Minireview Article

Effects of alcohol on the developing brain: the adolescent at risk

Abstract

Adolescence is a phase of great physical, emotional and social transformations that put individuals in vulnerability and with risks of aggravations that can be definitive. Among the various characteristics of the adolescent, the experimentation of new sensations and challenges is one of the most outstanding, being responsible for several common problems in this phase of life. Among the several factors that can adversely affect adolescents, alcohol is one of the most prevalent, offering serious immediate and late risks. This article presents some characteristics of alcohol consumption among adolescents and the effects on the development of the central nervous system, highlighting the main damages that can be caused in the brain in formation (reduced white matter volume and cortices, neuronal apoptosis, demyelination). In view of the relevance of the effects of alcohol on the developing brain all efforts should be directed towards avoiding or minimizing the risks to which adolescents are subject. It also presents some measures that can be with the aim of preventing the consumption of alcohol among adolescents.

Keywords: adolescent - alcohol – alcohol consume – binge drinking – alcohol dependence – adolescente drinking – alcohol use consequences – risky drinking

Introduction

In whole world more than two billion people are regular consumers of alcohol wich makes it the most widely consumed recreational drug being that the use of alcohol and its adverse health and social consequences among early adolescents have become of increasing interest on the global stage [1]. Alcohol is the most commonly consumed substance among youth with 37% of 18-years old endorsing use and most than 24% reporting being drunk in the past month [2].

In recent years, with the emergence of new research techniques through magnetic resonance imaging, several studies have been completed focusing various brains regions, allowing a deeper understanding of the deleterious effects of various substances on the central nervous system [3].

Alcohol is a licit drug. Its consumption is sanctioned by social practices and cultural norms and the use tipically begins in adolescence as a rite of passage and a proff of maturation, from their former childhood and ongoing process of becoming adults, helping to explain, comfort and strengthen the transformations not yet understood by adolescents. However, the impact on brain development results in interference in social adjustment, delays the development of their abilities and can cause definitive damage [4,5].

Alcohol is the substance of choise among early adolescentes and is highly correlated with a range of other risky behaviors (low school performance, unsafe sexually activity, illicit substance use and, driving chashes). Adolescence is a time of experimenting with various behaviors due to the characteristics of this phase of life, such as curiosity and the search for immediate pleasure, which leads to the search for new sensations [6]. Adolescence to young adulthood is a window of vulnerability in the context of alcohol and substance misuse.

Adolescence

Adolescence is characterized by a period of developmental physical, emotional and social transformations, significant increases in physical size and appearance,

confrontation with issues of personal, ethnic, and sexual identity, renegotiating relationships with parents toward a greater acceptance of personal autonomy, becoming more peer involved and influenced, initiating and maintaining dating relationships [7].

This phase of life is a period of developmental transition, comprising physical, mental, emotional, and social aspects. The development of both physical and interpersonal skills required to successfully integrate into society is essential for living in groups, and these skills improve through adolescence to adult levels. Adolescence in humans and other social animals is characterized by high expression of risk taking, exploration, novelty and sensation seeking, social interaction, and play behavior that contributes to this transition. Is a period of great vulnerability with an enhanced taste for risk associated to impulsive actions and decisions that can lead to serious consequences, including unintentional (car crashes, drowning, falls) and intentional injuries (domestic violence, sexual assault, firearms injuries). All these characteristics are linked, mainly, to transformations and maturation of brain structure [8].

Alcohol

Alcohol is classified as a sedative hypnotic drug which has having in its structure one or more hydroxyl groups attached to saturated carbons. Ethanol, known as ethyl alcohol, is the most common type of alcohol, is soluble in water and in lipids, contained in alcoholic beverages, which is formed by the anaerobic fermentation of the sugar [9].

After ingestion alcohol is absorbed, by simple diffusion, in smaller scale by the stomach than by the small intestine (80%), not requiring digestion, reaching peaks of blood concentration between 30 to 90 minutes. The alcohol concentration in the body is proportional to the amount of water in each tissue, which explains its greater presence in the blood than in other structures [10].

The metabolism of alcohol is performed in the liver through two main oxidative processes: 1) the action of alcoholic dehydrogenase and 2) the microsomal oxidation system of ethanol, that transform the alcohol into acetaldehyde and acetic acid. Acetaldehyde is the main by-product that contributes to tissue damage, alcohol dependence and addiction. Oxidation of etanol leads to the formation of reactive

oxygen species that can cause various harmful processes (inflammation, atherosclerosis, cancer, etc). At most 10% of the amount of alcohol ingested is unchanged in the urine, saliva, sweat, and expired air [11].

The rate of alcohol metabolism can be increased by the simultaneous metabolism of sugars, whereas fasting and starvation states reduce this rate of metabolization. Body size, percentage of body weight composed of water and activity of alcohol deydrogenase also interfere with these processes. Males and females differ in sensitivity to alcohol and these differences become generally more pronounced with sexual maturation in adolescence and into adulthood. In female sex the activity of alcoholic dehydrogenase is slower [12].

Ethanol is a small molecule that easily cross the plasmatic membrane and diffuse rapidly, affecting brains tissues, interefing with neuronal communication and depressing the neuronal activity of excitatory synapses including the serotonergic, opioid, cholinergic, dopaminergic and gamma-aminobutiric acid systems [13].

The velocity of alcohol ingest is very importante since adolescents often drink high amounts in a short time, including a quick rise in the etanol blood levels [14], and triggers adverse effects on the CNS, wich can remain overtime [15].

Adolescents experience several physiological symptoms the day after excessive alcohol consumption, even when blood alcohol levels have returned to zero [14]. These simptoms are commonly know as a "hangover" which is characterized by a headache, nausea, fatigue, muscular pain, and decresead physical and mental abilities [16]. However, these physical symptoms disappear approximately 24 hours later, and adolescents are then willing to drink again [17].

Nowadays, alcohol consumption in adolescents has another purpose: to get drunk fast to have fun [18,19]. This characteristic pattern of alcohol consumption among adolescents is known as "binge-drinking" which is defined by a pattern of drinking that brings blood alcohol concentration levels to 0,08g/dL or at least five drinks for male and at least four drinks for females on the same occasion (in a period of 2 hours) [20].

Therefore, alcohol consumption by adolescents presents three important characteristics that should be considered when studying the effects of this substance on the central nervous system: early onset, very high consumption peaks and intermittency [21].

Adolescent brain evolution

Adolescence is a period of accelerated brain and cognitive development which comprises high risk taking, sensation seeking and impulsivity, because subcortical structure matures more quickly than the prefrontal control regions [22]. The asynchrony between maturation of the different structures and functions predisposes the adolescent brain to develop differently according to the different stimuli and factors with which it interacts, causing changes that may be definitive [23].

The major modifications that occur during the development of the adolescent's nervous system are a decline in the number of excitatory synapses in some brain regions as well as in gray matter volume within the cortex and some subcortical regions; continued maturation of axons and de development of myelin, and increasing white matter synaptic pruning [7,24].

Although overall brain size achieves its peak in early childhood, maturational changes in brain cortical volume, axonal growth, and refinement of cortical connections (e.g., via synaptic "pruning") continue, especially with regard to the limbic system, including the amygdala and the prefrontal cortex. These brain systems are involved in a broad range of cognitive, affective, and behavioral processes (e.g., learning, decision making, impulsivity) that, in turn, influence alcohol use and other co-occurring problems (e.g. risky sexual behavior) [25,26].

Subcortical limbic structures, such the amygdala and hippocampus mature during adolescence. Prefrontal cortex is the last structure to mature; white matter structures mature hierarchically and become more organized; mielin increases efficient neural transmission with processin speed and congnitive function [3,27-29]. The prefrontal area of the brain, which undergoes the most change during adolescence, plays an important role in the formation of adult personality and behavior and is the second area most affected by alcohol abuse [30]. This brain region is related to the planning of complex behaviors and thoughts, personality expression, decision making and modulation of social behavior [31].

With regard to the maturation of the brain, important developmental asynchronies exist between some earlier developing limbic and affective portions of the brain relative to the later developing prefrontal cortex. This is significant because in earlier

adolescence, the affective portions of the brain may be more dominant with respect to behavioral responses, including the immediate rewarding aspects of alcohol use, whereas the brain functions associated with the prefrontal cortex that involve higher cognitive processing related to executive functioning (e.g., planning, goal setting, inhibitory control), decision making, and cognitive-affective behavioral regulation still are developing [32,33].

Adolescent have a great sensitivity to the rewarding features, and less experience of the negative aspects. Cerebral white matter is a primary site of alcohol-associated brain damage. White matter provides the structural foundation for the complex connections that run throughout the human brain. Cerebral white matter constitutes the complex connecting network that carries information between brain regions. The integrity of the components comprising the cerebral white matter is therefore essential to normal functioning of the brain [34].

An increased activation in reward sensitive areas of the brain contributes to adolescents seeking, or being highly motivated to pursue, appetitive rewards (e.g., alcohol) [35,36]. Hence, the existing neuroscience literature is contributing to a more nuanced understanding of why adolescence is a unique period of development and is identifying cognitive (e.g., impulsive decision making) and affective (e.g., heightened reactivity) mechanisms that may serve as targets for intervention and/or provide clarity for components of intervention programs [5].

Effects of alcohol on the central nervous system

Adolescent alcohol exposure causes widespread and persistente changes in neurotrophic, neuroimmune, and epigeneti pathwys in the brain, manifested by altered synaptic remodeling and neurogenesis [37].

Several studies have shown that alcohol drinking in adolescence alters brain plasticity, and causes structural and functional changes by means of neuroinflammation in specialized proteins, oxidative stress, and neurodegeneration that result in cognitive and behavioral deficits. The cerebral cortex, limbic system and cerebellum are the structures more vulnerable to effects of alcohol use, and acetaldehyde is the main responsible for the severe damage observed in neuronal cells [25,38,39]. It has been shown that neurogenesis during this critical developmental

stage of brain maturation is potently inhibited by etanol, that exerts long-term effects on the brain stress circuits [40].

Alcohol interacts with almost all brain neurotransmitter systems in diferente ways and produces two main problems in the central nervous system: 1) irreparable damage to brain cells [17], and 2) the risk for developing pathologies associated with alcohol consume [41].

There are substantial changes in brain structure due to etanol-induced defects in angiogenesis, and hypoxic suppression of cortical activity; neuroapoptosis through an innibition of the physiological activity, innibition of receptors and voltage-dependent calcium channels; potentiation of GABA receptors and increases quantal GABA release for interneurons [7,24,42]. Other changes may also be observed such as: reduce white matter volume and integrity in the prefrontal cortex (prefrontal cortex, the more evolutionarily advanced part of the brain, continue to be myelinated though adolescence and even into young adulthood), reduced hippocampus size, smaller cerebelar volume, reduced cortices in all lobes, neuronal apoptosis, increased rates of gray matter volume loss in the cortical lateral prefrontal and temporal regions, decresead rates of white matter growth in the corpus callosum and demyelination [43-46].

During adolescence, there has been substantial interest in relating changes in the development of brain activation to cognitive and behavioral change. In general, the subcortical limbic system is considered especially sensitive to activation in early adolescence and perhaps related to the early and average increase of adolescence in the search for sensations. Women appear to be more sensitive to alcohol-induced effects and have more cognitive impairment in some functions [30,34,47,48]. Alcohol exposure during the second decade of life was also found to alter adult hypothalamic-pituitary-adrenal axias responsiveness with changes in adrenergic brain stem nuclei involved in stress responses [49].

The main changes that occur in adolescents caused by alcohol consumption are: deficits in attention, memory and visuospatial function; impaired immediate visual and working memory; deleterious effect on a range of learning, recall and recognition measures; heightened emotional reactivity; poor distress tolerance, and predisposition to dependence on other drugs [3,17,24,28,50,51].

Table 1 presents the main changes that alcohol can cause in brain development (modified from [2]).

Table 1. Summary of alcohol damages in adolescente brain development

Brain structure	Brain functioning	Neuropsychological testing
Impair: white matter integrity; accelerated decreases in gray matter frontal and temporal; attenuated white matter development	Increases activation during inhibition and working memory	Impair: working memory; verbal learning and memory; psychomotor speed; visuospatial functioning

Why does the adolescent start to consume alcohol

Drinking among adolescents is less frequent than adults, but the amount consumed per occasion is considerably more [5]. In recent years it has been observed that alcohol consumption among adolescents has been started earlier and that alcohol tasting occurs in the family context, with the approval of parents. Such attitudes demonstrate that there is parental approval and a familiar model of behavior that will be absorbed and incorporated into adolescents' lives [30]. In addition, many authors have identified several other reasons highlighted by adolescents, such as [52-55]:
1. genetic contribution; 2. environmental influences by means of advertisements in TV, magazines, sports stadium signs, subway systems; 3. older alcohol-using peers; 4. externalizing disorders; 5. prestigie, sex appeal,"drinking is fun"; 6. reduce stress, tension, pain; 7. feel pleasure; 8. social self-affirmation, and 9. easy acquisition, low cost.

What to do

In the face of all the harm that alcohol can cause to adolescents' health, whether in the present or in their future life, it is fundamental that measures are adopted that can act preventively. In order to do this, it is necessary to seek to involve the family, friends, teachers and all workers in the health and education areas, directing efforts to identify current patterns of use and alcohol-related harms, and problems related to

consumption or after effects use and to assist adolescents to link patterns of consumption with current life style, social or health-related problems [56].

Alcohol ingestion, especially aroud the time of puberty, could sex-specifically increase the risk for later alcohol use disorders by altering normal, steroide-sensitive development of brain regions occurring at the time of use [57].

In order to obtain good results programs must providing credible information about alcohol issues in adolescents, adress scientific data and local norms to ligitimize the message, and to stablish a positive social network with family, peers, and the school [58]. The use of motivational interviewing techniques, selecting and targenting peers leaders, and other social support networks can contribute to this relevant health promotion action. Demystify consumption of alcohol as a rite of passage into adulthood, restricting access from comercial sources and regulating advertising by means of social midianand digital communication have been considered as targets to reduce alcohol-related harms [59].

Conclusion

The health, social and economics consequences related to the consumption of alcohol are a global concern and people that start drinking during adolescence are more likely to be become an alcohol dependent person during the adulthood [20,60]. Alcohol involvement in adolescence is a multifactorial phenomenon that leads to a psychological dysregulation, that is, a deficiency in the ability to regulate attention, emotions, and behavior in response to environmental challenges [5].The developing brain increases the propensity for adolescents to engage in risk-taking and to seek new experiences, including alcohol use. Therefore, preventive efforts might be directed towards limiting access to harmful risk-taking situations and to stimulate alcohol-free social contexts that minimize change by harm.

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