Swallowing in Sleep and Wakefulness in Adult Cats

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Summary: Clinical evidence indicates that swallowing, a vital function, may be impaired in sleep. To address this issue, we elicited swallows in awake and sleeping adult cats by injecting water through a nasopharyngeal tube. Our results indicate that swallowing occurs not only in non-rapid eye movement (NREM) sleep, but also in rapid eye movement (REM) sleep. In NREM sleep, the injections often caused arousal followed by swallowing, but, in the majority of cases, swallowing occurred in NREM sleep before arousal. These swallows in NREM sleep were entirely comparable to swallows in wakefulness. In contrast, the injections in REM sleep were less likely to cause arousal, and the swallows occurred as hypotonic events. Furthermore, apneas were sometimes elicited by the injections in REM sleep, and there was repetitive swallowing upon arousal. These results suggest that the hypotonic swallows of REM sleep were ineffective. Key Words: Sleep—Swallowing—Cats—REM sleep—Arousal.

Swallowing is a vital function. In addition to its role in alimentation, swallowing also protects the airways and lungs by removal of matter that could be aspirated. Swallowing is the final act in the process of mucociliary clearance. Mucociliary clearance decreases in sleep, and patients with lung diseases that cause sputum production frequently state that expectoration is greatest in the morning after arousal from sleep. In addition, aspiration can occur during sleep in patients with and without esophageal reflux (1). These results suggest that swallowing is impaired in sleep. Therefore, because swallowing is important in protecting the airways against aspiration and because aspiration during sleep may cause apnea, we investigated swallowing in sleep and wakefulness.

Our interest primarily focused on whether swallowing occurred in sleep or if instead swallows were necessarily preceded by arousal. Some results indicate that swallowing does not occur in sleep (2); other results indicate that swallowing occurs and is well-coordinated with breathing in unconscious patients (3), sleeping infants (4) and sleeping adults (5); still other results indicate that swallowing occurs in association with movement arousals from stages 1 and 2 of non-rapid eye movement (NREM) and rapid eye movement (REM) sleep (6). In addition, although sleep states are not equivalent to an absence of cortical function, swallowing does occur in decerebrate animal preparations (7). Thus, the results of previous studies are varied, and it is uncertain whether or not sleep affects swallowing. The present study addresses this issue using intact, unanesthetized cats in whom swallowing was elicited in sleep and wakefulness.

METHODS

Subjects, surgical and recording procedures

Four unanesthetized adult cats implanted with electrodes for recording electroencephalographic (EEG) and electromyographic (EMG) activity were studied. Electrodes for the EEG and EMG were implanted in the cats under anesthesia (30 mg/kg ketamine and 2.5 mg acepromazine maleate) using aseptic techniques in an approved operating room. An acrylic headcap attached to the skull of each subject held a connector for the electrodes and contained fasteners that allowed atraumatic restraint of the head during recording sessions. The EEG and EMG recordings were used to identify the three states of consciousness: wakefulness, NREM sleep and REM sleep. A tracheostomy just below the cricoid cartilage was performed on each subject at the time of implantation of the electrodes. All experimen-
tal and surgical procedures were approved by the institutional Animal Care and Use Committee.

After recovery from surgery (1–2 weeks), the animals were adapted to head restraint in a recording apparatus. A flexible 8-Fr [inner diameter (ID) 0.063 inch, outer diameter (OD) 0.105 inch] silicone elastomer tube was inserted through the fistula into the trachea and was connected to a differential pressure transducer. The small size of the tube did not occlude the airway and allowed normal nasal breathing to occur. Measured intratracheal pressures were used to discriminate inspiration and expiration and as an index of swallowing.

Submental EMG activity and pharyngeal pressures were also used as indices of swallowing. Submental EMG activity was recorded with bipolar needle electrodes inserted into the submental muscles between the mandible and the hyoid bone (8). Pharyngeal pressure was monitored by inserting a flexible 6-Fr (ID 0.047 inch, OD 0.078 inch) silicone elastomer tube connected to a differential pressure transducer 6 cm into the left nostril. Prior to insertion of the tube, benzocaine (Cetacaine), a topical anesthetic, was applied to the nostril to minimize any discomfort during this procedure.

Three different volumes of tap water (0.5, 0.19, and 0.06 ml) were used to elicit swallowing. The fluid was delivered by way of a flexible 6-Fr silicone elastomer tube that, after application of benzocaine, was inserted a distance of 5 cm through the right nostril. The subjects slept in the presence of the experimenter, who upon observing REM or NREM sleep activated a computer that was programmed to deliver the fluid through the nasopharyngeal tube at the onset of an inspiration. The volume of fluid delivered was randomized. Experimental sessions were typically 2–3 hours in duration.

**RESULTS**

Four unanesthetized, adult cats were studied during wakefulness, NREM and REM sleep. A total of 286 injections of water were delivered through the nasopharyngeal tube: 136 in wakefulness, 84 in NREM sleep and 66 in REM sleep. The threshold for swallowing was not determined but we determined empirically the volumes needed to elicit only one or two swallows. It seemed that larger volumes of fluid produced a greater number of swallows rather than a larger single swallow, but we did not systematically examine this issue. Swallowing could occur in inspiration as well as expiration, but whether or not most swallows occurred in a particular phase of the respiratory cycle was not determined (7).

Swallowing occurred in sleep as well as in wakefulness, as illustrated by the integration of the submental EMG, and the swallows elicited in NREM sleep were comparable to swallows in wakefulness (Fig. 1). The fluid injections in NREM sleep also caused arousal. In the majority of cases (47/84), swallowing occurred prior to arousal (Fig. 2A), but in other cases (37/84) swallowing occurred after arousal, or the temporal relationship between arousal and swallowing was ambiguous. The injections that caused arousal prior to swallowing were distributed throughout the trials over days, eliminating the possibility that the arousal was related to the novelty of the stimulus or that there was some type of learning that occurred with experience over time. The swallows in NREM sleep that occurred after arousal were comparable to swallows in NREM sleep that occurred before arousal (Fig. 2B).

In contrast to swallows in NREM sleep, swallows in REM sleep were hypotonic (Figs. 1, 3 and 4). In addition, in REM sleep the injections were less likely to cause arousal (Fig. 3). In two-thirds of the trials in REM sleep, arousal occurred only after multiple injections of fluid. The arousal was then followed by repetitive, normal swallows. In one-third of the trials in REM sleep, arousal occurred after one injection; this was comparable to NREM sleep when arousal always occurred after one injection of fluid.

The hypotonic swallows in REM sleep were apparently ineffective (Figs. 3 and 4). Not only was arousal followed by repetitive swallows—suggesting that this fluid had pooled in the pharynx—but in many instances there was an apnea for several seconds after fluid injection, suggesting that the fluid had been aspirated (Fig. 4).

**DISCUSSION**

By the limited measures taken, our results showed that swallows in NREM sleep were indistinguishable from swallows in wakefulness. Swallowing in response
Swallowing in wakefulness, NREM and REM sleep. Swallows are similar in wakefulness and NREM sleep. In REM sleep, the swallows are hypotonic. Note that submental EMG activity is greatly diminished. Arrows indicate time of injection of fluid into pharynx. In each section, the top trace is the moving time average of the integrated submental EMG activity (100 milliseconds time constant); the middle trace is the raw EMG tracing and the bottom trace is intratracheal pressures with inspiration signaled by upward deflections. Note the "schluckatmungs" (swallow-breaths) that are seen as negative (upward) deflections on the intratracheal pressure tracing.

FIG. 1. Swallowing in wakefulness, NREM and REM sleep. Swallows are similar in wakefulness and NREM sleep. In REM sleep, the swallows are hypotonic. Note that submental EMG activity is greatly diminished. Arrows indicate time of injection of fluid into pharynx. In each section, the top trace is the moving time average of the integrated submental EMG activity (100 milliseconds time constant); the middle trace is the raw EMG tracing and the bottom trace is intratracheal pressures with inspiration signaled by upward deflections. Note the "schluckatmungs" (swallow-breaths) that are seen as negative (upward) deflections on the intratracheal pressure tracing.

to injected fluid occurred in NREM sleep and was associated with arousal. In some cases, swallowing preceded arousal; in other cases, it occurred after arousal. In REM sleep, swallowing occurred as a hypotonic event, and arousal was less common than in NREM sleep. In REM sleep, multiple injections were given without arousal; this confirms earlier observations by Sullivan and colleagues (2) that the threshold for arousal is higher in this state of sleep than in NREM sleep. In some cases in REM sleep, apneas resulted from the injections. These apneas may have been the result of aspiration. Furthermore, upon arousal from REM sleep, there were multiple swallows, indicating that the pharyngeal fluid had not been cleared by the hypotonic swallows.

Sullivan and his colleagues (2) found that water injected into the larynx in NREM sleep generally caused arousal followed by swallowing. If laryngeal stimulation did not cause arousal from NREM sleep, swallowing did not occur. In REM sleep, laryngeal stimulation with a bolus of distilled water did not reliably elicit arousal, but swallowing did occur in this state, "as judged by observation of the epiglottis" (2). Our results confirm the observation that arousal to a fluid bolus is unlikely in REM sleep but highly likely in NREM sleep. However, our results differ from those of Sullivan and his colleagues (2) in showing that swallowing can occur normally in NREM sleep, and that, although the central pattern generator for swallowing is apparently activated in REM sleep, the swallows in that state are hypotonic and ineffective.

Issa (personal communication) has found that stimulations of the tongue with tap water, saline, a glucose solution or acetic acid fail to elicit swallowing in either NREM or REM sleep. Our results obviously differ from his, indicating that different results can be obtained...
REM

EEG

NUCHAL EMG

0.06 ml 0.06 ml 0.19 ml 0.19 ml 0.5 ml

SUBMENTAL EMG

0.06 ml 0.06 ml 0.19 ml 0.19 ml 0.5 ml

INTRATRACHEAL PRESSURE

Arousal

FIG. 3. Repetitive hypotonic swallowing during REM sleep. Six injections of water during REM sleep fail to cause an arousal. In each case, hypotonic swallows are elicited. After the seventh injection, arousal occurs and is followed by repetitive swallows, suggesting that the hypotonic swallows in the previous REM sleep period did not clear the airway.

depending on the site of stimulation. Pharyngeal stimulation such as was used in our study is apparently a stronger stimulus that can induce swallowing in all states.

It is apparent from our results that swallowing can occur in NREM sleep. Because swallowing represents a form of behavioral control of the respiratory system, these results do not support the idea that behavioral control does not occur in that state (2,9) and that arousal is required for clearance of the airway through swallowing. It is clear, however, that arousal is an important, although apparently unnecessary, response to fluid in the pharynx in NREM sleep.

The situation in REM sleep is more serious; the respiratory system is at risk of aspiration in that state because swallows occur but are ineffective. The hypotonic muscular responses and very small “Schluckatmung” (swallow-breath) indicate that the stimulus is sensed and that the central pattern generator for swallowing is activated but that the swallow is blunted or inhibited by mechanisms that we presume to be those that inhibit other muscles in REM sleep (10-12). Changes in baseline submental muscle activity from NREM sleep to REM sleep were not evident in our recordings. This may have been either because of the absence of tonic activity in these muscles or, more likely, because the recording was not amplified sufficiently to show this baseline activity. It could be that afferent input is also reduced in REM sleep and that this reduced input produces a smaller swallow. This idea is contrary to our experience that larger stimuli produce not larger swallows but instead multiple, apparently equivalent, swallows. Whatever the case, these ineffective swallows result in the pooling of fluid in the pharynx with the potential or actual occurrence of aspiration in that state.

Acknowledgements: Supported by HL21257 (J.O.), HL42400 (T.E.D.) and by grants from Friends of Physiology, Department of Physiology, Texas Tech University School of Medicine (C.A.A.), Medical Student Summer Research Fellowship, Graduate School of Biomedical Sciences, Texas Tech University School of Medicine (C.A.A.) and American Heart Association Medical Student Research Fellowship 93512 (C.A.A.). We gratefully acknowledge the contributions of Becky Tilton for her excellent care of the animals and Jonathan Rude for his technical support.

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