ALCOHOL AND HEALTH

ALCOHOL, ALZHEIMER'S DISEASE, AND OTHER NEUROCOGNITIVE DISORDERS

Éduc alcool

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INTRODUCTION

In 1817, a British surgeon named James Parkinson published the first description of a disease that appeared to have a serious impact on the motor function of those who suffered from it. Severe tremors, slowed movement and difficulty walking were the primary symptoms.

Less than a century later, in 1906, German psychiatrist and neurologist Alois Alzheimer hurried to examine the brain of one of his patients, who had suffered from impaired memory and language problems, as well as psychiatric disorders. He described a series of anomalies in the patient's neurons and drew a portrait that would help identify the disease that bears his name.

For some time now, news stories have been exploring the links between alcohol, Alzheimer's disease, Parkinson's disease and other neurocognitive disorders.

"Alcohol protects against Alzheimer's," says one headline. "Red wine slows the development of Alzheimer's," reads another. "Alcohol prevents Alzheimer's," proclaims yet another.

On the other end of the spectrum are articles such as these: "Alcohol abuse multiplies the risk of dementia by three," or "Excessive drinking doubles the risk of Alzheimer's disease," and even "Dementia: frequent drinking increases risk."

Of course, retail alcohol outlets are not pharmacies and alcohol is not a medication. No one should ever consider drinking for health reasons.

But it is important to have accurate information about the impact of alcohol on health. The desire for such information is normal–and healthy.

Nearly three quarters of Quebecers have indicated that they are curious about the relationship between alcohol and health. In response, Éduc'alcool presents this report. The subject is of significant import, and is clearly of growing interest to people as they age.

We hope it will help everyone make the most enlightened decisions about drinking, and convince them, in light of the latest scientific data, that moderation is always in good taste.

ABOUT NEURODEGENERATIVE DISEASES

Alzheimer's and Parkinson's are among the best-known neurodegenerative diseases. In both cases, certain brain cells, primarily neurons, deteriorate progressively and cease to function properly. As a result, some regions of the brain can atrophy and cause death.

Aside from their similarity in terms of neuronal destruction, however, the two diseases are very different. Alzheimer's belongs to a family of diseases called neurocognitive disorders. In 2013, the DSM-5[1] used by all psychiatrists and psychologists in North America replaced the term "dementia" by major neurocognitive disorder and mild neurocognitive disorder. These are diseases characterized by a decline with regard to memory, cognitive processing, and the adequate execution of acts of daily living. The losses are more severe than the cognitive decline normally observed as people age, and they cannot be explained by another mental disorder.

Parkinson's, on the other hand, is characterized primarily by a loss of motor capacity. The most common symptoms are severe tremors, muscle stiffness and loss of balance. The disease results from a drop in the production of dopamine, a neurotransmitter that plays an important role in those regions of the brain involved in voluntary movement. Parkinson's is sometimes, but not necessarily, accompanied by varying degrees of neurocognitive disorders.

[1] The fifth version of the Diagnostic and Statistical Manual of Mental Disorders
https://en.wikipedia.org/wiki/DSM-5

The biochemical causes of Alzheimer's

There are a number of factors that can lead to neurocognitive disorders such as Alzheimer's:[2]

1. The accumulation of beta-amyloid cells in the brain, which causes the formation of plaques that interfere with the normal functioning of neural networks;
2. The deterioration of tau proteins, which are involved in transporting nutrients that neurons need;
3. The chronic inflammation of neural networks, caused by an impaired glymphatic system (which is like the brain's immune system);
4. A variety of vascular problems, i.e. related to blood circulation, which may also explain impaired nutrient delivery to the brain.

A genetic component

Several genes are recognized as being linked to the onset of Alzheimer's disease.[3] One of the most critical of these is the one involved in producing apolipoprotein E (APOE). This protein is particularly important in eliminating beta-amyloid cells, which, when they accumulate, can increase the likelihood of Alzheimer's.[4]

As for Parkinson's, most cases occur in people with no apparent history of the disease in their family.[5] However, Parkinson's does occasionally follow a hereditary pattern marked by autosomal dominant or recessive transmission, depending on the gene. Autosomal dominant transmission means the genetic code that puts someone at risk may be transmitted by just one parent. Such is the case for the LRRK2 and SNCA genes. In autosomal recessive transmission, both parents must pass on the genetic code. This is true for the PARK7, PINK1, and PRKN genes.

Neurocognitive disorders induced by alcohol

Among long-time heavy drinkers, a deterioration in the white matter of the brain is observed.[6] The white matter is the tissue composed of nerve fibres that connect different regions of the brain so that they can communicate with each other, like a network of electric wires. The particular regions generally affected are essential for inhibitory control, memory, and coordination between the two hemispheres of the brain. These are the same faculties strongly affected by neurocognitive disorders.

The largest study ever conducted on the subject involved more than 30 million patients hospitalized in France between 2008 and 2013. It found that more than half (about 57%) of the neurocognitive disorders diagnosed in people under 65 were related to abusive drinking.[7] In fact, the risk of developing a neurocognitive disorder is three times higher among people with an alcohol use disorder, compared to those with none.

It is not clear at which point we can conclude with certainty that a neurocognitive disorder is due solely to excessive drinking–as opposed to one that would have arisen in any case, without alcohol. Nonetheless, some researchers suggest that heavy drinking, i.e. more than 35 drinks a week for men and 28 drinks a week for women, over a period of more than five years, is enough to determine that a neurocognitive disorder is due to alcohol.[8]

[2] National Institute on Aging, 2018
[3] Lourida et al., 2019
[4] Lui et al., 2013
[5] Genetics Home Reference, 2020
[6] Harper, 2009
[7] Schwarzinger et al., 2018
[8] Oslin et al., 1998

ALZHEIMER'S AND ALCOHOL

The importance of a healthy lifestyle

According to the Alzheimer Society of Canada,[9] moderate drinkers have the lowest risk of developing Alzheimer's disease. Next come non-drinkers and then heavy drinkers. Let's take a look at that.

A healthy lifestyle can help reduce the risk of developing a neurocognitive disorder after the age of 60, even among people who may have a genetic predisposition.[10] "Healthy lifestyle" here means a non-smoker who is physically active, eats a healthy diet and drinks moderately.

However, these results may exclude the risk of early-onset neurocognitive disorders, given that the study sample was limited to people 60 and older. Furthermore, it is important to isolate the impact of drinking on the risk of neurocognitive disorders from other factors, such as smoking and physical inactivity. To do that, we need studies that take these other variables into account. In other words, all other things being equal, what role does alcohol play in the risk of developing a neurocognitive disorder?

[9] Alzheimer Society of Canada, 2018
[10] Lourida et al., 2019
[11] Mukumal et al., 2003
[12] Anstey, 2009

A closer look at alcohol

To answer the question, a study[11] of 393 patients with neurocognitive disorders and compared them to a group of the same size without neurocognitive disorders. Taking multiple factors into account (specifically, smoking, education and socioeconomic status, and various cardiovascular diseases), they determined that people who had between one and seven drinks a week were the only ones who displayed a lower risk for neurocognitive disorders than longtime non-drinkers. In terms of risk, this group of moderate drinkers was followed by those who had an average of less than one drink a week, and then those who had seven to 13 drinks a week. Life-long non-drinkers were further down the list: their risk factor was lower only than for those who had more than 14 drinks a week. The same trends were observed when Alzheimer's alone was analyzed.

When various studies on the subject are combined, a similar picture emerges. A meta-analysis of 15 studies[12] found that moderate drinking among older people was associated with a reduced risk of developing a neurocognitive disorder. More specifically, the risk was reduced by 28% for Alzheimer's, 25% for vascular dementia, and 26% for all neurocognitive disorders. With regard to Alzheimer's in particular, the effect is more pronounced among men than among women (a risk reduction of 42%, compared to 17%).

Moderate drinking

The definition of moderate drinking varies according to the different studies, with a maximum between 13 and 27 drinks per week. Note that Éduc'alcool currently recommends a maximum of 10 drinks a week for women and 15 for men.

The results shown above should be interpreted with caution, since it is not clear whether the protective effect of alcohol appears among people who have drunk moderately all their lives, or those who began drinking moderately later in life. We may simply infer that moderate drinking among older people could be linked to a reduced risk for Alzheimer's and other types of neurocognitive disorders.

Also, a fair comparison of moderate drinkers and non-drinkers should exclude former drinkers from the latter group. Given that a not-insignificant number of former drinkers stopped drinking because of health issues, including them among the non-drinkers would artificially increase the risk of disease for the abstainers.

It turns out that the observations about the connection between moderate drinking and the risk of neurocognitive disorders stay the same, even when former drinkers are excluded from the non-drinker category. And yet, a number of studies have failed to make the distinction. Thus, it is possible that the protective effect observed may, in reality, be less pronounced than is being generally reported in the scientific literature.

Once first symptoms appear…

A study[13] followed 360 patients presenting with symptoms of Alzheimer's disease. Some were monitored twice a year over more than 19 years. Their cognitive capacity was assessed each time, as was their alcohol intake. The study results suggest that people who had more than one drink a day showed increased cognitive loss, compared to those who had just one drink a day and those who did not drink at all. There was no difference between the latter two groups. The harmful effect was particularly pronounced among those who drank spirits.

Another study[14] was conducted, this one involving more than 3,000 people in the United States. They noted that the effects of alcohol on the risk of neurocognitive disorders differed depending on the base level of cognitive impairment: the beneficial effects of moderate drinking were observable only among people whose cognitive capacity was not yet impaired.

Taken together, these results suggest that, even if their risk is no higher, moderate drinkers lose their advantage over non-drinkers when the first symptoms of a neurocognitive disorder have already appeared.

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[13] Heymann, 2016
[14] Koch et al., 2019

PARKINSON'S AND ALCOHOL

Unfortunately, an analysis of all the scientific research on the link between alcohol and the risk of developing Parkinson's disease, conducted between the years 2000 and 2014, shows little consensus among researchers.[15] Unlike other diseases, Parkinson's has been the subject of very few studies, and most of them have methodological flaws.

More recently, researchers from Harvard and Oxford universities conducted the only study[16] that distinguished drinkers in terms of their consumption: light, moderate and heavy. This study of more than a million women in Great Britain found no link between drinking and the incidence of Parkinson's. Nor was any difference observed between the different types of alcohol consumed.

OTHER IMPACTS OF HEAVY DRINKING ON THE BRAIN

Wernicke-Korsakoff syndrome

Wernicke's encephalopathy and Korsakoff's psychosis are two brain disorders in which cognitive capacity, including memory, is affected, often permanently. If diagnosed early and treated properly, the disease may be reversible. When both disorders occur at the same time, they are given the name Wernicke-Korsakoff syndrome (WKS).

The primary cause of WKS is a thiamine (vitamin B1) deficiency.[17] In developed countries, where people generally eat a balanced diet, the disease occurs primarily among regular heavy drinkers. This suggests that the interaction between alcohol and thiamine is linked to WKS.

Cerebellar atrophy

Autopsies have shown that as many as 42% of longtime heavy drinkers suffer from cerebellar atrophy,[18] a medical condition in which the cells of the cerebellum (the more primitive part of the brain) are damaged and cease functioning. This generally occurs after more than ten years of abusive drinking.[19] Because one of the cerebellum's primary functions is maintaining balance and muscle coordination, cerebellar atrophy manifests as a loss of coordination and difficulty walking. Like WKS, this problem is also attributed to a thiamine deficiency.

[15] National Institute on Aging, 2018
[16] Kim et al., 2019
[17] Lourida et al., 2019
[18] Harper, 2009
[19] Schwarzinger et al., 2018

HOW IT ALL WORKS

Protective effect ❶
Activation of the immune system

The brain has its own separate immune system, known as the glymphatic system, which is activated primarily during sleep.[20] Studies with lab rats have shown that small quantities of alcohol allowed the glymphatic system to be activated even when the animals were awake.[21] It is possible that the glymphatic system is activated specifically in order to eliminate alcohol, and in the process, other molecules that may be toxic to the brain are also eliminated.

[20] Jessen et al., 2015
[21] Lundgaard et al., 2018

Protective effect ❷
Easier elimination of neuronal debris

Small amounts of alcohol may play an important role in the elimination of waste from the brain, specifically because of alcohol's vasodilation effect, which allows larger toxic molecules to leave the brain.[22]

Both processes noted above would help eliminate beta-amyloid cells, which, in excessive numbers, can impair brain function.

[22] Cheng et al., 2019

Harmful effect 1

Inflammation and beta-amyloid cells

When beta-amyloid cells accumulate, they turn into plaques that impair brain function. This activates the brain's immune system to get rid of the harmful cells, and that creates areas of inflammation around the toxic plaques. For various reasons, the glymphatic system sometimes fails to remove all the plaques, resulting in constant inflammation in certain parts of the brain. By creating even more congestion between neurons, the combination of amyloid plaques and inflammation further impairs the proper functioning of neuronal connections.

In addition, while the information comes from a study using rats,[23] an excessive amount of alcohol may prevent the expression of genes that produce glial cells, which play a critical role in maintaining the central nervous system and eliminating beta-amyloid cells.

Harmful effect 2

Thiamine deficiency

Heavy drinkers tend to have low levels of thiamine.[24] Even if this were due simply to the poor dietary habits of heavy drinkers,[25] some biochemical functions may explain how too much alcohol could cause thiamine levels to drop.

Many researchers agree that alcohol interferes directly with the delivery of thiamine to the body through the walls of the digestive system,[26] but the harmful impact of alcohol can also be less direct. For example, the body needs a certain amount of magnesium to make best use of the thiamine available. But heavy drinking causes magnesium levels to drop.[27] Thus, alcohol interferes with the adequate processing of thiamine.

Interestingly, a study in Taiwan found that heavy drinkers who took thiamine supplements had a reduced risk of neurocognitive disorders.[28] Considering all these factors, it may well be that thiamine plays a significant role in the onset of neurodegenerative diseases.

[23] Kalinin et al., 2018

[24] Martin et al., 2003
[25] Rees et al., 2012
[26] Martin et al., 2003; Subramanya et al., 2010
[27] Rivlin, 1994; Romani, 2008
[28] Chou et al., 2019

THE SPECIFIC CASE OF RED WINE

Some studies have shown that, compared to other types of alcohol, wine can have a beneficial impact on the risk of developing a major neurocognitive disorder.[29] However, these studies have not considered other factors characteristic of individuals who prefer each type of alcohol, such as physical activity and diet. Such variables may well explain some of the results observed.

When studies comparing the effect of different types of alcohol do consider confounding variables (such as the different lifestyles and habits of beer drinkers and wine drinkers), no difference is observed between the different types of alcohol.[30] The so-called "red wine benefit" is generally attributed to resveratrol, a substance found in red wine and grape skins. Some cite studies showing the protective effect of resveratrol with regard to the risk of neurocognitive disorders.[31] However, let's take the study by Sawda et al. (2017) as an example. Participants received resveratrol in doses starting at 500 mg a day. But the average litre of red wine contains less than 1 mg of resveratrol,[32] which means one would have to drink a ridiculous amount of wine (about 500 litres a day) in order to consume the same amount of resveratrol used in the study. More realistically, the antioxidant effect of resveratrol is most likely counterbalanced by the pro-oxidant effect of the 13.45 grams of alcohol in a standard glass of wine.

[29] Truelsen et al., 2002
[30] Ruitenberg et al., 2002
[31] Reale et al., 2020
[32] Weiskirchen et al., 2016

In short

- To minimize the risk of developing a neurocognitive disorder, it's best to
  - stick to the recommended low-risk drinking guidelines
  - avoid smoking
  - be physically active
  - eat a healthy, balanced diet
- Data regarding the effects of different types of alcohol are controversial. While resveratrol seems to have a protective effect when it comes to the risk of neurocognitive disorders, it is not certain that the effect is as pronounced with red wine.
- Once the first symptoms of a neurocognitive disorder appear, the potentially beneficial effects of moderate drinking disappear.
- People who drink heavily on a regular basis should consult a doctor to make sure they are getting an adequate amount of such nutrients as thiamine.

CONCLUSION

There is a fairly clear connection between drinking and neurocognitive disorders, such as Alzheimer's disease.

While we still do not understand completely how these diseases arise, many studies of both humans and laboratory animals indicate possible avenues for exploring how different levels of alcohol consumption can affect the likelihood of developing such diseases.

Studies that separate drinkers according to how much they drink produce occasionally divergent results, sometimes highlighting the protective or neutral impact of drinking on the risk of developing a neurocognitive disorder, and sometimes showing an increase in risk, depending on the amount of alcohol consumed.

Thus, having one to seven drinks a week could prevent neurocognitive disorders, while having eight to 14 drinks a week might be beneficial, but would not, in any case, increase the risk.

On the other hand, heavy drinking beyond the recommended limits does increase the risk of developing a neurocognitive disorder.

In other words, even for the brain, moderation is always in good taste.

DEFINITIONS

Dementia:
A generally irreversible acquired disorder of the mental processes caused by brain disease or injury and marked by memory disorders, personality changes and impaired reasoning. The decline in cognitive abilities is severe enough to impair daily life and independent function.

Meta-analysis:
A statistical analysis that combines the results of multiple independent scientific studies on the same subject in order to determine overall trends.

Neurotransmitter:
A chemical substance that is released at the end of a nerve fiber, allowing nerve cells to send messages to each other.

White matter (of the brain):
Tissue in the brain composed of nerve fibers that connect nerve cells and are covered by myelin (which gives white matter its white color). Myelin speeds up the signals between the cells, enabling the brain cells to send and receive messages quickly.

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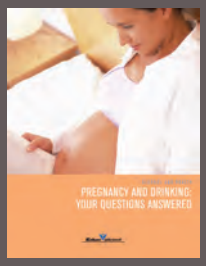

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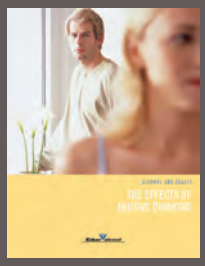

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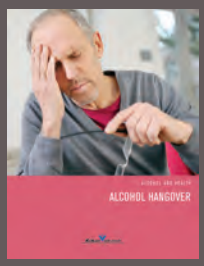

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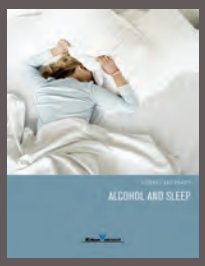

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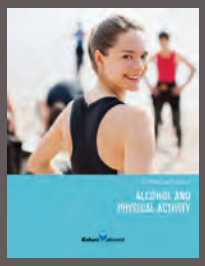

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