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## Does excessive alcohol consumption contribute to the development of anxiety disorder?

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## ABSTRACT

### Introduction

Over past decades the number of patients suffering from psychiatric disorders all around the world is constantly increasing. Thank to general awareness and less stigmatization people seek for specialist's help more willingly. Recently, one of the most common diagnoses has been anxiety disorder and many of them also tend to abuse alcohol. So far, scientists have focused mostly on alcoholism as a consequence of anxiety disorder, due to patients' predilection to addictions. However, ethanol can also trigger anxiety itself.

### Aim of the study

The aim of this study is to summarize the current state of knowledge on the role of alcohol in anxiety disorder development and its pathomechanisms.

### Material and methods

This article is based on available publications in Pubmed and Google Scholar databases.

### Conclusions

Excessive alcohol consumption may lead to the development of anxiety disorder in some patients, as well as, many other psychiatric disturbances. However, further research must be done to find out precise pathomechanism responsible for those states.

Key words: anxiety disorder, alcohol

## Introduction

Excessive consumption of ethyl alcohol has become a social and health problem, especially in many developed countries all around the world. Violence, low productivity, child neglect, psychiatric disturbances as well as long term problems as addiction or organs failure are just a few after-effects of alcohol abuse [2]. In Poland around 12% of working age population meet the criteria of Alcohol Use Disorder (AUD) [3]. On the other hand, population suffering from psychiatric problems is still increasing. Anxiety disorder is a persistent mental disorder related to the feeling of worry, anxiety and panic that interfere with daily activities, is difficult to control and is disproportionate to the actual situation. [4]. According to the American Psychiatric Association there are few different types of Anxiety Disorders, such as Generalized Anxiety Disorder, Panic Disorder, Phobias, Agoraphobia, Social Anxiety Disorder (previously called social phobia) and Separation Anxiety Disorder [5]. Recent studies show that there might be a correlation between lifelong anxiety disorders and AUD. Although, finding correlation between alcohol and anxiety seems to be very complex. A following article is a review of current knowledge relate do coexistence of both disease entities.

## How alcohol affect the brain?

Even though, up to 10% of alcohol is eliminated from the body with lungs, sweat and urine the rest is metabolized to acetaldehyde by alcohol dehydrogenase (ADH) [6]. ADH is one of ethanol's direct target. As a consequence, alcohol concentration in blood decrease about 4-5 mmol/L ethanol per h. Then, acetaldehyde is converted to carbon dioxide and water with aldehyde dehydrogenase (ALDH). Some variants of ADH genes (ADH1B\*2 and ADH1C\*1) contributes to more rapid metabolism of alcohol and faster production of acetaldehyde. [7]. Despite fast metabolism, even low doses of alcohol have sedating effects which is related to enhancing activity in the inhibitory systems [8]. This mechanism leads to muscle relaxation, somnolence and intoxicated feelings. Development of ethanol tolerance leads to increased activity of  $\gamma$ -aminobutyric acid and increased stimulating activity of glutamate N-methyl-D-aspartate receptor system that leads to insomnia and anxiety [9]. Furthermore, drinking causes release of such substances as dopamine (rewarding neurotransmitter), serotonin, opioid peptides (endorphins), that all contribute to craving and disinhibition during intoxication [6,10,11].

Moreover, it has an impact on the proteins involved in excitatory and inhibitory synaptic transmission, it enhances cys-loop ligand-gated ion channels (LGICs) such as GABAA and glycine receptors (GlyRs) and inhibits glutamate receptors [12,13]. GABAA, an inhibitory neurotransmitter, when stimulated by alcohol is the cause of ethanol's depressive effects. Potentiation of GlyRs has been found in several brain regions and contributes to changes in behavior [14,15,16]. Knowing mechanisms of ethanol we can explain not only acute ethanol-related behavioral changes but also chronic changes such as psychiatric ones [16].

## Alcohol's impact on anxiety

Research has shown that up to 50% people who are under treatment for alcohol-dependence also met diagnostic criteria for anxiety disorders. [17,18]. It is established that alcohol is a stressor. It activates the hypothalamic-pituitary-adrenocortical axis (HPA) which is a major neuroendocrine stress factor. [19]. Consequently, neurons of the hypothalamus are stimulated which leads to release of corticotropin-releasing factor (CRF), vasopressin and adrenocorticotropic hormone (ACTH).[20]. Studies in rodents conducted in the XXth century have shown that chronic alcohol consumption leads to elevated blood levels of corticosteroids, known as stress hormones. [21,22]. At the same time, chronic alcohol consumption may result in persistent changes in HPA neuroendocrine function which activate independent stress processes in the brain, outside the HPA [23]. Stress reactions are controlled by HPA. If all the stress processes are out of HPA, the patients have behavioral and psychological changes. There is large evidence that changes in CRF function without neuroendocrine function may cause stress, dysphoria and anxiety. [24]

Another system engaged in chronic alcohol and stress is the DYN/KOR system. Dynorphins (DYN) are peptides that bind to kappa opioid receptors (KOR). As DYN bind with receptors, signaling cascades are initiated. [25,26]. As well as CRF, KOR has been shown to produce dysmorphic effects, anxiety and depression. [27]

Another research has shown that adolescents with alcohol use in the past have weaker cognitive functions in comparison to abstinent adolescents. They tend to make risky decisions, their memory and executive function are worse, they present poorer arithmetic, deficits in attentional function and verbal memory. [28,29, 30,]. Moreover, variety tests in rodents have proved that later anxiety-like behavior after alcohol exposure is significantly increased. What is interesting, a study on rats exposed to alcohol during adolescence entering the dark, unlit compartment spent there more time comparing to rats that weren't exposed to alcohol. [31,32,33]. That shows depressive impact of alcohol.

So far, many studies proved clear tendencies to abusing alcohol in a group of patients with depression or anxiety disorder, which are much than in a control group. [3,5,34] According to the National Co-morbidity Study, lifetime prevalence rates of AUD among patients with social anxiety disorder were 24% compared to a group

without anxiety disorder where it rated 14,19% [35]. It means, that alcohol abuse is a consequence of anxiety disorder. However, no reliable research towards proving that anxiety disorder develop as a result of ethanol consumption has been done.

### Summary

Alcohol abuse and anxiety disorder often coexist making patients daily life tough. Both conditions are a serious problem worldwide and they still seem to be hard to treat. So far, scientists have believed that high consumption of alcohol is rather a consequence of poor mental health of patients with anxiety disorder rather than a cause. Taking into consideration the latest analysis it became noticeable that chronic alcohol exposure lowers the quality of many cognitive functions and may be a trigger point in anxiety disorder development. Proving that could help avoiding mental problems by proper treatment of AUD. This field of medicine is unexplored and further research must be done.

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