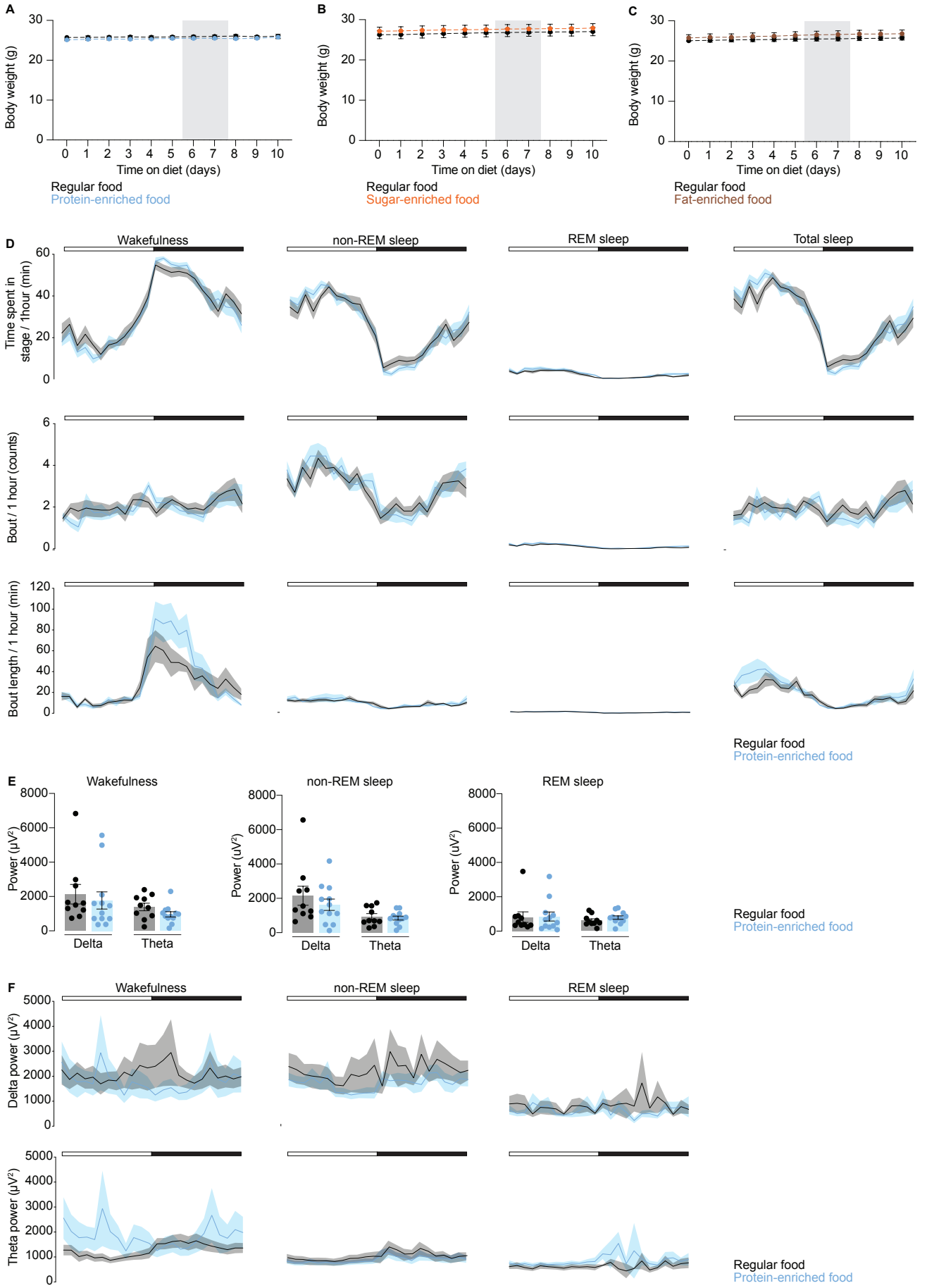Supplementary Figure 4, related to Figure 4