Effects of Oat β-glucan on Non-alcoholic Steatohepatitis Aggravated by Circadian Disruption in C57BL/6J Mice

Abstract No. 91

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Introduction

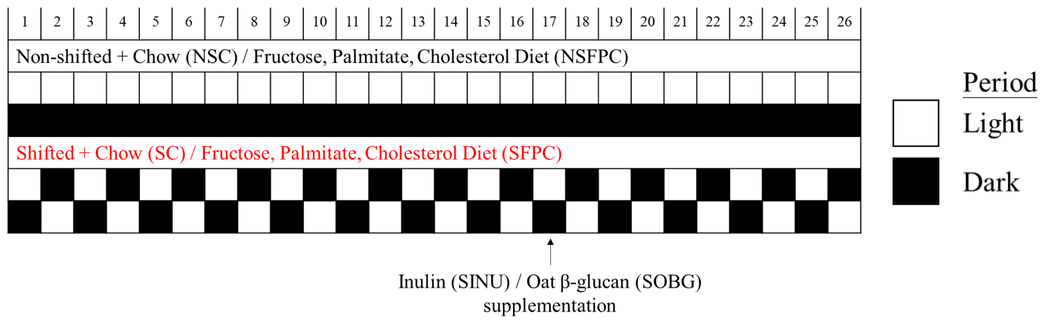
Non-alcoholic steatohepatitis (NASH) is becoming a common cause of chronic liver diseases. Circadian disruption (CD), a common phenomenon among shift workers, has been shown to promote hepatic steatosis in rodent model. Recent studies have shown an association between gut microbiota and liver function. Anti-inflammatory property with prebiotic potential is found in oat β-glucan (OBG). We hypothesize that oral supplementation of OBG results in the alleviation of NASH mediated by gut microbiota composition and function. Preliminary results showed that CD might intensify NASH but could be attenuated by OBG supplementation.

Objectives

1. To assess the intensifying effect of CD on NASH
2. To compare the effects of prebiotic inulin (positive control) and β-1,3/1,4 OBG on NASH at dose level of 500mg/kg bw/day

Methods

Circadian manipulation and feeding protocol



- Male C57BL/6J mice were randomly divided into 6 groups (n = 5)
- Weekly shifted light-dark cycle was adopted to mimic chronic shift work to induce CD
- Liver histology was assessed by H&E staining
- Concentration of cecal SCFAs were quantified using GC-MS
- Expression of hepatic genes was measured by RT-qPCR

Results

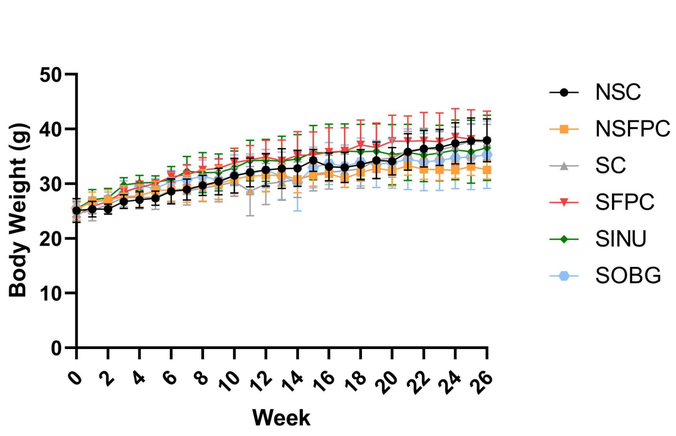


Figure 1. Trend of body weight over 26 weeks.

Figure 2. Representative H&E-stained liver sections from mice in different groups.

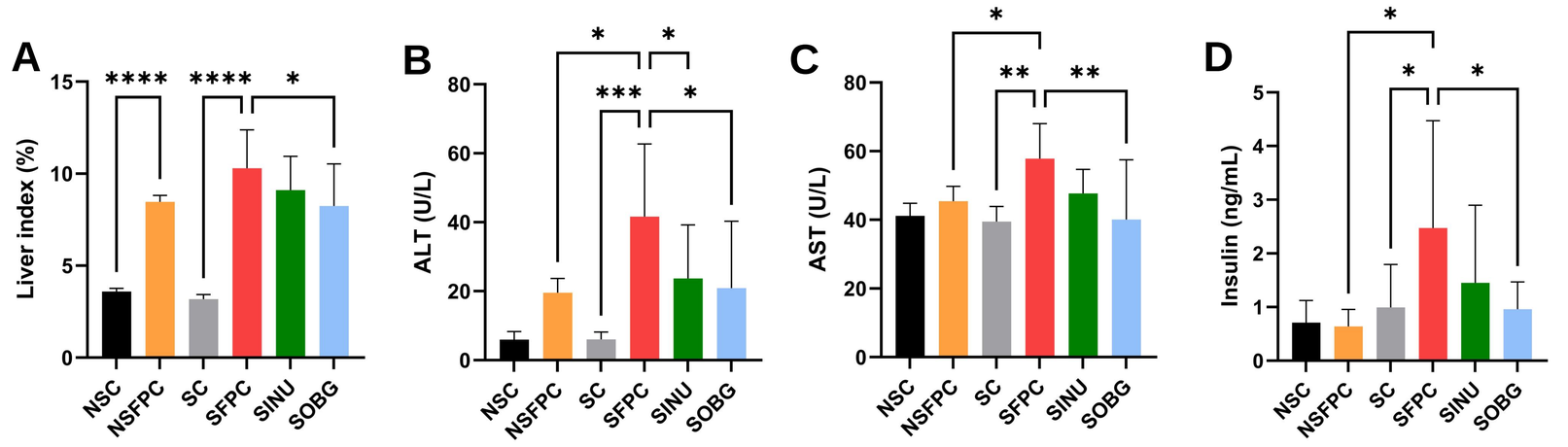


Figure 3. Host metabolic parameters. (A) Liver index, (B) serum alanine aminotransferase (ALT), (C) aspartate aminotransferase, and (D) fasting insulin.

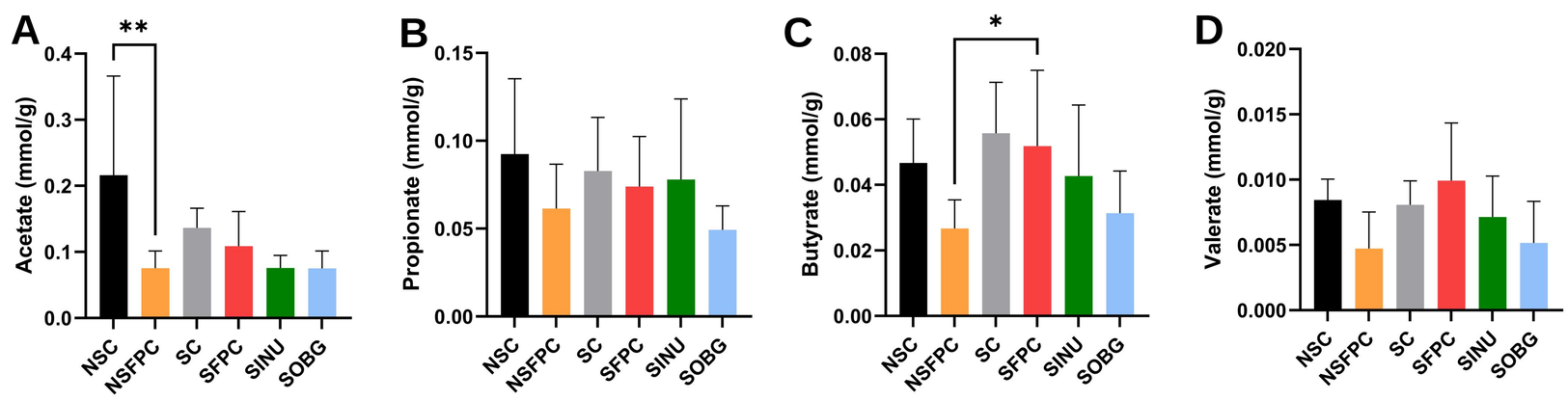


Figure 4. Profile of cecal short-chain fatty acids. (A) Acetate, (B) propionate, (C) butyrate, and (D) valerate.

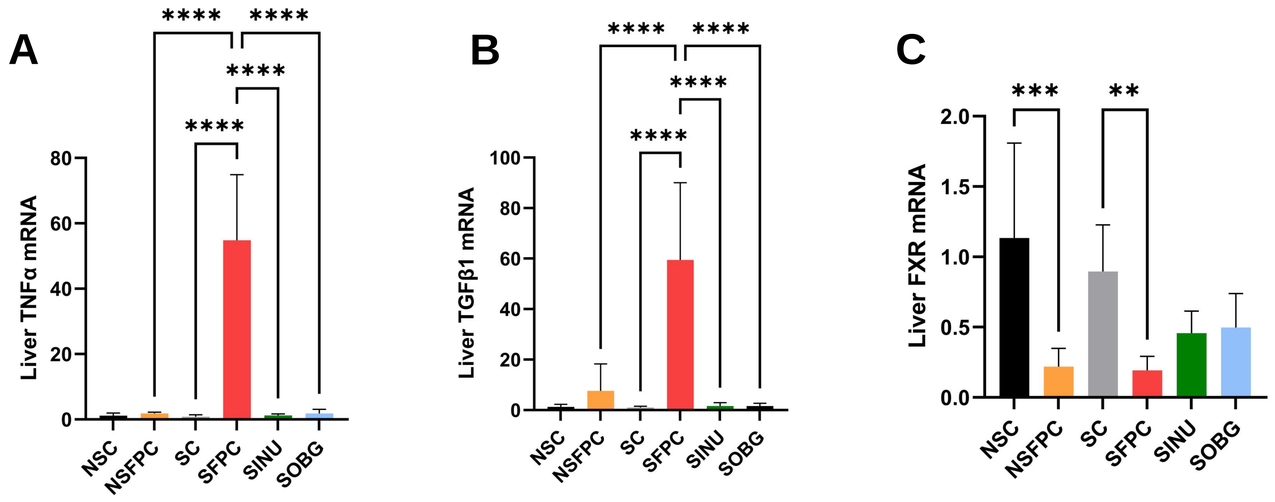


Figure 5. Hepatic gene expression. (A) Tumor necrosis factor alpha (TNFα), transforming growth factor beta 1 (TGFβ1), and farnesoid X receptor (FXR). GAPDH was chosen as a house-keeping gene for normalization.

Statistical analysis: Data is expressed as mean ± SD. One-way ANOVA followed by Fisher's Least Significant Difference test was used to assess the difference between groups. *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$, and ****$p < 0.0001$.

Key Findings

1. Hepatomegaly could be alleviated by OBG supplementation.
2. Shift work could increase the degree of inflammation and fibrosis in NASH mice but could be reversed by OBG supplementation.
3. The level of SCFAs was not influenced by prebiotic supplementation.

Conclusion

Our results suggested that OBG has the potential to alleviate liver injury, liver inflammation, and hyperinsulinemia in CD-intensified NASH mice which could be partially attributed to FXR activation. Ongoing work to decipher the gut microbiota-associated mechanisms of OBG for the improvement of NASH is in progress.