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Area postrema-lesions increase operant responding to sucrose in rats

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Abstract

Rats with lesions of the area postrema (APX) are known to exhibit an enhanced intake of highly palatable foods such as sweetened condensed milk and cookies. These observations suggest the possibility that APX rats find these foods more rewarding and will work harder to obtain these foods. Sham and APX rats were tested on fixed ratio (FR) and progressive ratio (PR) schedules. APX rats consistently pressed more times to receive sucrose solution and attained both FR 3 and FR 5 criteria significantly faster than sham-lesioned control rats. Furthermore, rats with APX had significantly higher break points than sham-lesioned control rats on a progressive ratio schedule. These results support the hypothesis that rats with lesions of the area postrema will consistently work harder to obtain a highly palatable food reward.

Keywords: Food reward; Hindbrain; Nucleus of the solitary tract; Fixed ratio; Progressive ratio; Food intake

The area postrema (AP) is a hindbrain circumventricular organ located in the dorsal vagal complex (DVC) that was initially associated with emetic responses to ingestion of toxic substances [4]. More recent reports indicate that rats with lesions of the AP (APX) have a marked appetite for highly palatable foods in short-term trials [9,20]. This behavior suggests the possibility that lesions of the AP lead to increased motivation to consume highly palatable, sweet foods such as sucrose, cookies or sweetened condensed milk. This is an interesting hypothesis as the AP lies in the caudal medulla, far from forebrain structures typically associated with motivation and reward.

In 1981, Edwards and Ritter [9] demonstrated that although rats with thermal lesions of the AP consume the same amount of ad libitum fed laboratory chow over a 24-h period as sham-lesioned rats, APX rats consume significantly greater quantities of a palatable food (i.e. sucrose, cookies or instant breakfast) than sham-lesioned rats over a short time period. Interestingly, it has also been reported that increased intake of sucrose solution is associated with a decrease in anxiety-like behavior [7], and indeed, APX rats exhibit reduced anxiety-like behavior in an open field [17] and in an elevated plus maze (unpublished observations). Hence, increased palatable food intake demonstrated by the APX rat indicates a distinct role for the area postrema in palatable food intake. This role is often overlooked when considering the role of the hindbrain in food-motivated behavior.

Considering that rats with lesions of the AP consistently overconsume palatable foods or liquids when offered, we examined whether APX rats would actually work harder to obtain a sucrose reward than sham-lesioned rats. Results from the current studies indicate that APX rats are motivated by a palatable (sweet in this case) reward and will work harder than a rat with an intact AP to achieve the reward.

Male, Sprague–Dawley rats weighing approximately 250–300 g ($n = 19$) at the time of surgery were used for these studies. The animals were group housed in pairs in shoe-box cages in a temperature-controlled room with a 12-h light/12-h dark cycle with lights on at 7.00 a.m. Standard laboratory rat chow and water were provided ad libitum. All animal work was approved by the University of Georgia Institutional Animal Care and Use Committee.

Lesions centered on the AP ($n = 10$) were produced with a modification of a previously described technique [11].

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Briefly, this involved anesthetizing each rat with methoxyflurane (Shering-Plough, Union, NJ, USA). The dorsum of the head and neck was clipped and vacuumed to remove loose hair and the anesthetized rat was placed in a stereotaxic apparatus with the neck flexed. The surgical area was cleaned with chlorhexidine to disinfect the skin, and an incision approximately 3 cm long was made from just rostral to the occipital crest to approximately the midcervical level. The underlying muscles were then dissected to expose the foramen magnum. Next, the atlantooccipital ligament and underlying meninges were incised to expose the dorsal surface of the medulla. The cerebellum was gently elevated if necessary, and the AP was visualized through a dissecting microscope. The AP and immediately adjacent NTS were aspirated through a blunt section of 30-gauge stainless steel tubing connected to a vacuum line. The surgical wound was closed with suture. In control animals, sham lesions ($n = 9$) were produced by exposing the medulla and blotting the surface of the brain with a cotton swab. The animals were then returned to their home cages and their body weights were monitored daily for the first 15 days and at least three times per week thereafter. All rats used in these studies were allowed to recover for at least 6–8 weeks prior to behavioral testing. At this time, rate of body weight gain in APX animals matched those of sham-lesioned animals.

Rats were trained to lever press for a 15% sucrose solution reward. Standard operant chambers equipped with automated solution delivery systems were used for training and testing. First, sucrose solution was delivered until each rat consistently drank from the food receptacle. Each rat was then shaped to lever press for reinforcement and these fixed ratio (FR) 1 responses were recorded for several days. After stable FR 1 responding was observed, rats were tested on a criterion of five consecutive FR 3 responses within a 20 min period. After this criterion was achieved, the rats were tested on a criterion of five consecutive FR 5 responses within 20 min. Overnight food deprivation was used in rats that did not reach the criterion in the first session. After reaching this criterion, rats were tested on the following progressive ratio (PR) schedule: 1, 2, 4, 6, 9, 12, 15, 20, 25, 32, 40, 50, 62, 77, 95, 118, 145, and 178. The number of cumulative bar presses made until an animal failed to achieve criteria was determined and recorded as the breakpoint.

All AP-lesioned rats included in the statistical analysis had complete lesions of the AP. Additionally, there was slight damage to the immediately adjacent NTS ventrolaterally and laterally in the nucleus gracilis. No damage was noted to the dorsal motor nucleus of the vagus nerve ventrally.

Fig. 1 depicts data collected during lever pressing on the last day of shaping. APX rats pressed the lever significantly more times during a 30 min period of time than the sham-lesioned rats ($p < 0.009$) to obtain the 15% sucrose reward. Accordingly, the APX rats achieved fixed ratio 3 criteria ($p < 0.05$) and fixed ratio 5 criteria ($p < 0.03$) significantly faster than sham-lesioned control rats (Figs. 2 and 3). Moreover, APX rats displayed significantly increased progressive ratio breakpoints ($p < 0.05$) than sham-lesioned control rats (Fig. 4) supporting the interpretation that rats with lesions of the AP are more motivated to work for a 15% sucrose reward than sham-lesioned control rats. These results indicate that not only do APX rats exhibit increased motivation for a sucrose reward, but that they also learn an operant task quicker when responding for a sucrose reward.

The reward systems activated after consumption of a sweet, palatable solution have been postulated to involve multiple neural circuits that rely on neurotransmitters such as dopamine (DA) and neuropeptide Y (NPY) that are found

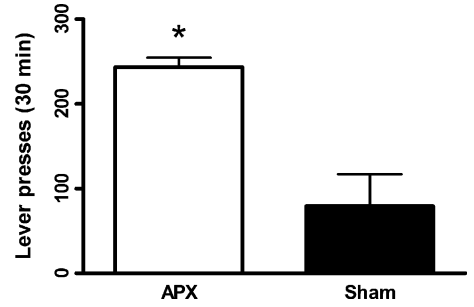

Fig. 1. Total lever presses in last 30 min training trial (mean ± S.E.M.) using 15% sucrose as reinforcement. Note that APX ($n = 10$) rats pressed significantly more times than Sham-lesioned control ($n = 9$) rats ($p < 0.009$).

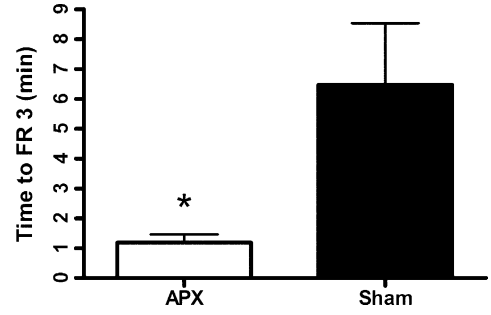

Fig. 2. Fixed ratio 3 (FR 3) results using 15% sucrose as reinforcement. The results are expressed in time in minutes (mean ± S.E.M.) to achieve the FR 3 criteria of five responses in a 20 min period. Note that the APX group ($n = 10$) achieved criteria significantly faster than Sham-lesioned control ($n = 9$) rats ($p < 0.05$).

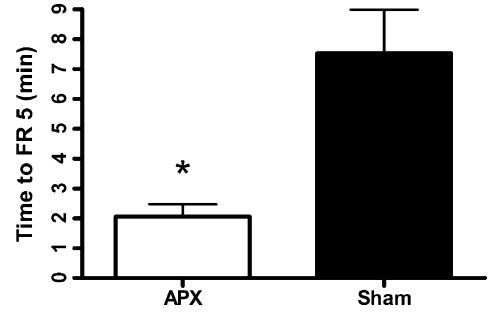

Fig. 3. Fixed ratio 5 (FR 5) results using 15% sucrose as reinforcement. The results are expressed in time in minutes (mean ± S.E.M.) to achieve the FR 5 criteria of five responses in a 20 min period. Note that the APX group ($n = 10$) achieved criteria significantly faster than Sham-lesioned control ($n = 9$) rats ($p < 0.03$).