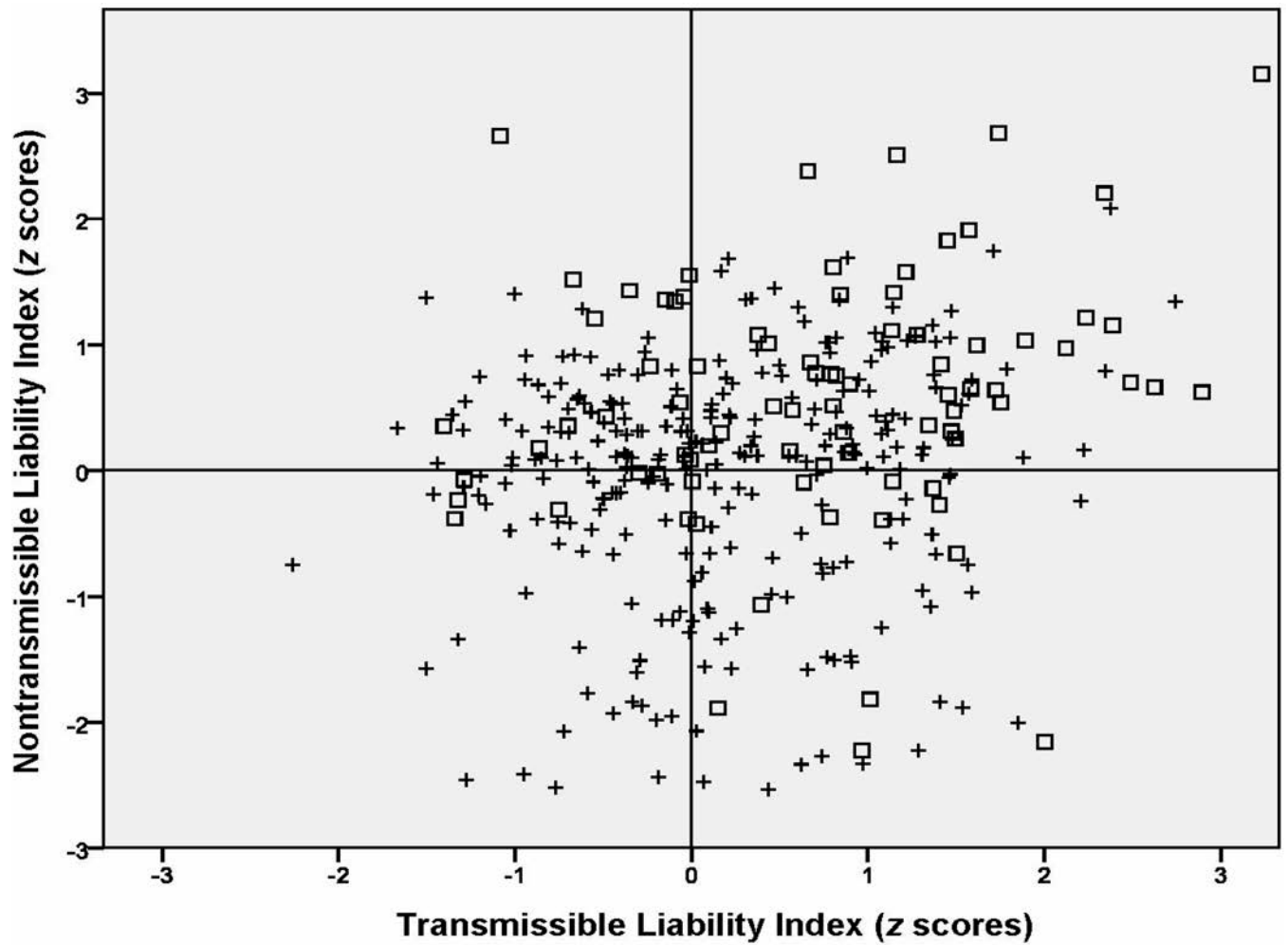


Figure 5. Scatter plot of transmissible liability and non-transmissible risk of youths at age 10–12 (N=352) who develop cannabis use disorder (□) or no disorder (+) (Adapted from Tarter et al., in press) [4].

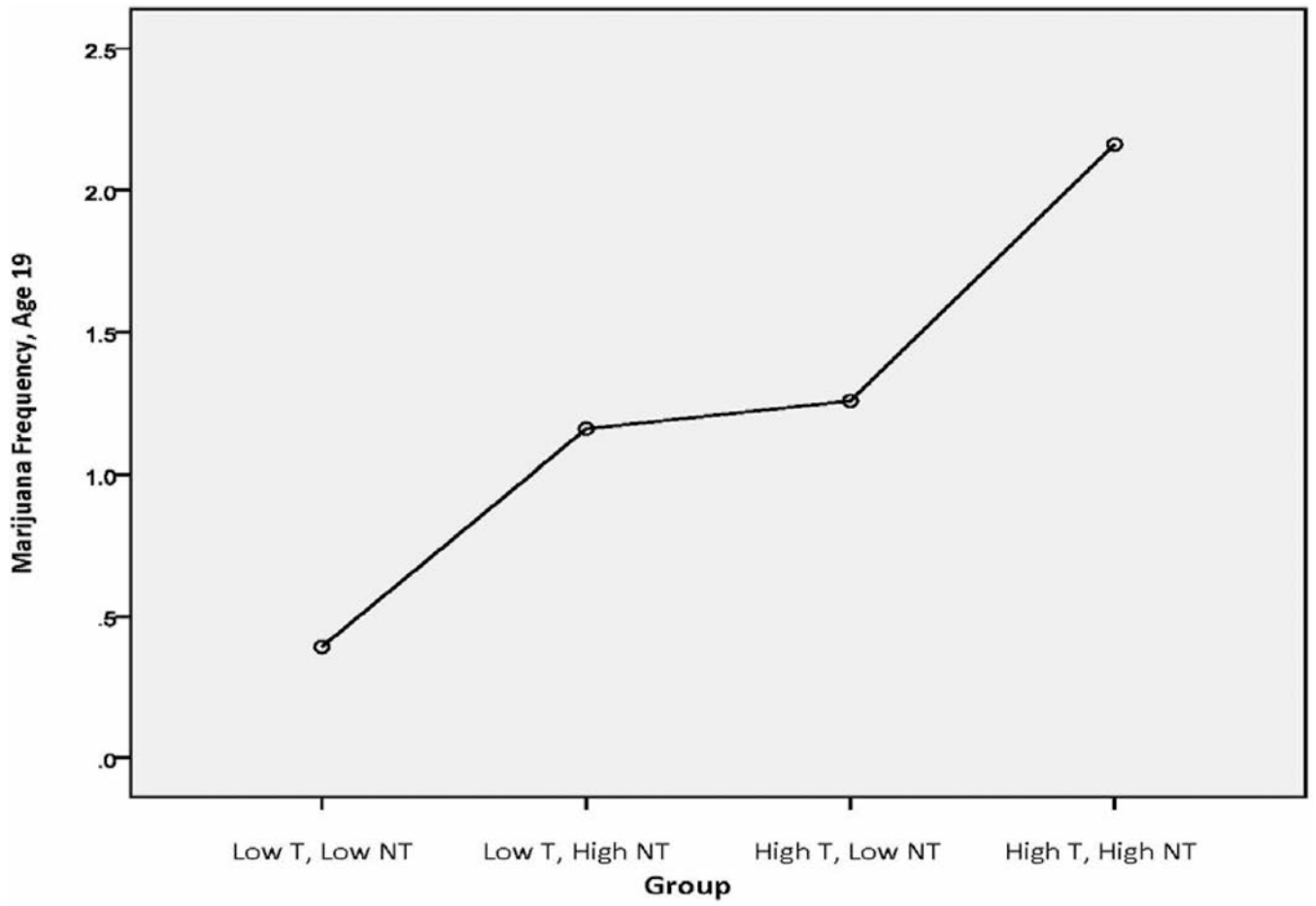


Figure 6. Marijuana use frequency at age 19 based on transmissible and non-transmissible risk scores.

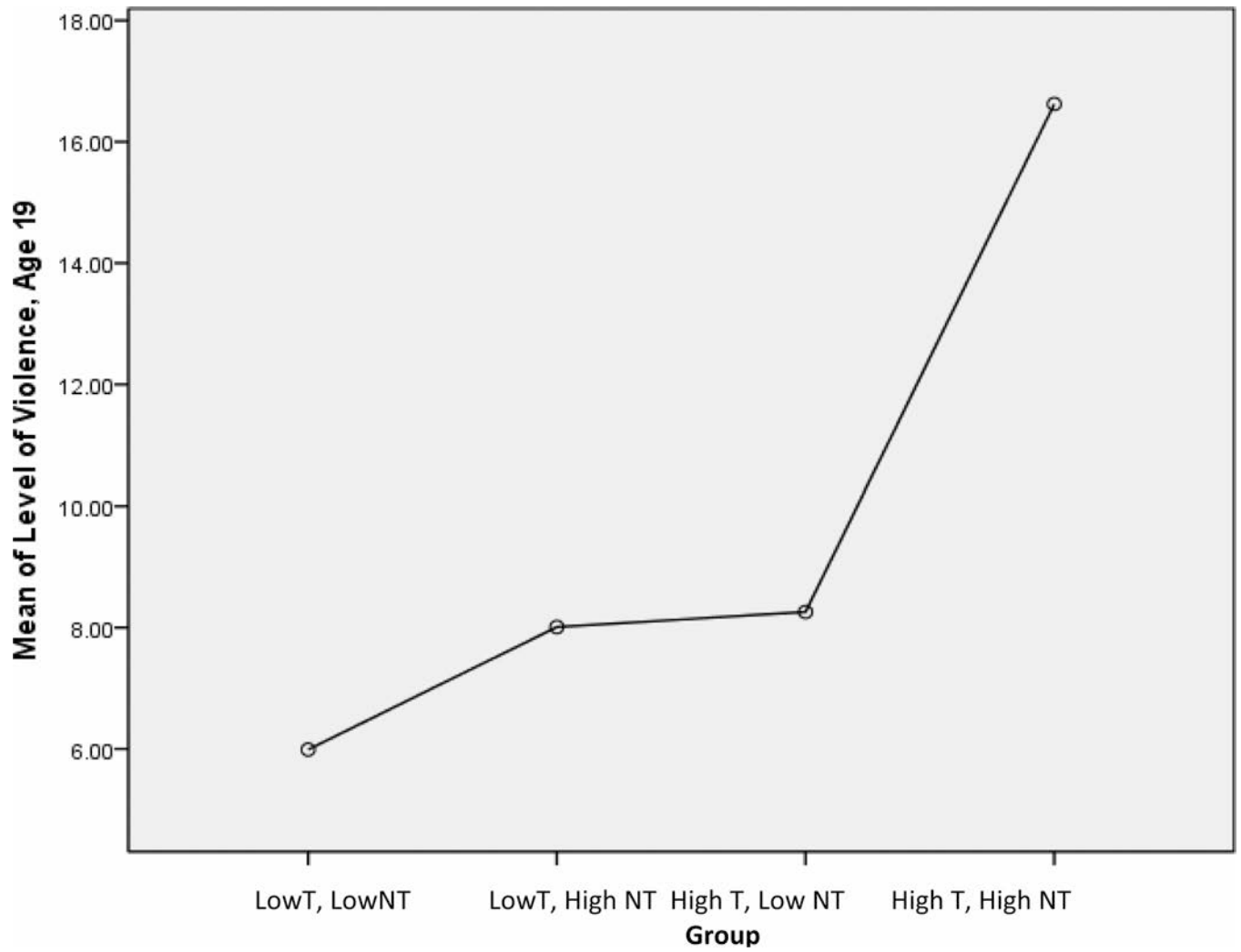


Figure 7. Violence severity at age 19 based on transmissible and non-transmissible risk scores.