ELSEVIER

Neurobiology of Aging 27 (2006) 155–162

NEUROBIOLOGY OF AGING

www.elsevier.com/locate/neuaging

Functional degradation of visual cortical cells in old cats

Tianmiao Hua[a], Xiangrui Li[a], Lihua He[a], Yifeng Zhou[a,b,*], Yongchang Wang[a,c], Audie G. Leventhal[a,c,*,1]

[a] *Department of Neurobiology and Biophysics, School of Life Science, University of Science and Technology of China, Hefei, Anhui 230027, PR China*
[b] *Laboratory of Visual Information Processing, Institute of Biophysics, Chinese Academy of Science, Beijing 100101, PR China*
[c] *Department of Neurobiology and Anatomy, University of Utah, Salt Lake City, UT 84132, USA*

Received 19 May 2004; received in revised form 1 October 2004; accepted 10 November 2004

Abstract

Visual function declines with age. Using extracellular single-unit in vivo recordings, we compared the function of primary visual cortical (area 17) cells in young and old paralyzed, anesthetized cats. The results reveal that cortical neurons in old cats exhibit higher visually evoked responses, higher spontaneous activities, lower signal-to-noise ratios, and weaker orientation and direction selectivity than do cells in young adult cats. These findings are consistent with previously reported age related declines in cortical function in senescent macaque monkeys. Thus, similar declines in cortical function accompany old age in different mammalian species with well developed cortices.

Keywords: Old cat; Visual cortical cells; Functional declines; Orientation selectivity; Direction selectivity; Signal-to-noise ratio

1. Introduction

Studies of visual perception show that human visual function declines with age. Senescent humans show decreased visual acuity, binocular summation, contrast sensitivity and wavelength sensitivity [14,16,27,29,39,41,42,52,55,71] as well as poor or slowed performance at tasks requiring orientation discrimination and/or motion direction detection [3,40,64,65,73]. Age related changes in the retina [48,63,66] and subcortical visual pathways [61] cannot explain the foregoing declines.

Schmolesky et al. [57] compared the responses of cells in primary visual cortex (VI) of young adult macaque monkeys with those of very old macaque monkeys. That study provided the first evidence for a significant degradation of orientation and direction selectivity in senescent animals. Their results also indicated that the decreased stimulus selectivity of cells in old monkeys was accompanied by increased responsiveness to all orientations and directions as well as an increase in spontaneous activity. The ability of old neurons to differentiate signals from noise was also reduced.

To date there have been no studies of age related declines in visual cortical function in higher mammalian species other than the monkey. We, thus, have for the first time, used extracellular single-unit recording techniques to examine orientation and direction sensitivity as well as visual responsiveness of VI cells in old and young adult cats. Our aim was to test whether age related changes in monkey cortex can be generalized to other species with well developed visual systems. We chose cats as subjects because cats have a well developed visual system and thus are used widely in studies of visual cortex.

2. Methods

2.1. Subjects

Subjects for this study were four young, sexually mature cats (1–3 years old) and four old cats (12 years old). Several lines of evidences indicate that a cat about 12 months old can be considered sexually mature and functional aging of the brain takes place in cats of 10 years or older [6,7,22,32].

* Corresponding author. Tel.: +86 551 3601436; fax: +86 551 3607 014.
E-mail addresses: zhouy@ustc.edu.cn (Y. Zhou), audie.leventhal@m.cc.utah.edu (A.G. Leventhal).
[1] Tel: +1 801 581 6006; fax: +1 801 585 3513.

0197-4580/$ – see front matter © 2005 Elsevier Inc. All rights reserved.
doi:10.1016/j.neurobiolaging.2004.11.012

All cats were examined ophthalmoscopically before the experiment to confirm that they had no optical or retinal problems that would impair visual function. All experiments were done strictly in accordance with the National Institutes of Health Guide for the Care and Use of Laboratory Animals.

2.2. Preparation for extracellular recording

The preparation for extracellular single-unit recording was carried out as previously described [58]. Briefly, cats were lightly anesthetized with ketamine HC1 (20 mg/kg). Lidocaine (1%) was applied to all incisions of surgical entry. After the intravenous and tracheal cannulae were inserted, cats were placed in a stereotaxic apparatus. Pupils were maximally dilated with atropine (1%), and appropriate contact lenses were used to protect the corneas. Neosynephrine (5%) was administered to retract the nictitating membranes.

A mixture of urethane (20 mg/h/kg body weight) and gallamine triethiodide (10 mg/h/kg body weight) was infused intravenously to maintain anesthesia and paralysis. Expired pCO_2 was maintained at approximately 4%. Heart rate (about 180–220 pulses/min) and EEG was monitored throughout the experiment to assess the level of anesthesia. A small hole was drilled in the skull 4 mm posterior to the ear bars and 2 mm lateral to the midline. A glass-coated tungsten microelectrode (with an impedance of 3–5 MΩ) was positioned and advanced using a hydraulic micromanipulator (NARISHIGE, Japan). The small hole was filled with a 4% solution of agar in saline and sealed with wax. After the preparation was complete, the optic discs of the two eyes were reflected on a tangent screen positioned 114 cm from the retina and the central areas for both eyes were located. Spectacle lens were used as needed.

At the end of the experiment, the cat was deeply anesthetized and perfused through the heart. Blocks of tissue containing area 17 (striate cortex) were removed, post-fixed overnight in cold 4% paraformaldehyde in PBS and then embedded with wax for later morphological studies.

2.3. Visual stimulation

Visual stimulus patterns were drifting sinusoidal gratings shown on a CRT monitor (1024 × 768, 85 Hz), placed 57 cm away from animal's eyes. The program to generate the stimulus was written in MATLAB, using the extensions provided by the high-level Psychophysics Toolbox [8] and low-level Video Toolbox [44]. When a single unit was isolated, the cell's receptive field was carefully mapped by consecutively presenting a series of computer-generated light spots on the CRT. We selected optimal stimulus size, temporal and spatial frequency for each cell. Each stimulus was presented monocularly to the dominant eye. Then, a set of sinusoidal gratings with optimal stimulus parameters, moving in 24 different directions (0–360° scale with an increment of 15°) was used to compile the orientation and direction tuning curves. The orientation of each drifting stimulus was orthogonal to its direction of motion. Before each stimulus presentation, 5 s spontaneous activities were obtained while mean luminance was shown on the display. The duration of each stimulus presentation was less than 5 s with a 5 min interval between stimuli for functional recovery. The contrast for each stimulus was set at 80%. The mean luminance of the display was 19 cd/m^2, and the environment luminance on the cornea was 0.1 lx.

2.4. Data collection and analysis

After the signal was amplified with a microelectrode amplifier (NIHON KOHDEN, Japan) and differential amplifier (FHC, USA), action potentials were fed into a window discriminator with audio monitor. The original voltage traces were digitized using an acquisition board (National Instruments, USA) controlled by IGOR software (WaveMetrics, USA). The original data (Fig. 1A) were saved for later analysis.

The post-stimulus time histograms (PSTHs) of response were obtained for further analysis (Fig. 1B). The responses of a cell to the sinusoidal gratings were fast Fourier transformed and defined as the amplitude of the fundamental Fourier com-

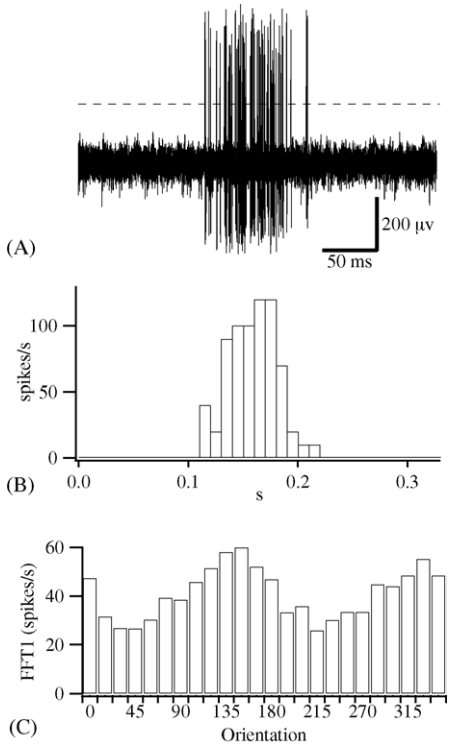

Fig. 1. An example showing the visual responses of an area 17 neuron in an old cat and analysis of the responses. (A) Each cycle of the neuron's original response was superimposed in one stimulus period (0.333 s). A spike above the broken horizontal line is counted as an action potential. (B) The PSTH derived from (A) for further analysis. Bin width was 10 ms. (C) The neuron's orientation tuning curve. The curve was established on a 360-degree scale with an increment of 15°. The orientation of the drifting gratings were orthogonal to its moving direction. The responses were defined as the fundamental Fourier components (FFT1). The FFT1 at each stimulus direction was computed from the PSTH such as the one shown in (B).