INTRODUCTION

• Benzodiazepines (BZs) have long been known to produce hyperphagia by increasing the gustatory hedonic evaluation of foodstuffs. Behavior analyses of taste reactivity, licking microstructure, and brief access licking after BZ treatment all support this conclusion (3, 4, 6).

• Studies suggest that benzodiazepines may modify taste evaluation through hindbrain neural systems. Chronic decerebrate rats in which the forebrain is disconnected from the hindbrain exhibit enhanced gustatory responses after benzodiazepines, and direct infusion of benzodiazepine into the hindbrain fourth ventricle or parabrachial nucleus (PBN) of intact rats also produce this response (2, 7, 8, 10, 12).

• Although the behavioral evidence for BZ modulation of gustatory coding in the PBN is compelling and clear, no studies to date have evaluated electrophysiological PBN gustatory responses to benzodiazepine receptor ligands. We therefore evaluated PBN gustatory neuron responses before and after injections of chlordiazepoxide (CDP), a prototypic BZ agonist with well-established gustatory behavioral effects (1, 5).

METHODS

Single unit subcortical acute recording in the PBN was performed in urethane-anaesthetized rats. Using tungsten microelectrodes, gustatory responsive cells were located using standard search procedures. Each task cell was profiled for its responses to 0.1M sucrose, 0.1M NaCl, 0.1M citric acid, 0.1M quinine hydrochloride (QHC), and water. Task cells were delivered using a fluid delivery system involving two glasses fed by a programmed external delivery system. Each task was applied for 20s followed by a 20s water rinse and a 60s rest interval. Water trials allowed subtraction of tactile/thermal responses.

Only a single systemic CDP injection can be made per rat. To maximize the efficiency of the preparation, task strategies were employed to avoid recruiting "saturation" responsive cells using compound responses of a neuron before and after CDP infusion (Higgs, 2000), while a record was "satisfactory" comprised of at least 300 spikes. Only those cells that were characterized as primary gustatory responsive profile (before CDP/PKz) were analyzed for the repeated measures before CDP/PKz (n=106). Randomly selected neurons (20% of all identified for each condition) were chosen to be recorded, each CDP/PKz group was recorded up to 4 h after injection. Responses were the number of spikes during the taste flow period minus the number of spontaneous spikes preceding each taste trial. Water responses were then subtracted to isolate the taste component of the responses. Responses were then quantified for the repeated presentations. More than 50% of cells had at least 200 spikes or saline tests. For repeated measures, the 3 s for the baseline phase and the first 3 s after onset (0-3 s) of the taste stimulus were averaged. Benefits of tasting protocols were derived from the 3 s after onset (0-3 s) of the taste stimulus were derived from the 3 s after onset (0-3 s) of the taste stimulus.

RESULTS

• CDP increased the proportion of cells best-responsive to sucrose (Figure 4). CDP increased the proportion of cells responding best to citric acid and QHC. These findings suggest that behavioral responses to aversive gustatory stimuli should be affected by BZs. We are working to systematically characterize behavioral responses to aversive last moments by brief access and licking microstructure paradigms.

• CDP increased the proportion of cells responding best to sucrose without altering the number of spikes elicited by sucrose. The results suggest that increased recruitment of S-best cells, perhaps via dynamic change in individual cell responses, may underlie the behavioral responses to sweet stimuli after BZ treatment. The results could be through a selective suppression of responses to aversive stimuli in individual cells, which may also contribute to the finding that the more broadly tuned cells showed a small reduction in entropy after CDP injection.

• It is not clear whether the effects observed here are mediated by direct action of BZ in the PBN or through actions at other forebrain, hindbrain, or peripheral sites. We are exploring this question through the use of direct nerve recordings, injections targeted directly to the PBN (9, 11), and analysis of the subnuclear distribution of CDP neurons modulated in the PBN.

REFERENCES


