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**Reply:**

L.M. Kong

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**Reply:**

I would like to reply to the letter by Basar Sarikaya regarding our published article “Acute Effects of Alcohol on the Human Brain: Diffusion Tensor Imaging Study.”

First, the author of the letter said that it is not clear why we used 2 different software programs for our analysis and at which step and why we switched to the other software. In fact, we performed the analyses only on FuncTool in the AW 4.3 Workstation (GE Healthcare, Milwaukee, Wisconsin) of DTIStudio software (Johns Hopkins University, Baltimore, Maryland), which is capable of coregistration to remove eddy currents and motion artifacts and has excellent means for drawing the ROIs.

Second, was the issue that the placement of ROIs was not clearly explained. In our study, we placed ROIs on anatomic sequences first, and then the same size and shape region of interest was automatically displayed on the ADC and FA maps. We are sorry to say that the region-of-interest size defined as 32 cm<sup>2</sup>, except for the internal capsule for which region-of-interest size was 26 cm<sup>2</sup>, was an error on our part in manuscript preparation. The region-of-interest sizes measured in our images were in square millimeters and not square centimeters.

Third, as to the results in the article by Duning et al (2007), the authors were not able to identify any significant changes in ADC values in the 4 subjects they examined, and, in our study, we found that the sensitivity of different parts of the brain to alcohol was different. The ROIs in some parts of the brain showed significant changes in ADC values, and some did not change after drinking. In our opinion, the different results between the 2 studies are due to the regions of interest of different parts of the brain and individual differences in alcohol clearance of the participants. In our study, to ensure that the alcohol dose received in the study would be within the participants' normal range of experience, we excluded very heavy drinkers. Participants were asked to refrain from any alcohol for 24 hours before their appointment and to eat a light meal 5–6 hours before their appointment.

Fourth, regarding the statement in the conclusion, “DTI has been shown to be more effective in detecting alcohol-induced changes on the human brain compared with BAC (blood alcohol concentration)

or BrAC (breath alcohol concentration),” we found, in both the high- and low-dose groups, that the BrAC was at the highest concentration at 0.5 hours, representing the peak of blood-ethanol concentrations, but the ADC values reached the lowest values at 1 hour post-alcohol administration (Fig 3A, -B, and -E). Significant changes in ADC values in the frontal lobes, thalamus, and middle cerebellar peduncle in our study showed that these areas are more vulnerable to the effects of acute alcohol consumption. Moreover, in our study, when the BrAC descended to 0, we could see that the ADC values in the brain were still lower than those before drinking, which reflects the existence of brain edema. The alterations of blood alcohol content or BrAC cannot directly reflect these changes in brain.

Fifth, the author of the letter said that both studies used alcoholic beverages instead of pure ethanol. Understandably the author's comment is subject to 1 common limitation. In our study, we used Maotai, a kind of Chinese spirits (Chinese spirits have been distilled mainly from fermented cereals). To our knowledge, besides ethanol, other components of Maotai have little CNS effect.

Finally, we agree that better designed studies with a greater number of subjects would yield more information on the acute effects of alcohol on DTI parameters. We believe that some other mechanism is more likely to cause the alterations that could possibly be detected on functional MR imaging. Ethanol has different actions on different neurotransmitter receptors; while it potentiates some, it deactivates the rest. It is very likely that different imaging findings might be encountered, depending on microstructural changes in different parts of the brain. In our other study, we tried to use MR spectroscopy to investigate the change of metabolites in the rat brain after acute alcoholism at 7T MR imaging, and we also used DTI combined with MR spectroscopy in a study of the acute effects of alcohol on the human brain. We have found some interesting microstructural changes in the brain after administering alcohol.

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