

From “Social Drinker” to Addict: How Is the Line Drawn?

By S. Andrei Anghel

Up until recently, this may have been a philosophical question. However, like many other equally complex issues, it has now entered the realm of science. Through careful observation and experimentation, science is making it possible to define alcohol addiction. In one particular study (1), a group of researchers establish both the brain structure and the molecular pathways involved. While this research may eventually lead to the develop-

ment of novel drugs, it also raises some important ethical questions. Though many might prefer to consider alcohol to be either “good” or “bad,” the situation, unfortunately, is more complex. If exercise is considered to be a problem in itself (think caffeine), but it becomes a problem when it leads to consumption of high quantities of alcohol. There is currently very little information on what alcohol addiction actually is and how it develops, so it is usually given a behavioral definition: compulsive alcohol-seeking behavior and a hyperexcitability withdrawal syndrome when deprived of consumption (4). Though the exact mechanism of addiction is not known, it seems that one of the key players is the NMDA receptor (5,6), a brain cell protein present at synapses. However, this same protein is also one of the most widely distributed in the human brain and has also been involved in learning, memory, epilepsy and schizophrenia (4), so until now it was unclear how relevant this receptor was.

Fortunately, this new study (1) sheds light on the mechanism of alcohol addiction. The authors build upon their previous experiments, in which they had shown that adding alcohol to slices of a particular brain structure (the dorsal striatum) activated a cellular signaling pathway through a particular NMDA receptor (7). The striatum is very important in controlling movement, but also has a crucial role in controlling appetite, sexual behavior, and learning (8).

Their latest study uses administration of alcohol to live rats, first by injection and then by placing a bottle of 20% alcohol (similar to rum) in the cages every other day. In this way, they are able

to show that the previous conclusions based on brain slices hold with live rats. Moreover, two important details emerge. First, a single injection of alcohol is inconsequential – in order to activate the signaling pathway, alcohol must be administered repeatedly. Secondly, the

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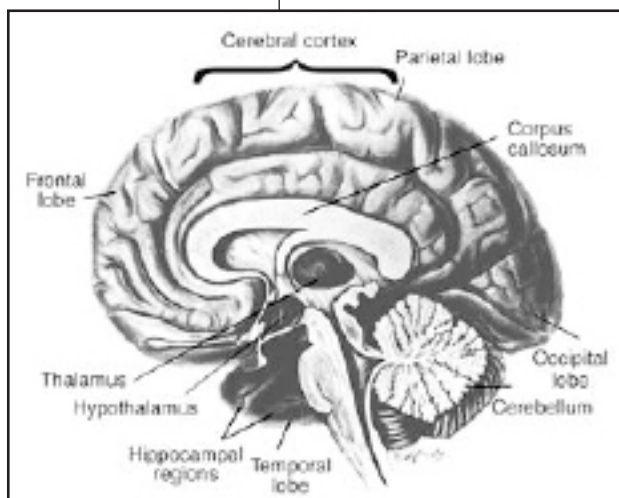
If exercise is

definitely good for you (the more the better, to a limit), and smoking is definitely bad for you (the more the worse) (2), alcohol seems to have a dose-dependent effect. Specifically, when it comes to likelihood of dying, one finds that one drink a day actually makes you live longer, three drinks a day means you’ll live about as long as someone who doesn’t drink at all, and drinking more than three drinks daily means that – on average – you’ll die sooner (3).

The problem with alcohol is that it is chemically addictive. Addiction is generally not

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▲ **Figure 1.** Regions of the brain that have been proven to be sensitive to the effects of alcohol. As can be seen, alcohol affects numerous brain structures.

molecular effects of alcohol persist even after nine days of being “sober.” Thus, activation of the pathway is not simply an effect of alcohol exposure – it might be the molecular signature of addiction. To test this model, the authors inject an inhibitor of the pathway, ifenprodil, into the striatum of rats. This direct inhibition made the “alcoholic” rats seek the “rum” bottle less, meaning that, to a certain extent, ifenprodil injected into the striatum can cure alcoholism in rats. This is not a completely new finding—it had previously been reported that this same drug can inhibit alcohol relapse in rats when administered systemically (9).

What is impressive about this study is how the authors tie together previously known associations into one coherent story: they identify the exact region of the brain where the molecular pathway acts (the dorso-medial striatum), they identify the exact receptor subtype as well as another key component of the signaling pathway, and they show how these are related not to alcohol drinking but to alcohol addiction. Of course, the knowledge of the phenomena involved is not complete and the important details remain to be worked out, but it may be time to start considering therapeutic applications of ifenprodil or similar drugs. Efficiency still needs to be proven in humans and side effects need to be closely investigated. However, it is a start.

This kind of research also raises some interesting ethical questions. If, for example, it were possible to detect activity of this pathway just by drawing blood (currently it isn't), would it be ethical to test if someone is an alcoholic? I, for one, would not want to receive surgery from an alcoholic doctor. However, I would not want my health insurance company telling me I am not eligible for coverage because I have “high NMDA”. Classic considerations of privacy vs. welfare are at the center of this bioethical stage. In my opinion, this kind of testing would be justified only in the most extreme cases when one's health is at risk, such as testing surgeons whose attentiveness and alertness may make the difference between the life or death of patients.

Drunkenness
Is a Disease and
Can be Cured.

It is now a well-known fact to the medical fraternity and the laity, that Drunkenness is a disease of the entire nervous system, and it is curable, the same as any other malady.

We have at very great expense, discovered a SURE and INFALLIBLE cure for this curse, having found it by many years of constant study and research. This treatment is not to be compared with the worthless quack cures advertised at so much per package, or "Free," &c. It is a different matter from all this to perfect a course of thorough, special treatment that

WILL REALLY DO THE WORK AND CURE

forever. This remedy can be given with or without the knowledge of the patient, and can be placed in any food or liquids that the person uses. It is PERFECTLY HARMLESS.

But how about the case where a doctor has two patients waiting for a liver transplant and only one liver is available? An alcoholic is a bad candidate for a liver transplant, so one may say the doctor has the right to perform the test to discriminate rationally. However, if in light of this evidence we can consider alcoholism a disease like any other, is it reasonable to sentence someone to death because of his illness?

Science is the most objective form of inquiry ever developed. Its conclusions are safe from ethical debate. However, we must never forget that the applications of science are not quite as objective. To repress knowledge is not an option, so how to properly apply new information it is an ever-lingering quest of the scientific community. **H**

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◀ **Figure 2.** Advertisement for the cure for alcoholism, dating back to 1904. The author claimed that alcoholism is simply a disease of the nervous system and can be cured as such. The author was surely either a misguided person who thought he possessed the cure, or a charlatan. However, after more than 100 years, it seems we might be close to developing such a cure.