Response to Dr. Kawada

Garth Swanson, Muneer Rizvydeen, Helen Burgess, and Ali Keshavarzian
Department Digestive Diseases, Rush University Medical Center, Chicago, Illinois

Submitted 26 June 2015; accepted in final form 26 June 2015

TO THE EDITOR: We thank Dr. Kawada for his interest in our recent article (5) and for raising several important issues related to the analysis of actigraphy in alcoholics. First, as noted in his letter we did use the default setting of 40 for sleep/wake sensitivity. We did this to permit comparison with our other studies and with the general literature, which largely tends to use this setting (1). We appreciate this is a topic of concern for Dr. Kawada as he has raised the same concern with others (2). Accordingly, we reanalyzed our data with at the 20 cutoff for sleep/wake sensitivity; we found no significant change in our findings nor in our conclusions made between alcoholic group and our control group.

We also agree age and obesity are important factors in sleep characteristics. Subjects with depression (Beck score of >15) were excluded from this study. As acknowledged in our paper, there were significant differences in age and BMI between the alcoholic group and the control group. We discussed this potential confounder in the DISCUSSION section of our paper and noted this as a potential limitation of our study. Nonetheless, no subjects over 60 were included in the study. Similarly, none of our alcoholic subjects were morbidly obese [BMI > 35]. Thus, although we cannot make any definite conclusions whether age or obesity were important factors in our actigraphy findings, it is unlikely that age and BMI could fully explain the differences we observed.

Finally, while we agree that further study is needed to examine the role of low melatonin secretion correlating with increased intestinal permeability, we disagree that this finding lacks statistical strength. Our data show a statistically significant correlation between melatonin in both small bowel (5-h lactulose/mannitol ratio) and whole gut permeability (24-h sucralose) with a \( P = 0.03 \) and \( P = 0.01 \), respectively. Furthermore, we have previously published how circadian disruption can impact alcohol-induced intestinal permeability in a human intestinal cell line (4) and an environmentally or genetically shifted animal model (3). These human data therefore further support the important role that sleep and circadian disruption may play in the biological and medical consequences of alcoholism, which include increased intestinal permeability and gut-derived inflammation.

REFERENCES