PII S0091-3057(96)00385-1

Tremulous Characteristics of the Vacuous Jaw Movements Induced by Pilocarpine and Ventrolateral Striatal Dopamine Depletions

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FINN, M., A. JASSEN, P. BASKIN AND J. D. SALAMONE. *Tremulous characteristics of the vacuous jaw movements induced by pilocarpine and ventrolateral striatal dopamine depletions.* PHARMACOL BIOCHEM BEHAV **57**(1/2) 243–249, 1997.—Vacuous jaw movements induced by the muscarinic agonist pilocarpine and striatal dopamine depletions were examined using a slow motion videotape system. With this procedure, rats were videotaped in a Plexiglas tube so that the profile of the head region could be seen. Vacuous jaw movements were analyzed by examining the tape at 1/6 normal speed. An observer recorded each jaw movement using a computer, and the computer program re-calculated the temporal characteristics of jaw movement responses back to normal speed. The interresponse time was recorded for each jaw movement, and each jaw movement interresponse time was assigned to a 50 ms wide time bin. Thus, the distribution of interresponse times could be used to analyze the temporal characteristics of jaw movement responses. In the first experiment, rats were administered saline vehicle, 1.0 mg/kg and 2.0 mg/kg pilocarpine. The rats were videotaped 10–15 min after injection, and the data were analyzed as described above. Pilocarpine induced very high levels of vacuous jaw movements, and the vast majority of all movements occurred in "bursts" with interresponse times of 1.0 s or less. Analysis of the interresponse time distributions showed that most of the jaw movements were within the 150–350 ms range. The modal jaw movement interresponse time was in the 150–200 ms range, which corresponds to a local frequency of 5–6.66 Hz. In the second experiment, the neurotoxic agent 6-hydroxydopamine was injected directly into the ventrolateral striatum in order to produce a local dopamine depletion. The dopamine-depleted rats were observed for jaw movements 7 days after surgery. The overall level of jaw movement activity resulting from dopamine depletion was much lower than that produced by pilocarpine. There was a significant inverse correlation between ventrolateral striatal dopamine levels and total number of vacuous jaw movements. Videotape analysis indicated that the temporal characteristics of jaw movements induced by dopamine depletions were similar to those shown with pilocarpine. These experiments indicate that vacuous jaw movements induced by pilocarpine and striatal dopamine depletion occur in a frequency range similar to that shown in parkinsonian tremor. © 1997 Elsevier Science Inc.

IN rats, several pharmacological and neurochemical conditions can lead to the production of orofacial movements (16,18, 19,20,35,51). One type of oral activity that has been widely studied is vacuous jaw movements (also known as vacuous or purposeless chewing). These movements are characterized by a vertical deflection of the lower jaw that resembles chewing but is not directed at any particular stimulus (8,7,23,35,40). Vacuous jaw movements are induced by a number of conditions, including muscarinic agonists (8,35,40,41,47) dopamine

(DA) antagonists (35, 45,46), the monoamine-depleting agent reserpine (7) and striatal DA depletions (23). Although the links between vacuous jaw movements in rats and human movement disorders remain uncertain (51), it has been suggested that drug-induced perioral behaviors in rats may be related to tardive dyskinesia (5,16,49) or dystonia (36). Additionally, it has been suggested that the vacuous jaw movements induced by muscarinic agonists or striatal dopamine depletions could be related to parkinsonian tremor (7,9,23,39,40,41). Al-

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TABLE 1

EFFECTS OF PILOCARPINE ON VARIOUS PARAMETERS OF
JAW MOVEMENT (MEAN ± SEM FOR EACH MEASURE
IS SHOWN; $N = 7$)

Parameter	Pilocarpine Dose (mg/kg)		
	Saline	1.0	2.0
Total jaw movements	12.3 (3.7)	177.3 (28.7)*	214.4 (26.7)*
Single jaw movements	5.0 (0.8)	6.1 (0.6)	4.7 (0.8)
Jaw movements in bursts	7.3 (3.7)	171.1 (29.1)*	209.2 (26.7)*
Number of bursts	2.1 (0.9)	24.6 (2.8)*	30.0 (2.0)*
Average burst size	2.3 (0.5)	6.7 (0.5)*	6.8 (0.6)*

*$p < 0.05$, different from saline vehicle, Dunnett test.

though human parkinsonian tremor usually occurs in the hand, it also has been reported to occur in the jaw (1,22,50). Thus, it is possible that vacuous jaw movements in rats could be used to study the generation of tremulous movements.

According to Findley and Gresty (17) a tremor is a "periodic oscillation of a body member". Different tremors have characteristic local frequencies, and in humans parkinsonian resting tremor generally occurs in the 3–7 Hz frequency range (1,22). This local frequency is quite different from tardive dyskinesia, which tends to occur in the 1–2 Hz frequency (4,53). Clearly, it would be very important to determine the local rate of vacuous jaw movements in rats. Yet studies of vacuous jaw movements have generally involved direct observations, which are not suitable for quantifying the local rate of the movements observed (see also ref. 16). It has been reported that vacuous jaw movements tend to occur in rapid bursts (40,41,45). In one recent study, a slow motion videotape system was used to characterize the jaw movements induced by reserpine plus a very low dose of apomorphine (39). It was observed that the vacuous jaw movements induced by reserpine plus apomorphine tended to occur in rapid bursts, with the peak frequency appearing in the 3–7 Hz frequency range (39).

In the present study, the slow motion videotape method was used to characterize the jaw movements induced by the muscarinic agonist pilocarpine, and also those movements induced by striatal dopamine depletions. For the first experiment, a group of rats received injections of saline, 1.0 and 2.0 mg/kg pilocarpine. These rats were videotaped 10–15 min after injection. For the second experiment, the neurotoxic agent 6-hydroxydopamine (6-OHDA) was injected directly into the ventrolateral striatum (VLS) in order to produce a local dopamine depletion. This site was chosen based upon a previous study demonstrating that the VLS was the most effective site at which DA depletions could induce vacuous jaw movements (23). DA-depleted rats were observed on day 7 after surgery, and a 5 min sample of videotape was obtained. Correlational analyses were performed to study the relation between VLS DA levels and vacuous jaw movements, and data from the 6-OHDA-treated rats were divided into low and high DA depletion groups for further statistical analyses.

Subjects

Male albino rats (total $n = 16$, Harlan Sprague–Dawley, Indianapolis IN) were used for these experiments. All rats were housed in a colony room with a constant temperature of 72°F and a 12 L:12 D cycle (lights on at 0730 h). Standard lab chow and water were available ad lib. Average weights at the start of the experiment were 300–325 g.

Drugs

Pilocarpine hydrochloride was obtained from Sigma Chemical Company. This drug was dissolved in a vehicle of 0.9% saline solution for systemic injections (intraperitoneal; IP) in a volume of 1.0 ml/kg. Saline vehicle was used for control injections. Sodium pentobarbital (IDE Interstate, Amity, NY) was used for anesthesia. The neurotoxic agent 6-OHDA (Research Biochemicals Int.) was used for depletions of ventrolateral striatal DA (see below for surgical methods).

Behavioral Procedures

For testing of vacuous jaw movements, rats were placed in a clear 9 cm diameter Plexiglas tube so that a consistent view of the orofacial region could be achieved for videotaping. Each rat was recorded using a Panasonic AG-180 video camera focused on the orofacial region for a 5 min period. A blind observer then played the videotape on a Panasonic AG-1730 videocassette recorder in slow-motion at 1/6 normal speed to observe vacuous jaw movements, which were defined as vertical deflections of the lower jaw that resembled chewing but were not directed at any stimulus. At the point of maximal jaw opening, the observer pressed the space bar of the computer keyboard, and a basic computer program written in the laboratory calculated various parameters of the jaw movements. These parameters included the total number of jaw movements, the total number of single jaw movements (one not preceded or followed by another movement within a 1 second interval), the number of jaw movement bursts (defined as a group of at least 2 jaw movements with an interresponse time of less than or equal to 1.0 sec), total number of jaw movements occurring in bursts, and the average burst size. The computer program converted the temporal parameters observed in slow-motion into real time and calculated the interresponse time for each jaw movement that occurred in a burst. The reciprocal of the interresponse time is equal to the local frequency of the movements (i.e., an interresponse time of 0.200 s represents a frequency of 5 Hz). The interresponse time for each jaw movement was then assigned to a 50 ms-wide time bin, and the program recorded the number of movements within each of the following interresponse time bins: 0–50, 50–100, 100–150, up to 950–1000 ms and >1000 ms. The 50 ms time bin was chosen based upon pilot work, and also based upon previous research involving jaw movements produced by other pharmacological conditions (28,39). Previous experiments have demonstrated a high degree of test-retest reliability using this measurement system ($r = 0.996$ on responses in each interresponse time bin between two ratings of the same tape segment).

Ventrolateral Striatal Dopamine Depletions

Rats received IP injections of 20.0 mg/kg pargyline 30 min prior to surgery, and also received 50.0 mg/kg sodium pentobarbital anesthesia. Depletions of DA in the VLS were ob-

JAW MOVEMENTS

A

3–7 Hz

INTERRESPONSE TIME (msec)

▨ VEHICLE

JAW MOVEMENTS

B

3–7 Hz

INTERRESPONSE TIME (msec)

▨ 1 mg/kg PILOCARPINE

JAW MOVEMENTS

C

3–7 Hz
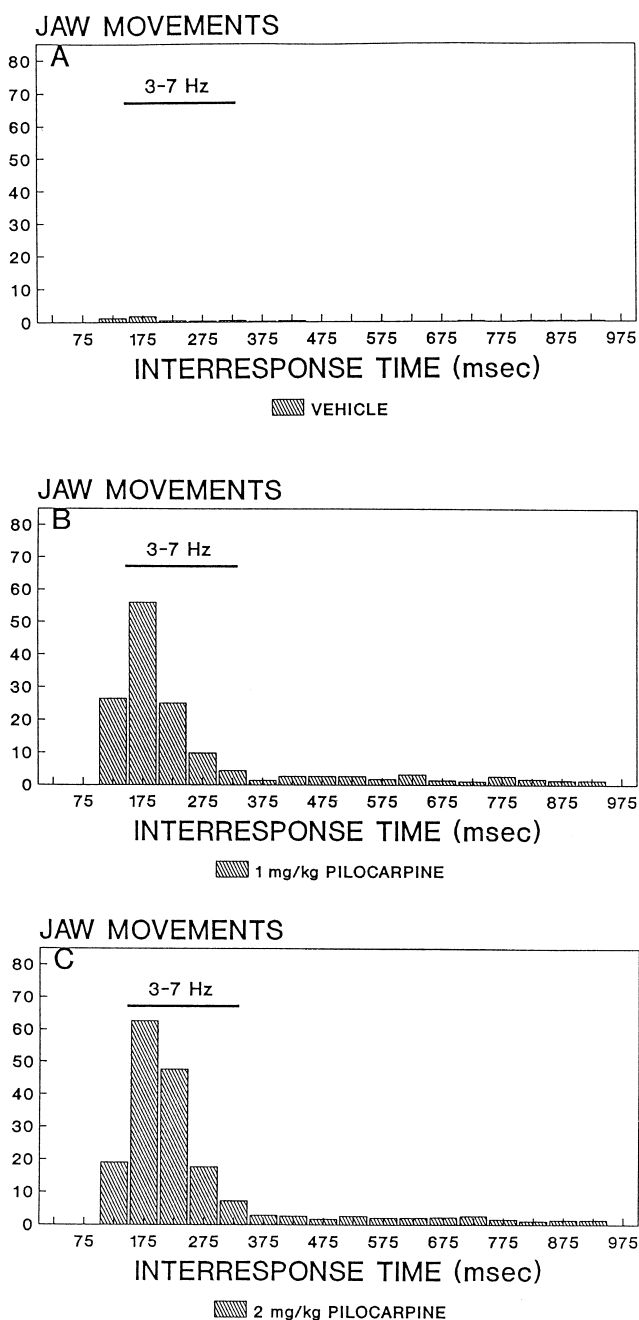
INTERRESPONSE TIME (msec)

▨ 2 mg/kg PILOCARPINE

FIG. 1. These figures are frequency distribution histograms showing the number of jaw movement IRTs that are distributed into twenty 50 ms time bins. Data shown are the mean number of jaw movement IRTs in each time bin for rats treated with saline (A), 1.0 mg/kg pilocarpine (B), and 2.0 mg/kg pilocarpine (C); $n = 7$ for each condition. On each figure, the IRT range corresponding to the parkinsonian tremor frequency range (3–7 Hz) is shown.

tained by bilateral injections of the neurotoxic agent 6-OHDA. Solutions of 6-OHDA were injected through 30 ga stainless steel injectors into the VLS (AP ± 1.4 mm, ML ± 4.0 mm, DV −7.2 mm with respect to bregma; incisor bar + 5.0 mm relative to the interaural line). Each injection consisted of 12.5 μg of free base 6-OHDA dissolved in a total of 2.5 μl of 0.1%

ascorbic acid (2.5 μl of 5.0 μg/μl 6-OHDA solution). The injection was delivered at a flow rate of 0.5 μl/min by a Harvard Apparatus syringe pump, and injectors were left in the VLS for 2 min after the infusion to allow for diffusion into the tissue.

Neurochemical Assays for Tissue Dopamine

Rats were placed in a carbon dioxide chamber on day 3 following drug treatment (day 10 postsurgery) for 30 s before being decapitated. Brains were quickly removed and immediately frozen. Coronal sections 0.7 mm thick were cut through the brain and a 16 ga stainless steel tube was used to dissect cylindrical samples from adjacent segments of VLS (dorsal or dVLS, and ventral or vVLS). Tissue samples were placed in 200 μl of chilled 0.1 N perchloric acid and homogenized. The samples were centrifuged for 4 min at 16,000 rpm and then frozen at −20 degrees°C. The supernatant obtained from each sample was analyzed using a high performance liquid chromatography system with electrochemical detection that has been previously described (12,23). The mobile phase was a phosphate buffer (pH 4.5) that contained 7.0% methanol, EDTA, and 0.4 M sodium octyl sulfate. Standards of DA (Sigma Chemical Co) were assayed before and after the tissue samples.

Experiments

In the first experiment, a group of rats ($n = 7$) was used to study the effects of pilocarpine. Each rat received all of the three drug treatments (1.0 ml/kg saline, 1.0 mg/kg pilocarpine, 2.0 mg/kg pilocarpine) in a randomly varied order, with three days between each drug treatment. After IP injection, the rats were placed in the Plexiglas tube for a 10 min habituation, and were videotaped for the 5 min period 10–15 min after injection. This time period was chosen as the period of maximal response based upon a previous study (40).

In the second experiment, a group of 9 rats received 6-OHDA injections into the VLS, as described above. On day 7 after surgery, the rats were tested for vacuous jaw movements. After being placed in the tube, the rats were left in the tube for a 10 min habituation, and were videotaped for a 5 min period following habituation. Three days after observation, the 6-OHDA-treated rats were decapitated and their striatal samples were dissected and analyzed as described above. DA levels in VLS were correlated with vacuous jaw movements, and data from the 6-OHDA-treated rats were divided into low and high DA depletion groups for further analyses.

Data Analysis

The computer program that was used to analyze the behavioral data generates several parameters of jaw movement activity, including total number of jaw movements, the number of single jaw movements, the number of jaw movement bursts, total number of jaw movements occurring in bursts, and the average burst size (see Behavioral Procedures above for definitions of these parameters). Data were square root transformed prior to statistical analysis in order to reduce variability and establish more homogeneous variance across groups. These parameters were analyzed in the first experiment with repeated measures analysis of variance (ANOVA). For both experiments, the interresponse times of jaw movements within bursts (i.e., less than 1.0 s interresponse time) were analyzed by constructing frequency distribution histograms. The jaw movement interresponse times were assigned to twenty 50 ms

TABLE 2

PARAMETERS OF JAW MOVEMENT (MEAN ± SEM FOR EACH MEASURE)
IN RATS WITH LOW (N = 5) AND HIGH (N = 4) DOPAMINE DEPLETIONS

Parameter	Group		
	Low Depletion	High Depletion	Correlation (r)
Total jaw movements	17.8 (5.9)	55.0 (15.7)	−0.72*
Single jaw movements	1.8 (0.7)	4.5 (1.3)	−0.49
Jaw movements in bursts	16.0 (5.6)	50.5 (16.2)	−0.71*
Number of bursts	2.8 (1.0)	12.0 (2.8)	−0.83*
Average burst size	5.4 (1.9)	3.9 (0.8)	−0.03

*$p < 0.05$. (Also shown is the correlation between total VLS dopamine and jaw movement activity for each parameter.)

wide time bins, and the number of interresponse times within each bin were graphically depicted for all treatment conditions. The distributions of interresponse times were analyzed using the chi-square goodness of fit test. For this analysis, the interresponse time distributions were divided into three categories: bins 1–3 (< 150 ms), bins 4–7 (150–350 ms), and bins 8–20 (350–1000 ms), and the observed frequencies of interresponse times were compared with the expected frequencies that would have been generated by an equal probability of assignment to each 50 ms time bin. These three time bin categories were selected because the middle category (150–350 ms range) roughly corresponds to the parkinsonian tremor frequency. In experiment 2, there was a significant inverse correlation between dopamine levels in the VLS and number of vacuous jaw movements; thus, the data from the rats were divided into two groups (high dopamine depletion and low dopamine depletion) for further analyses.

RESULTS

Effects of Pilocarpine

The effects of pilocarpine on the parameters of jaw movement activity are shown in Table 1. Pilocarpine had significant effects on several measures of jaw movement, and there were significant overall treatment effects on total number of jaw movements ($F(2, 12) = 66.0$, $p < 0.01$), number of jaw movements in bursts ($F(2, 12) = 64.6$, $p < 0.01$), number of bursts ($F(2, 12) = 90.5$, $p < 0.01$), and average burst size ($F(2, 12) = 16.6$, $p < 0.01$). There was no significant increase in the number of single jaw movements ($F(2, 12) = 1.33$, NS). The pilocarpine-induced increase in jaw movement activity was due entirely to an increase in jaw movements in bursts; jaw movements in bursts accounted for more than 96% of the jaw movements shown at 1.0 mg/kg pilocarpine and more than 97% of all the jaw movements shown at 2.0 mg/kg pilocarpine.

The temporal characteristics of the jaw movements that occurred in bursts are shown in Fig. 1. This figure is a frequency distribution histogram of the jaw movement interresponse times less than 1.0 s. Figs. 1A–C show the distribution of interresponse times in twenty 50 ms wide time bins (saline, Fig. 1A; 1.0 mg/kg pilocarpine, Fig. 1B; 2.0 mg/kg pilocarpine, Fig. 1C). For both doses of pilocarpine, the peak jaw movement activity occurred in the 150–200 ms time bin. This time bin corresponds to the 5–6.6 Hz frequency range. As shown in the figures, most of the pilocarpine-induced jaw movement activity was in the 3–7 Hz frequency range. Analysis of the distribution of interresponse times showed that the distribution significantly differed from an equal assignment to time

bins for both 1.0 mg/kg pilocarpine (chi-square = 1456.9, $df = 2$, $p < 0.001$) and 2.0 mg/kg pilocarpine (chi-square = 2324.3, $df = 2$, $p < 0.001$).

Effects of Ventrolateral Striatal Dopamine Depletions

For the entire group of 9 rats that received 6-OHDA, the levels of jaw movement activity (mean ± SEM) were as follows: total number of vacuous jaw movements (34.3 ± 9.6), number of single jaw movements (3.0 ± 0.80), number of jaw movements in bursts (31.3 ± 9.5), number of bursts (6.89 ± 2.0), and average burst size (4.7 ± 1.1). The results of the neurochemical analysis showed that the DA levels (in nanogram DA per mg wet tissue weight) for these animals were as follows: total VLS DA (1.64 ± 0.20), dVLS (1.55 ± 0.18), and vVLS (1.72 ± 0.22). There was a significant correlation between total VLS DA and total number of vacuous jaw movements ($r = -0.72$, $p < 0.05$). This correlation was largely due to dVLS DA, which was significantly correlated with total vacuous jaw movements ($r = -0.85$, $p < 0.05$) although VLS DA was not ($r = -0.38$, NS). Thus, on the basis of these analyses, data from the 6-OHDA-treated rats were divided into two groups: a low depletion group that consisted of the 5 rats with the highest level of total VLS DA (1.99 ± 0.22 nanogram/mg) and a high depletion group consisting of the 4 rats with the lowest level of total VLS DA (1.19 ± 0.18 nanogram/mg). These two groups significantly differed from each other in terms of total number of vacuous jaw movements ($t = 2.40$, $df = 7$; $p < 0.05$). Table 2 shows the data for these two groups on the overall parameters of jaw movement activity.

Figure 2 shows the temporal characteristics of the jaw movements that occurred in bursts. This figure is a frequency distribution histogram of the jaw movement interresponse times less than 1.0 s. Figs. 2A and B show the distribution of interresponse times in twenty 50 ms wide time bins (low depletion, Fig. 2A; high depletion, Fig. 2B). For both groups, the peak jaw movement activity occurred in the 150–200 ms time bin, which corresponds to the 5–6.6 Hz frequency range. As with pilocarpine, most of the jaw movement activity shown by 6-OHDA treated rats was in the 3–7 Hz frequency range. Analysis of the distribution of interresponse times showed that the distribution significantly differed from an equal assignment to time bins for both the low depletion (chi-square = 136.3, $df = 2$, $p < 0.001$) and high depletion (chi-square = 256.1, $df = 2$, $p < 0.001$) groups.

DISCUSSION

The present experiments examined the temporal characteristics of the vacuous jaw movements induced by pilocarpine

JAW MOVEMENTS

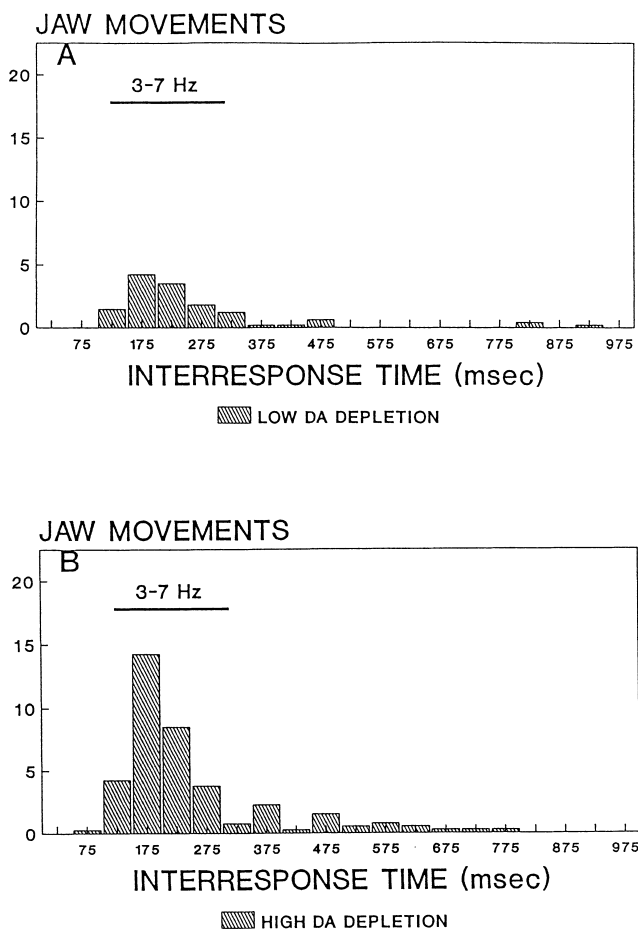LOW DA DEPLETION

JAW MOVEMENTS

HIGH DA DEPLETION

FIG. 2. These figures are frequency distribution histograms showing the number of jaw movement IRTs that are distributed into twenty 50 ms time bins. Data shown are the mean number of jaw movement IRTs in each time bin for rats that received 6-OHDA injected into the VLS (A, low depletion, $n = 5$; B, high depletion, $n = 4$). The IRT range corresponding to the parkinsonian tremor frequency range (3–7 Hz) is shown.

and VLS DA depletions. In the first experiment, pilocarpine induced vacuous jaw movements, which is consistent with several previous studies (8,9,35,40,47,48). The use of a slow motion videotape system allowed for the examination of various temporal characteristics of the jaw movements. Previous reports have indicated that cholinomimetic-induced vacuous jaw movements tend to occur in "bursts"; the present work strongly supports this observation, as it was demonstrated that greater than 96% of all the vacuous jaw movements induced by pilocarpine occurred in bursts with interresponse times of less than 1.0 s. The large number of jaw movements within bursts was related to substantial pilocarpine-induced increases in the number of movement bursts, as well as smaller increases in average burst size. Videotape analysis of interresponse times revealed that the bursts of jaw movements induced by both doses of pilocarpine occurred mostly in the 150–350 ms range, with a peak in the 150–200 ms time bin. This particular time bin corresponds to a local frequency of 5–6.6 Hz, which is well within the 3–7 Hz frequency range that is characteristic of parkinsonian resting tremor (1). In the second experiment,

it was observed that more than 90% of the vacuous jaw movements shown by rats with high DA depletions occurred in bursts. The vacuous jaw movements associated with DA depletion, like those induced by pilocarpine, occurred largely within the 3–7 Hz frequency range. Thus, the present studies indicate that the jaw movements induced by pilocarpine and VLS DA depletion are not only "vacuous" (i.e., non-directed), but they also are "tremulous."

Previous work has demonstrated that injections of 6-OHDA directly into the VLS induce vacuous jaw movements (23). In that study, DA depletions in other terminal regions were ineffective, and DA levels in VLS were inversely correlated with the production of vacuous jaw movements. The present experiment confirmed those results, in that a significant negative correlation was observed between VLS DA levels and number of vacuous jaw movements produced. Rats with high VLS DA depletions had a significantly higher number of vacuous jaw movements than rats with low depletions. Overall, these results are consistent with previous work showing that the VLS is a very important structure for the induction of vacuous jaw movements. The VLS is the most effective site for the induction of vacuous jaw movements by physostigmine (24), pilocarpine (41) and VLS DA depletion (23). The vacuous jaw movements induced by systemic administration of the anticholinesterase tacrine were blocked by very low doses of scopolamine injected directly into the VLS (28). As well as leading to vacuous jaw movements, VLS DA depletions have been shown to impair various aspects of oral and forepaw motor control (12,13,38,42,43). Anatomical evidence also supports the notion that ventral and lateral regions of neostriatum are involved in motor functions. The lateral striatum of the rat receives substantial input from sensory and motor cortices (10,30,52,54), and it is likely that this structure is the homologue of the putamen. Evidence indicates that the putamen of primates and the lateral striatum of the rat are somatotopically organized (3,30,33,34,23). The ventral putamen in primates and the VLS in rats receives input from head areas of motor cortex (26,30), and in primates the hand region of cortex is dorsal to and overlapping with the head representation (3,26). Thus, the VLS of the rat appears to be a subregion of the putamen in which a variety of functions related to head, orofacial and forepaw motor control are performed. The present results suggest that the more dorsal portion of the VLS is highly related to the production of vacuous jaw movements, and future research should attempt to identify more precisely the localization of motor functions within these particular striatal subregions.

Vacuous jaw movements can be induced in rats by muscarinic stimulation and also by pharmacological or neurotoxic depletion of DA (7,23,35,40,41). Vacuous jaw movements induced by haloperidol or reserpine can be reduced by muscarinic antagonists (35,39,45), and cholinomimetic-induced vacuous jaw movements can be reduced by the DA agonist apomorphine (48). Thus, the pharmacology of vacuous jaw movements is characterized by an acetylcholine/dopamine interaction that also is evident in a number of other neurochemical and behavioral studies (2,11,14,25), including studies of human parkinsonism (6,15,27,50). In humans, parkinsonian symptoms can be reduced by muscarinic antagonists (15,27,29) and these symptoms also can be induced or exacerbated by cholinomimetic drugs (15,31,21,32). Cholinergic stimulation in rats appears to be more effective than interfering with DA systems as a method for inducing vacuous jaw movements. Consistent with the present findings, previous work has shown that the total number of vacuous jaw movements induced by

cholinomimetics (8,28,40) is much larger than the number resulting from DA antagonism or DA depletion (7,39,45). The significance of this observation is unclear, although it may suggest that vacuous jaw movements are directly instigated by muscarinic stimulation and only indirectly stimulated by interference with DA. Neurochemical studies have shown that striatal DA depletions increase striatal acetylcholine release (2,14), and it is possible that this mechanism underlies the production of vacuous jaw movements by DA depletions. Further studies using microdialysis will be necessary to determine the relation between striatal acetylcholine release and vacuous jaw movements.

In conclusion, the present experiments demonstrated that the vacuous jaw movements induced by pilocarpine and VLS DA depletion occurred largely in bursts, with most of the jaw movement activity in the 2.86–6.67 Hz range. This is consistent with other studies using similar methods, which have demonstrated that the jaw movements induced by tacrine (28) and

reserpine plus a low dose of apomorphine (39) also occur within a similar frequency range. Using different behavioral and computer methods, See and Chapman (44) also reported that pilocarpine-induced jaw movement activity was largely in the 5–6 Hz frequency range. Although some types of low amplitude neuroleptic-induced orofacial movements do occur within the 1–2 Hz range that is characteristic of tardive dyskinesia (16), the present results indicate that the vertical jaw movements induced by pilocarpine and DA depletion occur in a frequency range that is consistent with parkinsonian resting tremor and not with tardive dyskinesia. Thus, vacuous jaw movements induced by cholinomimetics and DA depletions in rats could be useful for studying the neurochemical and physiological basis of tremulous movements.

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