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The Neural Basis of Underlying Acquisition of Anticipation

Background: The occurrences of regularly scheduled resources and stimuli, such as food, mates, and pain, have profound effects on behavioral and physiological rhythms, as well as on neural activity. For example, when access to food is restricted to a specific time each day, animals will increase their locomotor activity in anticipation of the feeding time, known as food anticipatory activity (FAA). The specific brain circuits necessary and sufficient for the development of FAA are unknown, though various brain regions have been implicated in anticipatory processes including, the dorsomedial hypothalamus (DMH), the lateral hypothalamic area (LAH), ventral tegmental area (VTA), and the nucleus accumbens (NAc).
Goal and Methods: The present study aims to understand the development of anticipation in an FAA paradigm by examining cFos, a marker of neuronal activity, in brain regions previously implicated in learning, anticipation, and emotionality, reward, and feeding. Animals were placed on a LD cycle, where food was available for 6 hours each day, from the mid-point of the light period (zeitgeber time, ZT6) until dark onset at ZT12.
Groups: Mice were sacrificed on day 3 of restricted feeding (RF Day 3), during the acquisition of FAA phase or on day 10 (RF Day 10) when FAA was well established. Control animals were maintained on ad libitum for the duration of the experiment and were sacrificed at ZT6 and ZT4. Additionally, at each of these points, two times of day were examined, namely two hours prior to the time of food access (ZT4), and at the time of daily food access (ZT6), just prior to the delivery of food. CFos expression was compared by day and by time and was also examined in control animals.
Results: In the dentate gyrus (DG), cFos expression was elevated on RF Day 3 compared to RF Day 10, and at ZT6 compared to ZT4 on RF Day10. In the dorsomedial hypothalamus, elevated cFos was observed on RF Day 3, as compared to RF Day 10. The prefrontal cortex, prelimbic and infralimbic areas, and nucleus accumbens core, all showed increased cFos expression in the anticipatory groups compared to controls, but no significant differences were observed among experimental groups. The nucleus accumbens shell showed very dense cFos expression in a small sub-region (with no known specialization) on RF Day 3 compared to RF Day 10 (with no difference between ZT4 and ZT6), presenting a result that must be explored more thoroughly. The control group showed very low levels of cFos expression in all examined brain areas.
Conclusions: The elevated neuronal activation associated with anticipation in the dentate gyrus, implicates this region as a key brain area in first acquiring and then maintaining the timekeeping necessary for anticipation. The brain areas (DG, DMH, NAc Shell) that displayed greater neuronal activation during the acquisition phase (Day 3) compared to the established (Day 10) FAA phase may be implicated in the learning and acquisition of anticipation. The areas (PFC and NAc core) that did not show a difference among experimental groups (no significant differences between RF Day3 and RF Day 10 or between ZT4 and ZT6), but demonstrated an increase in neuronal activation as compared to controls, may be implicated in a general response to anticipation, although their specific activity in either acquisition or established FAA phases is unclear.