RESPONSE

Perez-Reyes and Cook point out a number of methodological differences between their study and ours and suggest that the fact that we used a between-subject rather than a within-subject design accounts for the disparity in the results. Drs. Perez-Reyes and Cook also offer evidence that, despite their precautions, they observed a wide inter-subject variation in measured plasma-ethanol levels. Although we do see some individual variation in plasma-ethanol levels, the range in our subjects is not as extreme as that stated by Drs. Perez-Reyes and Cook. However, there are two possible explanations for this difference. First, we study individuals who fit a rather strict height/weight ratio of between 2.0 and 2.5 cm/kg, so the body water content is likely to be very similar among our subjects. Second, we used a programmed dosing procedure to deliver the ethanol solutions to the subject at a steady rate via a peristaltic pump system. Thus, subjects receive their dose at a precise rate of 23 ml/min. We agree that when subjects have more control over their drinking session, they are likely to consume the solutions at different rates (e.g., "chuggers" versus "sippers") which might result in slight variations in absorption.

However, we believe that the different blood sampling procedures used represent a more important difference between the two studies. In our study (Lukas et al. 1992), blood samples were obtained at 5-minute intervals throughout the study whereas Perez-Reyes et al. (1988) withdrew the first sample 30 minutes after drinking began and at 15-min intervals thereafter. We reported significant reductions in plasma-ethanol levels during a relatively narrow time period after ethanol administration; plasma-ethanol levels after the different marihuana conditions had merged by 70 to 80 minutes after ethanol administration began. In Figure 1 of Perez-Reyes et al. (1988), it appears that the nonsignificant differences in peak values might have been more apparent had the blood been sampled more frequently. The graph in Figure 3 of Perez-Reyes et al. (1988) also shows that ethanol intoxication ratings were 13% lower in the Low Ethanol–Marihuana condition than in the Low Ethanol–Placebo condition. Although the authors stated that these differences were not significant, we noted a similar trend in our subjects.

Finally, the individual data presented by Drs. Perez-Reyes and Cook in Table 1 above demonstrate that *all six* subjects in the low-ethanol dose group who smoked marihuana had *lower* peak blood ethanol levels. The results of a repeated-measures analysis of variance with orthogonal polynomial regression revealed no significant differences. Although this is an appropriate statistical test for a complex interaction study, a paired *t*-test could have been used to test the hypothesis that marihuana does not alter blood-ethanol levels. Using this strategy, the null hypothesis (the mean of the differences between the two treatments is zero) should be rejected ($df = 5$, $t_{0.05} = 3.5$, $p = .0172$). Although the changes in C_{max} in the high-dose ethanol group were equivalent, there is enough margin of error in the sampling procedure (i.e., every 15 minutes) to have missed the real C_{max} values.

We believe that the difference in design (i.e., within- versus between-subject) does not adequately explain the different conclusions, especially in light of the new individual data presented above. Alternatively, we suggest that a rapid blood sampling procedure may be more likely to detect transient alterations in plasma-drug levels during drug interaction studies. It is now recognized that transient changes in gastric motility independent of pyloric patency may significantly affect gastric emptying of ethanol and subsequent ethanol absorption (Korsten and Lieber, 1992). The duration of the marihuana-induced decrease in plasma-ethanol levels is short. However, we believe that even a modest reduction in the plasma levels during the ascending curve may have relevant behavioral consequences. Even though the data from animal studies (Anderson et al. 1974; Shook and Burks 1989) are compelling, we agree with Drs. Perez-Reyes and Cook that further studies are needed to more fully understand the complex interactions of ethanol and marihuana combinations.

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