

# SYMPTOMS OF ALCOHOL-INDUCED LIVER AND HEART DISEASE IN RATS THAT REGULARLY DRINK ALCOHOL

Alcohol abuse induces liver disease and enlargement of the heart and spleen, but regular alcohol use, at socially acceptable levels, may also cause serious damage. In 2006, a NIDDK project<sup>1</sup> found that rats that drank the equivalent of three standard drinks per day, five days a week had significantly larger livers, spleens and hearts than rats that never drank alcohol. Our aim was to test whether the composition of these organs changed in ways that indicated alcohol-induced liver or heart disease. We used dual energy x-ray analysis to compare mineral composition, fat mass, and muscle mass in the livers, spleens and hearts of eight male Long-Evans rats that never drank alcohol, with the same organs of four, otherwise identically housed and treated, rats that regularly drank alcohol. We found compositional changes that were symptomatic of alcohol-induced liver and heart disease. This suggests that regular alcohol use at socially acceptable levels could lead to similar problems in humans.

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## BACKGROUND

Alcohol abuse is a widespread problem in the United States, with fatal health implications and is a particular problem in the Native American and Hispanic communities.<sup>2</sup> Alcohol abuse is known to cause liver, spleen and cardiovascular problems. It has been suggested, however, that regular but not excessive drinking has health benefits. Our aim was to test whether the composition of the liver, spleen and heart of rats that drank alcohol at a regular but not excessive level, changed in ways that indicated alcohol-induced liver or heart disease.

The liver is responsible for the metabolism of alcohol. The enzyme alcohol dehydrogenase converts ethanol into acetaldehyde, an unstable and toxic substance. The hydrogen produced replaces fatty acids as fuel; this increases the quantity of fatty acids and triglycerides in the liver which leads to alcoholic fatty liver disease.<sup>3</sup> In addition, as the body processes the alcohol, activity in the liver increases, causing the liver to increase in mass.<sup>3</sup>

Alcohol abuse also increases the spleen's activity as it increases the frequency of abnormalities in red blood cells. These abnormal cells are broken down and replaced in the spleen which increases in mass as a result of the increased workload.<sup>4</sup> Splenomegaly, or enlargement of the spleen, is, therefore, also symptomatic of alcohol-induced liver disease.

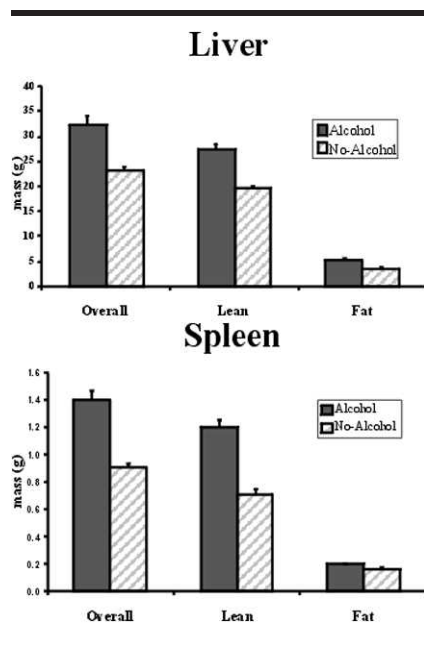
Cardiovascular disease is the leading cause of death in the United States. Alcohol abuse is harmful to the heart as it causes chronic high blood pressure, which in turn leads to hypertrophy of the heart.<sup>5,6</sup> However, moderate alcohol

use may be beneficial to the heart by increasing the ratio of high density lipoprotein to low density lipoprotein. High density lipoprotein helps bring cholesterol in the arteries to the liver to be processed, preventing the arteries from getting clogged.<sup>7</sup> Reduced stress from occasional drinking may also help the heart by decreasing the blood pressure.<sup>7</sup>

## METHODS

Twelve Long-Evans rats were obtained from the University of Alaska Anchorage, Department of Psychology. These rats had all been fed and housed identically. From the age of 3 months they were used in motivational experiments. For this experiment, they were placed in Skinner boxes for 30 minutes, 5 days per week, where they could obtain 3 seconds of access to a reward solution by pressing a lever.<sup>8</sup> For 8 of the rats, the rewards were 10% sucrose (wt/vol) solutions. These rats never drank alcohol and were all 12-months old when they were euthanized. For 4 of the rats, the rewards were 5, 10, 15 or 20% ethanol solutions. The rats usually drank the equivalent for their body weight of 3 standard alcoholic drinks (1 standard drink for a human contains 13.7 g of alcohol, eg 12 oz of beer or 1 shot of spirits<sup>9</sup>) in each 30 minute session.<sup>8</sup> One of these rats was 24-months old when he was euthanized. The other three were 18-months old. The rats were euthanized for reasons unrelated to this project.

The heart, liver and spleen, were dissected and removed from each rat in a consistent manner. Using dual energy x-ray absorptiometry, we measured the

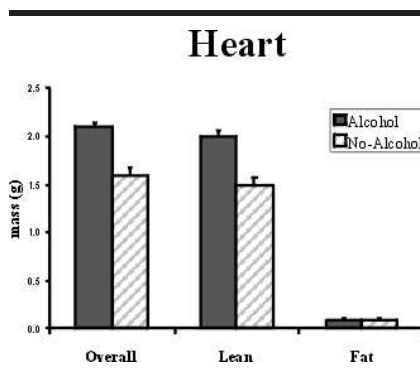


**Fig 1. Effect of alcohol use on the composition of the liver and spleen. Note: Columns show means; bars show standard errors;  $n=4$  for the alcohol treatment;  $n=8$  for no alcohol**

quantity of fat, lean mass and mineral composition (in grams) in the organs and calculated the percentage of fat.<sup>10</sup> We took the mean values for the rats that drank alcohol and for the rats that did not and compared them using a 1 tailed  $t$  test.<sup>11</sup>

## RESULTS

The mean overall, lean and fat mass of the liver and spleen were significantly higher for the rats that drank alcohol than for those that did not ( $P<.05$ ) (Figure 1). The mean fat mass of the liver and spleen was also significantly higher for the rats that drank ( $P<.05$ ) (Figure 1). The percentage of fat did not significantly increase in either organ. Mineral composition was negligible for all samples (0.000 g for all liver and spleen measurements,  $\leq 0.002$  g for all heart measurements). The hearts of rats that drank alcohol were significantly



**Fig 2. Effect of alcohol use on the composition of the heart. Note: Columns show means; bars show standard errors;  $n=4$  for the alcohol treatment;  $n=8$  for no alcohol**

heavier in terms of their overall and lean mass ( $P<.05$ ) (Figure 2). There was, however, no significant difference between the treatment and control groups in terms of the fat mass associated with the heart ( $P>.05$ ) (Figure 2).

## DISCUSSION

Drinking alcohol at regular but not excessive levels increased the mass of the rats' livers, spleens and hearts. Enlargement of the liver and spleen, especially when associated with increased fat levels, is symptomatic of alcohol-induced liver disease.<sup>3</sup> Enlargement of the heart is symptomatic of sustained high blood pressure and cardiac activity.<sup>5,6</sup> The elevated blood pressure is likely to be caused by the regular use of alcohol, though it could also be a side effect of alcohol-induced obesity. Drinking the equivalent of three standard drinks a day on a regular basis appears to have led to both alcohol-induced liver disease and alcohol-related cardiac problems in these rats. This level of alcohol consumption is common and socially acceptable for humans. Given the similarity between rat and human physiology,<sup>12</sup> this level of drinking is likely to increase the risk of liver, spleen and heart damage.

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