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# **"Chronic binge alcohol administration enhances pre-frontal cortex apoptotic signaling in SIV-infected rhesus macaques."**

## Abstract

Over 1.2 million people are infected with HIV in the US, and over 16 million adults suffer from alcohol use disorder. The frequency of heavy alcohol use in individuals living with HIV/AIDS is double that of the general population. Excessive alcohol use increases the rate of HIV-associated neurocognitive disorder (HAND) development. In our model of HIV infection, alcohol unmasks neurocognitive deficits in Simian Immunodeficiency Virus (SIV)-infected macaques. Alcohol and SIV can both increase apoptosis. Caspase-3, BAX, and BCL-2 were investigated in this experiment. These proteins are crucial in the apoptotic pathway; BAX and Caspase-3 are pro-apoptotic proteins whereas BCL-2 is an anti-apoptotic protein. We hypothesize there will be an increase in pro-apoptotic signaling in CBA/SIV infected macaques. An increase in these pro-apoptotic proteins would indicate a higher chance of neurocognitive disorders in subjects that are infected with HIV and abuse alcohol. Rhesus macaques were equipped with an intra-gastric catheter for the infusion of alcohol or sucrose solution on a chronic binge schedule, three months prior to inoculation with SIVmac251. Seven animals were separated into three treatment groups: Chronic Binge Alcohol (CBA) treatment (n=3), sucrose treatment (n=3), and Naïve animals (n=1). Both the CBA and sucrose groups were infected with SIV. Approximately 18 months after infection, the animals were euthanized and tissues from the prefrontal cortex were collected. Western blots were used to determine protein expression of active caspase-3, BAX, and BCL-2. We found that expression for the protein BAX was greater in two of the three CBA/SIV+ macaques, especially compared to the sucrose/SIV+ macaques. These results suggest enhanced apoptotic signaling in chronic binge alcohol-treated SIV-infected macaques.

**Comment [JKM1]:** Make the title a statement. For example "Chronic binge alcohol administration enhances pre-frontal cortex apoptotic signaling in SIV-infected rhesus macaques"

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**Comment [JKM2]:** Alcohol use? Alcohol abuse?

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**Comment [JKM3]:** Make this its own sentence

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**Deleted:** this could be a potential mechanism underlying these neurocognitive deficits.

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**Comment [JKM4]:** Simplify these sentences. We don't need info on cytochrome C in the abstract because we are not investigating it. Can you explain the importance of these proteins in one sentence?

**Comment [JKM5]:** Now that you explained what these proteins do, what is the aim of the experiment? What and why are we doing it? This is where you can make reference to apoptosis being a potential mechanism.

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**Deleted:** and separated into three groups: animals were treated with

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**Comment [JKM6]:** Re-word the descriptions of the groups.

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**Comment [JKM7]:** Play with the wording of this sentence a little bit. It doesn't sound quite right.

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**Investigation of Apoptotic Signaling In Alcohol and SIV Infected Macaque  
Brain Tissue**