Effects of light, food, and methamphetamine on the circadian activity rhythm in mice

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The circadian rhythm of locomotor activity in mice is synchronized to environmental factors such as light and food availability. It is well-known that entrainment of the activity rhythm to the light-dark cycle is attained by the circadian pacemaker in the suprachiasmatic nucleus (SCN). Locomotor activity is also controlled by two extra-SCN oscillators; periodic food availability entrains the food-entrainable oscillator (FEO) and constant consumption of low-dose methamphetamine reveals the output of the methamphetamine-sensitive circadian oscillator (MASCO). In this study, we sought to investigate the relationship between the SCN, FEO, and MASCO by examining the combinatorial effects of light, food restriction, and/or methamphetamine on locomotor activity. To investigate coupling between the SCN and FEO, we tested whether food anticipatory activity, which is the output of the FEO, shifted coordinately with phase shifts of the light-dark cycle. We found that the phase of food anticipatory activity was phase-delayed or phase-advanced symmetrically with the respective shift of the light-dark cycle, suggesting that the FEO is strongly coupled to the SCN and the phase angle between the SCN and FEO is maintained during ad libitum feeding. To examine the effect of methamphetamine on the output of the FEO, we administered methamphetamine to mice undergoing restricted feeding and found that food-entrained activity was delayed by methamphetamine treatment. In addition, restricted feeding induced dissociation of the MASCO and SCN activity rhythms during short-term methamphetamine treatment, when these rhythms are typically integrated. In conclusion, our data suggest that the outputs of the SCN, FEO and MASCO collectively drive locomotor activity.