Available online at www.sciencedirect.com
ScienceDirect
Physiology & Behavior 93 (2008) 461 – 466
PHYSIOLOGY & BEHAVIOR
www.elsevier.com/locate/phb

Age-related changes in orolingual motor function in F344 vs F344/BN rats

Hongyu Zhang [a], Crystal S. Bethel [a], Susan E. Smittkamp [a], John A. Stanford [a,b,c,*]

[a] Department of Molecular & Integrative Physiology, University of Kansas Medical Center, Kansas City, KS, United States
[b] Department of Physical Therapy & Rehabilitation Sciences, University of Kansas Medical Center, Kansas City, KS, United States
[c] Smith Mental Retardation Research Center, Landon Center on Aging, University of Kansas Medical Center, Kansas City, KS, United States

Received 3 July 2007; received in revised form 30 August 2007; accepted 5 October 2007

Abstract

Normal aging is associated with both locomotor and orolingual motor deficits. Preclinical studies of motor function in normal aging, however, have focused primarily on locomotor activity. The purpose of this study was to measure age-related changes in orolingual motor function and compare these changes between two rat strains commonly used in aging studies: Fischer 344 (F344) and Fischer 344/Brown Norway hybrid (F344/BN) rats. Rats (6-, 12-, 18- and 24-months of age) were trained to lick water from an isometric force-sensing operandum so that the number of licks per session, licking rhythm (licks/second) and lick force could be measured. In both strains, the number of licks per session was greatest in the oldest group, while this measure was greater for F344/BN rats at all ages. Peak tongue force increased with age in F344/BN rats, did not change with age in the F344 rats, and was greater for the F344/BN rats at all ages. Both strains exhibited an age-related slowing of licking rhythm beginning with the 18-month-old group. These findings suggest that despite lifespan differences between these two rat strains, diminished tongue motility emerges at the same age.

Keywords: Aging; Oromotor; Bradykinesia; Movement; Licking; Operant; Tongue; Animal models

1. Introduction

Normal aging is accompanied by decreases in both quantity and quality of motor activity in humans and in animals [5,19]. In addition to bradykinesia (slowed movements) and gait disturbances, diminished orolingual motor function is also associated with human aging. These alterations, which include dysarthria, dysphagia and masticatory deficits, contribute to increased mortality and morbidity in the elderly [3,11,20]. Like locomotor deficits, orolingual motor deficits also accompany Parkinson's disease (PD)[1,17], suggesting that altered basal ganglia function may play a role in their occurrence. In addition, age-related neuromuscular changes (e.g., motor neuronal innervation from the hypoglossal nucleus, changes in muscle fiber type) may also affect orolingual motor function [22,23].

Because of their functional relevance, orolingual deficits have been studied extensively in elderly human volunteers (e.g., [11]). Very few studies, however, have examined age-related changes in orolingual motor function using animal models. We recently addressed this issue by comparing orolingual motor function in young (6 months) versus aged (24 months) Fischer 344 (F344) rats [31]. Rats were trained to lick water from a disc that was attached to an isometric force transducer. While aged rats exhibited a greater number of licks per session (perhaps due to decreased tolerance to water restriction [27,34]), tongue motility as quantified by licks-per-second was significantly diminished in this group compared to the young group. This finding is consistent with studies reporting diminished tongue motility in elderly volunteers who performed an analogous repetitive tongue movement task [16]. We also reported a significant relationship between tongue motility and the ratio of dopamine (DA) metabolites to DA (thought to reflect DA

* Corresponding author. 2096 KLSIC, MS 3051, University of Kansas Medical Center, 3901 Rainbow Blvd., Kansas City, KS 66160, United States. Tel.: +1 913 588 7416; fax: +1 913 588 5677.
E-mail address: jstanford@kumc.edu (J.A. Stanford).

0031-9384/$ - see front matter
doi:10.1016/j.physbeh.2007.10.004

turnover) in the substantia nigra of the aged rats. This finding, along with the fact that orolingual motor function is altered in rats with 6-hydroxydopamine depletions of the nigrostriatal pathway [26], supports the basal ganglia hypothesis.

The purpose of the current study was to determine the age of onset of rhythm slowing, and whether this function differs between F344 rats and another strain commonly used in aging research, the F344/Brown Norway (F344/BN) hybrid. While F344/BN rats exhibit a longer lifespan than F344 rats (50% mortality at 146 weeks of age versus 103 weeks, respectively; [28]), both strains have been reported to exhibit diminished locomotor function and changes in nigrostriatal dopamine function beginning at 18 months of age [14,36]. What is not known is whether orolingual rhythm slowing likewise emerges in this middle-aged group in these strains, or whether it is a characteristic of senescence.

2. Materials and methods

2.1. Subjects

Male F344 and F344/BN rats were obtained from the National Institute on Aging colonies (Harlan Sprague-Dawley, Indianapolis, IN). Group numbers were as follows: F344 (6 months, $n=10$; 12 months, $n=8$; 18 months, $n=10$; 24 months, $n=4$; there was more age-related attrition than anticipated in the 24-month-old F344 rats); F344/BN (6 months, $n=11$; 12 months, $n=11$; 18 months, $n=8$; 24 months, $n=10$). Procedures were approved by the University of Kansas Medical Center IACUC and adhered to the *NIH Guide for the Care and Use of Laboratory Animals.*

2.2. Procedure

The apparatus has been previously described [10,26,31]. Briefly, data were recorded in a modified rodent operant chamber with a front panel containing a 6-cm square hole at floor level. Affixed to the square hole was a 6-cm cubic transparent enclosure that, on its lower horizontal surface, contained a 12-mm-diameter hole through which the rat's tongue extended down to reach the operandum. The operandum was an 18 mm diameter aluminum disc rigidly attached to the shaft of a Model 31 load cell (Sensotec, Columbus, OH) and was centered 2 mm beneath the hole in the plastic enclosure. A computer-controlled peristaltic pump (Series E; Manostat Corp., New York, NY), fitted with a solid-state relay (Digikey, Thief River Falls, MN), and controlled by a LabMaster computer interface (LabMaster, Solon, OH), delivered water to the center of the lick disc through a 0.5-mm-diameter hole. The force transducer was capable of resolving force measurements to 0.2-g equivalent weights. A PC recorded the transducer's force-time output sampled at 100 samples/s. Following gradual water restriction to 10 minutes access per day, rats were exposed to the water-licking task during 6 minute sessions until they licked reliably (i.e., >100 licks). Rats continued to receive 10 min water access per day throughout the study. The force requirement was 1 g to register a response and 12 licks were required to produce 0.05 ml of water. Each session started with a free 0.05 ml delivery of water. Upon stabilization of baseline (~2 weeks), data for the licking task were then collected over a period of 2 days. The mean values for each variable for these two days were analyzed.

2.3. Data analysis

The effects of age and strain on orolingual motor function were assessed in terms of three dependent variables: 1) number of licks per session, 2) the rhythm of licking in licks/second (Hz), and 3) the mean peak lick force. The number of licks was a count of the number of tongue contacts that equaled or exceeded 1 g. The lick rhythm was determined as follows: computation of the power spectra was performed by MatLab's Signal Processing Toolbox (The Math Works, Inc, Natick, MA). For this analysis, each 6-min session was divided into 35 series of 1024 samples from the lick-force transducer. With the Hanning data window selected, MatLab produced 35 corresponding power spectra. The power spectra were truncated to 25 Hz (based on prior work indicating little of behavioral interest beyond 25 Hz) and averaged together to yield a single power spectrum. A peak-find program written in Free Pascal was used to identify the peak in the averaged power spectrum, and the frequency at this peak was taken as the lick rhythm for a particular session. This method resolved lick rhythm to the nearest 0.1 Hz. This method was used because, unlike lick rate, the peak in the power spectrum is not influenced by pauses in licking behavior. The spectral analysis method is therefore more analogous to measures of within-burst inter-lick intervals (e.g. [7]). The peak lick force was the mean of the peak forces exerted during a session. Body weights were also analyzed as a function of age and strain. For between-strain comparisons, data for each measure were analyzed using a two-way analysis of variance (ANOVA) with age and strain as the between-subjects variables using SYSTAT (SYSTAT Software, Inc., San Jose, CA). The level of significance was $p<0.05$.

3. Results

Representative force-time waveforms illustrating licking bouts for one rat in each age group and strain are presented in Fig. 1. Note the substantially greater tongue forces in the F344/BN strain. The number of licks per session increased with age, $F(3,68)=6.239$, $p<0.001$, but was greater in the F344/BN rats at each age, $F(1,68)=25.292$, $p<0.0001$ (Fig. 2A). Both strains exhibited slowing of licking rhythm beginning at 18 months of age, $F(3,64)=18.331$, $p<0.0001$ (Fig. 2B). While the aging effect was more pronounced in the F344 rats, the age X strain interaction did not reach significance ($p=0.07$). Peak force of licks was significantly greater in the F344/BN rats than in the F344 rats at all ages, $F(1,62)=86.745$, $p<0.0001$ (Fig. 2C). Although tongue force increased with age in the F344/BN rats but remained constant with age in the F344 rats, this interaction was not significant ($p=0.07$). Body weights were greater for the F344/BN rats, $F(1,67)=137.697$, $p<0.0001$, but increased with age in both strains, $F(3,67)=46.120$, $p<0.0001$ (Fig. 2D). In