Risk and Protective Factors for Alcohol Use Disorders Across the Lifespan

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Abstract

Purpose of Review Losing and regaining control over alcohol intake varies as a function of individual-level predictors across the lifespan. Specifically, the interplay of protective and risk factors for losing and regaining control, particularly in real-life settings, is thus far poorly understood. Individual differences in cognition, affect, emotion regulation, social factors, and personality traits, together with individual differences in brain structure and function, and biological markers of stress exposure may have different effects on alcohol consumption in different age groups. We will review current evidence for age-specific effects for losing and regaining control over alcohol intake and propose a framework for investigation across age groups.

Recent Findings We find evidence for differences in relative impact of psychosocial predictors of alcohol consumption as a function of age that varies by gender. There is theoretical reason to assume that predictors vary in the time course of their taking effect: While e.g., early trauma and personality traits may be conceptualized as more distant antecedents of alcohol consumption, cognition, affect and emotion regulation can be conceptualized as co-correlates, where variation over periods of months may go along with changes in alcohol consumption. At the same time, craving, current stressors, and priming events may serve as short-term or immediate causes of alcohol consumption.

Summary We propose a combination of longitudinal age cohorts to (i) identify individual-level differences (using latent growth curve models) and profiles (using latent growth mixture models) of the psychosocial and biological variables of interest that predict regaining or losing control, and ambulatory assessments every 2 days, in order to (ii) investigate effects of triggers and risk factors on current alcohol consumption. This approach will allow us to characterize age-related differences in the interplay between these factors in real-life settings.

Keywords Alcohol use disorder · Risk factors · Protective factors · Lifespan · Age groups

Introduction

There is currently convincing evidence that increases and decreases in alcohol consumption, and the respective control over alcohol use, vary across the lifespan [1, 2]. Psychosocial protective and risk factors show differential impact on the development and maintenance of alcohol use disorder (AUD) in different age groups [1, 3, 4]. These psychosocial factors interact with genotype effects [5] as well as key neurobiological mechanisms implicated in the development and maintenance of AUD. Such key mechanisms include habituation (reflected by a reorganization of corticostriatal loops; [6, 7]), sensitization (promoting the attribution of incentive salience to drug cues; [8]), and alterations in goal-directed decision-making (preference of drug reward over alternative reinforcers and impaired cognitive control;[9, 10], 11]). Lab studies and retrospective accounts of patients
suggest that in vulnerable individuals, exposure to drug cues, stress, and priming doses trigger acute drug intake [12, 13]. Following a brief review of empirical evidence, we highlight the need for understanding the interaction between individual differences in age, psychosocial predictors, neurobiological and genetic mechanisms, and exposure to stress, cues, and priming drug doses [7, 8] with respect to losing and regaining control over alcohol intake across the lifespan.

On average, alcohol consumption patterns change across the entire lifespan (see Fig. 1). A meta-analysis of combined 59,397 participants revealed gender differences and estimated a moderate increase in women from age 15 to 35 and a moderate decline after age 55. Men displayed a sharp increase in consumption and especially binge drinking in men from age 16 to 25, with a subsequent sharp decrease from age 30 up until age 55. In older adults, estimates show slowing of this decrease at around age 55–70 [2].

**Psychosocial Predictors of Alcohol Consumption Across the Lifespan**

In adolescents and young adults, predictors differ with respect to (i) current alcohol consumption, especially binge drinking (i.e., consumption of five or more drinks on one occasion; compare [4]), and (ii) future alcohol abuse and the development of alcohol dependence into middle age [1]. In adolescents, age at first drink, levels of acute alcohol intoxication, externalizing personality traits, life events (romantic love), and anxiety symptoms were associated with both current and future alcohol consumption, and effects were moderated by current cannabis and tobacco consumption [1, 4, 14]. On the other hand, heritability estimates, structural brain changes, neurobiological correlates of inhibitory control and Pavlovian and reward-based learning were associated with future consumption only [4, 11]. In turn, early drinking episodes impact on the neurobiological correlates of reward-based learning, sensitization, and habit formation [15••], and gender differences have been proposed for AUD risk associated with depressivity [16, 17]. Thus, psychosocial variables and externalizing behaviors are powerful predictors of current consumption, and future consumption patterns and the development of AUD are associated with neuronal signatures of habitization and sensitization to drugs of abuse in adolescents and young adults.

In early middle-aged adults, adverse childhood experiences, parental alcohol use, and comorbid substance abuse seem to be reliable risk factors for an increase in consumption [1, 18]. Protective factors include marital status, higher education and socioeconomic status, and other aspects of resilience such as emotional and cognitive control under pressure, tolerance of negative affect, goal orientation, and strong social support, especially in the face of childhood adversity [19, 20] and exposure to drugs [21]. In middle-aged adults suffering from AUD, both Pavlovian learning and impairments in goal-directed behavior and their associated neurobiological correlates have been shown to be promising predictors for AUD maintenance and ongoing consumption [22, 23]. Both stress responsivity and cognitive capacity, as well as alterations in brain structure, interact with these neurobiological correlates of learning implicated in the development and maintenance of AUD [16••, 24]. Elevated biological markers of chronic stress are correlates of increased alcohol consumption in this age group, with higher cortisol levels in acute withdrawal of alcoholics compared with abstinent alcoholics or control samples [25]. In addition, gender effects have been reported for the type of stressors (i.e., family-related problems being a greater risk for women) [26] and for the association between depressivity and problem drinking in middle-aged adults [27]. Taken together, there is evidence that consumption patterns in midlife vary as a function of individual risk and protective factors, which interact with gender and individual stress exposure in the face of neurobiological processes of habitization and sensitization.

The overall decrease of alcohol consumption levels slows down in late middle age, and this effect seems to be driven by a proportion of middle-aged adults (estimated at around 20–25%) who significantly increase consumption patterns from around age 55 onward [2, 28]. Predictors of increased consumption in late middle age include anxiety, depression, loneliness, bereavement, and role transitions [28, 29]. In addition, there is evidence from longitudinal studies indicating that risky drinking behavior in midlife, high socioeconomic status, male gender, being unmarried, and the presence of loneliness...
and depressivity significantly increase the risk of AUD development in later life [3, 30]. It has been hypothesized that depression and loneliness are more likely to be predictors of alcohol use in women, while they may be consequences rather than causes of excessive alcohol intake in men [26, 27]. On a neurobiological level, age-associated decreases in the integrity and structure of the prefrontal cortex, including executive control, working memory functions, and dopaminergic neurotransmission [31, 32], may be related to increases in consumption patterns [33, 34]. Age-related changes in reward processing may be associated with altered sensitivity to alternative non-drug rewards and thus contribute to alcohol intake [35, 36]. Furthermore, effects of alcohol on cognition and brain structure as well as general morbidity and mortality are increased in late middle age [28, 29, 37], and can affect cognitive control mechanisms for regaining control over alcohol intake.

A series of studies confirm the additional impact of trigger factors including exposure to stress, biological markers of stress sensitivity, cues, and priming drug doses on key cognitive and behavioral mechanisms associated with alcohol intake [25, 38–40, 41]. Furthermore, the relative impact of stressors, cues, and priming doses on alcohol intake can differ with age, and indeed, age-related differences in the effects of setting and cues have been reported by first ambulatory assessment studies in substance use disorder [42, 43]. Using smartphone-based ecological momentary assessment, a study investigating older adults with and without HIV infection as population showed that greater anxiety predicted subsequent substance use (alcohol and cannabis), greater happiness predicted substance use in the evening and in the night, whereas higher pain levels led to higher consumption in the morning [43]. Conversely, coping with stressors and emotion regulation have been shown to have a significant protective impact on momentary alcohol intake [44], and these effects can be operationalized as the interplay between early life stressors [15] and biological markers of cumulative stress exposure (e.g., hair cortisol) [25]. Recent empirical findings have implicated differential effects for substance-specific and person-specific cues on momentary craving [45], highlighting the specific effects of cues on drug intake (or craving thereof) in real-life settings and underlining individual differences in cue responsivity in specific environments, with unique person-specific cues having a stronger effect on craving addictive substances than general substance-specific cues. In addition, aspects of cognitive control as evidenced by changes in working memory function have been associated with momentary increases in drug intake, thus reflecting momentary aspects of losing control in consuming individuals [46].

Taken together, as can be seen in Table 1, there is evidence for differences in the relative impact of psychosocial predictors of alcohol consumption as a function of age. There is also theoretical foundation to assume that predictors vary in the time course of their taking effect: On the one hand, early trauma and personality traits may be conceptualized as more distant antecedents of alcohol consumption. On the other hand, cognition, affect, and emotion regulation can be conceptualized as co-correlates, possibly leading to changes in alcohol consumption when vary over periods of months. At the same time, craving, current stressors, and priming events may serve as short-term or immediate causes of alcohol consumption. The following methodological framework to assess changes in psychosocial predictors and alcohol consumption over time uses this conceptualization as a basis for sampling and assessments.

Proposition of a Methodological Framework: Traditional Longitudinal Cohort Combined With Ambulatory Assessments

Ambulatory assessment offers the possibility to understand the interaction in real life between momentary effects of stressors, cues, and priming doses with age-related risk and protective factors and their impact on trajectories of losing and regaining control over alcohol intake. In addition to a classical longitudinal study, a collaborative research center has recently been established in order to inquire in a real-life setting whether currently alcohol-consuming subjects with at least mild AUD and no clinical need for detoxification plan to limit alcohol intake and we will assess whether they manage to keep their limit [47]. Using ambulatory assessments, sampling on every other day, effects of cue and stress exposure, and alcohol craving as well as impulsivity and mood on current alcohol consumption will be evaluated. Triggered by acute alcohol intake, we will also measure the effects of alcohol cues and priming doses of alcohol on craving, drinking motivation, impulsivity, mood, and stress levels as well as working memory span.

Using ambulatory assessment in real-life settings, effects of triggers of losing control over drug intake, specifically exposure to stress, drug cues, and priming doses, will be explored. To investigate effects over the lifespan, we will include currently drinking adolescents and young adults as well as early and late middle-aged adults with mild to moderate alcohol use disorder (AUD) and no clinical need for detoxification over the course of 1 year. All subjects will have four personal and online assessments (baseline and follow-up every 4 months) and provide ambulatory assessment data sampled every 2 days as well as triggered by alcohol use. Ambulatory assessments will thus allow us to measure the effects of triggers of alcohol use including momentary exposure to stress, alcohol cues, and priming doses on the amount of alcohol consumed at a given event.

In three longitudinal age cohorts (age cohorts ranging from 16 to 32 years, 33 to 49 years, and 50 to 65 years), it is thus
possible to identify individual-level differences (using latent growth curve models) and profiles (using latent growth mixture models) of the psychosocial and biological variables of interest that predict regaining or losing control, which will be operationalized as a composite measure of both planned and actual consumption and subjective control experience. Applying ambulatory assessments every 2 days, we will investigate effects of protective and risk factors on current alcohol intake using dual change score models, which allows us to characterize age-related differences in the interplay between these factors in real-life settings. We will be able to examine age-related differences in longitudinal trajectories of drug intake and their predictors over the course of 1 year, and we will assess effects of gender and comorbid cannabis and tobacco use on individual trajectories. The results of this investigation will critically inform novel prevention and intervention strategies by identifying individuals at specific risk for relapse and by identifying pathophysiology-driven targets for interventions.

Conclusion

The aim of assessing the interaction between momentary, psychosocial, and neurobiological predictors of losing and regaining control over alcohol intake fits the Research Domain Criteria (RDoC) approach [48, 49]. This approach suggests that characterizing key neurobiological mechanisms and their individual variance will enhance our understanding of the development and maintenance of mental disorders including AUD [50, 51]. The behavioral manifestation of losing and regaining control, for example, can be understood as a shift from non-drug reinforcement to drug reinforcement which has been associated with the expression of γ-aminobutyric acid (GABA) within the amygdala. In an exclusive choice procedure, rats that chose alcohol over a high-valued reward showed impaired GABA clearance within the amygdala, similar to decreased GAT-3 expression in the central amygdala of alcohol-dependent people [52].

Regarding our analytical approach, mean level prediction analyses can be extended to the identification of latent classes or subgroups (based on individual differences in predictor patterns and their association with outcome) either prone to develop AUD [53] or showing the propensity to regain control over alcohol intake [54]. Preliminary data suggest that within such subgroups (e.g., young adults with and without familial risk), predictors that have been established using mean level analyses vary in their impact on the development and maintenance of AUD depending e.g., on familial risk factors and their interaction with alterations in the reward system [55]. Accordingly, it is possible to explore the effects of heritable vulnerability factors on key neurobiological mechanisms including sensitization towards drug cues and habitization of alcohol intake. Specifically, this approach allows assessing the interactions with polygenic risk scores for AUD [56], externalizing disorders [57], and stress sensitivity [58].

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Compliance with Ethical Standards

Conflict of Interest  Dr. Banaschewski served in an advisory or consultancy role for Lundbeck, Medice, Neurim Pharmaceuticals, Oberberg GmbH, Shire, and Infectopharm. He received conference support or speaker’s fee by Lilly, Medice, and Shire. He received royalties from Hogrefe, Kohlhammer, CIP Medien, Oxford University Press; the present work is unrelated to these relationships. Dr. Ulrike Kluge received royalties from Elsevier and Psychiatrie Verlag; the present work is unrelated to these relationships. Dr. Michael Rapp received personal fees from Arbuma GmbH, personal fees from Philips GmbH, personal fees from Deutschlandfunk (National Radio Station), personal fees from Quakenbrück Hospital, grants from German Research Foundation, grants from BMBF (German Ministry for Education and Research), grants from

Table 1 Psychosocial predictors for alcohol consumption for different age groups

| Potential predictors of changes | Adolescent and young adults | Early middle-aged adults | Late middle-aged adults |
|--------------------------------|-----------------------------|-------------------------|------------------------|
| Social interaction             | Mood                        | Social isolation        |
| Inhibitory control versus impulsive decision-making | Marital status              | Executive functions     |
| Externalizing personality traits | Socioeconomic status        | Anxiety/depressivity    |
| Anxiety/depressivity           | Life stress                 |                         |
|                                | Childhood adversity         |                         |
| Potential triggers             | Stress                      | Stress                  |
| Stress                         | Cue responsivity            | Cue responsivity        |
| Priming dose                   | Life events (e.g., romantic love) | Role transitions |
| Life events (e.g., romantic love) | Co-substance use           | Co-substance use        |
| Covariates                     | Gender                      | Gender                  |
| Co-substance use               |                             |                         |
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Human and Animal Rights and Informed Consent  This article does not contain any studies with human or animal subjects performed by any of the authors.

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