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Aging Affects Fine and Coarse Coding of Orientation Information in Macaque Primary Visual Cortex

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Abstract—Human visual function degrades with age. Previous studies of visual perception have shown that aged people have worse performance in the coding of orientation information. However, the neuronal mechanism still remains elusive. In this study, we performed in vivo extracellular single-unit recording in the primary visual cortex of senescent and young monkeys, and we used the Chernoff distance to quantify the encoded information of neurons for fine and coarse orientation difference. Our results showed that the Chernoff distance for fine orientation difference in senescent monkeys is significantly smaller than that in young monkeys. In contrast, the Chernoff distance for the coarse coding was comparable in young and old groups. Meanwhile, increased spontaneous response and maximum evoked response was also observed. Further investigation of neuronal correlation showed higher noise and signal correlations in aging monkeys than that in young monkeys. These correlation changes predicted a detrimental effect on the efficiency of population coding of orientation information. Taken together, our results suggest that the information coding efficiency of orientation information is impaired during aging and might account for the degradation of performance in human fine orientation discrimination task.

Key words: aging, fine and coarse coding, orientation discrimination, the primary visual cortex (V1 area), visual degradation, macaque.

INTRODUCTION

A healthy visual function is crucial for life survival. Plenty of psychophysical studies have reported deficits in visual function in old people (Norman et al., 2003; Snowden and Kavanagh, 2006; Owsley, 2011). For example, most old people have difficulty in the coding of orientation information (Ball and Sekuler, 1986; Betts et al., 2007; Govenlock et al., 2009a,b). Much of these deficits cannot be attributed to the decline in the optical system, but rather to the age-related changes of neuronal properties of the receptive field in the visual cortex. Especially, it has been shown that the orientation tuning curve of neurons in visual cortex was altered during normal aging (Spear, 1993; Schmolesky et al., 2000; Leventhal et al., 2003; Norman et al., 2003; Wang et al., 2004; Yang et al., 2008; Yao et al., 2015). However, the neuronal mechanism underlying the effects of aging on orientation information coding remains unclear.

Orientation bias (OB), orientation specificity index (OSI) and response tuning width are widely used to measure the orientation selectivity in visual neuroscience (Leventhal et al., 1995; Leventhal et al., 2003; Yang et al., 2008). Using these measures, previous

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Abbreviations: DC, Chernoff distance; OB, orientation bias; OSI, orientation specificity index; SNR, signal-to-noise ratio maximum induced response spontaneous response; V1 area, the primary visual cortex.

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studies have reported a significant decline of orientation selectivity in the aged visual cortex (Schmolesky et al., 2000; Leventhal et al., 2003; Liang et al., 2010; Liang et al., 2012). However, OB and OSI are global measures of neuronal responses to various orientations (the overall shape of the tuning curve). Although the tuning width further described the shape of the wave crest, it is still not sufficiently refined (Ringach et al., 2002). Thus, these measures cannot capture age-related alteration of orientation selectivity at the fine dimension. To better understand how aging impacts fine and coarse coding of orientation information in the visual cortex, we applied the Chernoff distance, which is a measure of the difference between two probability distributions. Specifically, in the study of orientation coding, the Chernoff distance represented the information encoded in the difference of neuronal responses for two stimuli with different angles ($\delta\theta$). It has a direct relationship with Fisher information, which is widely used in neuroscience (Seung and Sompolinsky, 1993; Abbott and Dayan, 1999; Kohn et al., 2016). But Fisher information can be used only when two angles are very similar to each other. Thus, the Chernoff distance is more general because it can characterize small and large orientation differences simultaneously. (Chernoff, 1952; Cover and Thomas, 1991; Sompolinsky et al., 2001; Kang et al., 2004; Jacob et al., 2016).

It has been proposed that inhibitory circuits are impaired during normal aging. Indeed, neurophysiological studies have found that the spontaneous responses of neurons in the visual cortex of old animals were significantly increased. As a result, the signal-to-noise ratio (SNR) decreased a lot (Leventhal et al., 2003; Liang et al., 2010; Wang et al., 2014). Although the changes of single-unit response could to some extent account for behavior degradation during senescence, according to population coding theory, nervous systems signal and compute parameters using a large population of neurons (Sompolinsky et al., 2001; Kohn et al., 2016). Especially, the structure of correlated neural activity (i.e., signal correlation and noise correlation) affects the efficiency of neural encoding. Moreover, Samonds and his colleagues pointed out that fine coding depends more on neuronal interactions in a population (Samonds et al., 2003; Samonds and Bonds, 2004). These studies on neuronal information coding remind us of the necessity to analyze the structure of correlation.

In this research, using *in vivo* extracellular single-unit recording, we quantified neuronal fine and coarse coding of orientation information in the primary visual cortex (V1 area) as Chernoff distance. We found that the Chernoff distance for fine coding of orientation information was significantly decreased for neurons in the aged V1 area. However, the Chernoff distance for coarse coding was comparable in young and aged groups. These changes were accompanied by the increased spontaneous and maximum induced responses, enlarged noise correlation and decreased signal-to-noise ratio. These results may provide a potential neuronal mechanism for the performance changes in fine and coarse orientation discrimination tasks in old people.

EXPERIMENTAL PROCEDURES

Subjects

Acute experiments were conducted on three young adult (5–9 years old, 3.6–6.2 kg) and four aged (21–25 years old, 5–8.5 kg) rhesus monkeys. According to the life span of macaque, 5- to 9-year-old monkeys are sexually mature, and 21- to 25-year-old monkeys are considered aged (Dittus, 1975; Tigges et al., 1988). We examined all of the monkeys ophthalmoscopically before recording. We did not find any visible deterioration. All of the surgical and experimental operations were approved by the Institutional Animal Care and Use Committee of the University of Science and Technology of China and were in accordance with the National Institutes of Health Guide for the Care and Use of Laboratory Animals. We minimized pain and discomfort throughout the experiment's entire procedure.

Preparation for extracellular recording

The details for the preparation of macaque monkeys for single-unit recording have been described previously (Schmolesky et al., 2000; Priebe et al., 2002). In acute experiments, animals were initially sedated with ketamine HCl (10 mg/kg, i.m.) and maintained with isoflurane (3–5%, inhaled in oxygen) for venous and tracheal cannula. After venous and tracheal cannula, we placed the animals in a stereotaxic apparatus. The head was fixed with local anesthetic (2% lidocaine-HCl jelly) applied to all of the pressure points. Subsequent anesthesia was maintained by intravenous infusion of propofol (5 mg/kg/h, i.v.), sufentanil (10 ng/kg/h, i.v.) and a mixture air of O_2/N_2 O (30:70). To minimize the drifting of eye position, we infused gallamine triethiodide (7 mg/kg/h, i.v.). The animal was artificially ventilated using a medical ventilator. The level of anesthesia and physiological state of animals were assessed according to the heart rate, ECG, respiratory rate and rectal temperature. Expired CO_2 was maintained at approximately 4% and the rectal temperature was maintained at 37 °C using a thermostatic heating pad (Harvard Apparatus, Holliston, MA, USA). We protected the corneas from desiccation with topical hydroxypropyl methylcellulose (2.3%) in acute surgery and gas-permeable hard contact lenses in the subsequent recording. The pupils were dilated with 0.25% tropicamide eye drops. Atropine sulfate (1 mg, i.m.), dexamethasone (5 mg, i.m.), and penicillin (125 mg, i.m.) were administered every 12 hours. At the end of an experiment, the animal was deeply anesthetized with an overdose of pentobarbitone sodium and perfused with 0.9% saline followed by 4% paraformaldehyde (in 0.1 M phosphate buffer) through the heart. The brain tissue was removed and blocked for further analysis.

Visual stimulus

Before recording, the optic disks were back-projected to a plotting screen using an ophthalmoscope and corner cube

prism. We used corrected contact lenses to ensure that the eyes were focused on the stimulus plane. An artificial lens (2.3 mm diameter) was placed in front of the eye to improve the optical quality. Since multiple neurons were recorded simultaneously, the receptive field for the average response was determined (Samonds et al., 2003). Then, a series of sinusoidal gratings with the size of the receptive field and drifting in different directions were displayed on a CRT monitor (1024 × 768 pixels; Multiscan G220, Sony, Tokyo, Japan), which was placed 114 cm away from the animal's eyes. The grating was generated in MATLAB using the extensions provided by the high-level Psychophysics Toolbox (Brainard, 1997; Pelli, 1997). The mean luminance of the display was 38.7 cd/m^2. A blank screen with the mean luminance was first presented for 0.5 s, and then the stimulus appeared and started to move. After moving, the stimulus displayed on the screen for 1 s, and followed by 0.5 s blank screen with mean luminance. Each stimulus was presented 10 times in a randomized sequence. The receptive field was carefully mapped and the optimal spatial and temporal parameters were determined. After the initial characterization of each cell, optimal sinusoidal gratings moving randomly in 12 different directions (0°, 30°, 60°, 90°, 120°, 150°, 180°, 210°, 240°, 270°, 300°, 330°) were used to generate orientation tuning curves. The contrast of stimuli was stable at 99% (Fig. 1).

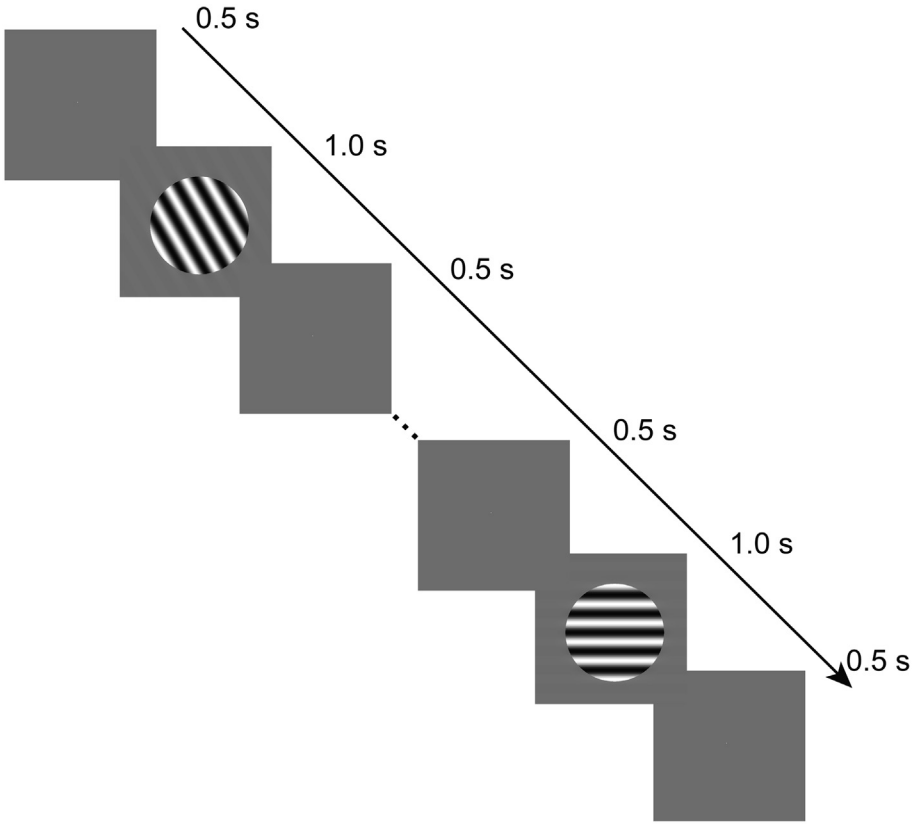

Fig. 1. Diagram of the stimulation protocol. The stimulus was a drifting grating with a contrast of 99%. A blank screen with the mean luminance was first presented for 0.5 s, then the stimulus displayed on the screen for 1 s, and followed by 0.5 s blank screen with mean luminance. The receptive field, optimal spatial and temporal parameters were characterized. After the initial characterization, optimal sinusoidal gratings moving randomly in 12 different directions (0°, 30°, 60°, 90°, 120°, 150°, 180°, 210°, 240°, 270°, 300°, 330°). Each stimulus was presented 10 times in a randomized sequence.

Data collection and analysis

Extracellular action potentials were recorded with 1 × 32 linear arrays (A1 × 32–6 mm–100–177, NeuroNexus). The electrode was advanced vertically to the brain surface using a hydraulic microdrive (David Kopf Instruments, Tojunga, CA, USA). The craniotomy of V1 was located 3 mm posterior to the ear bar and 2 mm lateral to the midline which is above the occipital lobe (Liang et al., 2012).

Spike rate (for brevity, we refer hereafter the spike rate as response) to each stimulus in the time window of the stimuli displayed (1 s) of the isolated neuron were recorded using a data acquisition system with on-line spike isolation (Cerebus, Blackrock Microsystems, Salt Lake City, UT, USA). All of the neuronal signals were filtered (0.3–10 kHz) and digitized at 30 kHz. The responses of neurons to the drifting stimuli were then stored in the computer for later analysis.

To describe the neuronal orientation responses, we firstly fitted the response tuning curves with a widely used function of von Mises (with a mean $r^2 = 0.905$ in this paper) (Li et al., 2008; Ecker et al., 2011; Hu et al., 2014; Zylberberg et al., 2016):

$$R(\theta) = Ae^{b\cos 2(\theta - x_c)} + R_0,$$

where R is the response of the neuron as a function of the direction θ, A is the value of response at the preferred orientation x_c, b is a bandwidth parameter, and R_0 is spontaneous.

Chernoff information is an objective method to characterize difference between two probability distributions $P(\vec{r}|\theta_1)$ and $P(\vec{r}|\theta_2)$. And it has a direct relationship with Fisher information and mutual information which are widely used in neuroscience. Simply, for a fitted response tuning curve $R(\theta)$ of a neuron, the Chernoff distance of the neuron is:

$$DC(\delta\theta) = \frac{1}{360^\circ} \times \int d\theta \left(\sqrt{R(\theta+\delta\theta)} - \sqrt{R(\theta)}\right)^2 + \left(\sqrt{R(-\theta-\delta\theta)} - \sqrt{R(-\theta)}\right)^2$$

where $R(\theta)$ is the response tuning curve, and $\delta\theta$ means the angle difference of two moving sinusoidal grating stimuli. The DC was calculated as the $\delta\theta$ changed. Thus, the DC described the information contained in the difference of responses induced by two stimuli. This equation

shows how the information of the Chernoff distance is related to the shape of the response tuning curve $R(\theta)$ (Kang et al., 2004).

The noise correlation (r_{sc}) of two paired neurons was calculated as the Pearson correlation from the fluctuations of evoked spikes counts (Bair et al., 2001; Kohn and Smith, 2005):

$$r = \frac{E(N_1N_2) - E(N_1)E(N_2)}{\sigma_{N1}\sigma_{N2}}$$

where E is the expected value, σ is the SD of the spike counts for a particular stimulus, N_1 and N_2 are spikes for neurons 1 and 2, respectively.

The signal correlation (r_{signal}) was calculated as the correlation coefficient of the average responses to stimulus (Lee et al., 1998; Ko et al., 2011). Statistics were performed after normalization of r to Z-score using Fisher transformation (Anderson, 1984):

$$Z = \frac{1}{2}\ln\left(\frac{1+r}{1-r}\right)$$

Statistical analysis

Statistical comparisons between young and old groups were carried out with Mann–Whitney U test. And the statistical significance is determined as $p < 0.05$. All of the results in this paper are expressed as the mean ± SEM. The effect size is measured as Cohen's d^2 (Cohen, 1990; Sullivan and Feinn, 2012). All statistical analyses are performed in SPSS 20.

RESULTS

We studied a total of 289 neurons from the V1 area. Specifically, we recorded 128 neurons from three young monkeys and 161 neurons from four old monkeys. All of the data were collected from three to five penetrations in each monkey. Eccentricities of cells we studied here were 2°–29° from the central area, and most were within 8°. The recording depths and eccentricities of neurons were comparable in the young and old groups.

We analyzed the age differences of orientation selectivity firstly. For aged group, the Orientation bias (OB) significantly decreased (Young: 0.206 ± 0.014; Old: 0.146 ± 0.011; $P < 0.0001$; Mann–Whitney U test) and the tuning width (HWHH) was wider (Young: 49.56 ± 1.76; Old: 56.83 ± 1.54; $P = 0.0016$; Mann–Whitney U test) when compared to the young group. These changes are consistent with previous studies about aging effects on V1 neurons.

Aging related effects on fine and coarse coding

Fig. 2A, B show orientation responses of two V1 neurons from young adult and old monkeys. Typically, the young V1 neuron in Fig. 2A showed sharper tuning to orientation than the aged V1 neuron in Fig. 2B. The information curves of Chernoff distance for example neurons were shown in Fig. 2C, D. Considering the property of orientation, we mirrored the same orientation but inverse drifting directions. Thus, the orientation tuning curves were depicted in the range of 0°–180° (Li et al., 2008). For the unimodal response curves in Fig. 2A, B, the information curves of Chernoff distance were also unimodal. And the Chernoff distance peaked at the $\delta\theta$ of 90°. For the young V1 neuron, the information curve (Fig. 2C) was clearly greater than the aged neuron (Fig. 2D). As $\delta\theta$ increases, the Chernoff distance shown in Fig. 2C rose more quickly than the Chernoff distance shown in Fig. 2D. This difference in growth rate was reflected expressly in the inset plot of the Chernoff distance at a $\delta\theta$ from 1° to 10° as shown in Fig. 2D. The maximum Chernoff distance shown in Fig. 2C was also greater than that shown in Fig. 2D (0.037 versus 0.018).

To study the generality of this relationship across neurons sampled in young and aged V1 areas, we performed statistical analyses for fine and coarse coding. The fine coding of orientation information represents the information encoded in the response difference for two orientations with small $\delta\theta$ (Samonds and Bonds, 2004). Fig. 3A shows that the Chernoff distance of young group is generally larger than aged group at all $\delta\theta$. Further, the Chernoff distance at $\delta\theta$ from 1° to 10° was significantly lower in the aged group than the young group (Fig. 3B). In Fig. 3C and Table 1, we showed the difference of DC(3°) and DC(90°) between young and aged V1 neurons. The DC(3°) of aged V1 neurons was significantly decreased compared with young V1 neurons ($P = 0.007$; Mann–Whitney U test). Also, the DC(90°) of aged V1 neurons was declined compared with neurons in young V1 area (Young: 0.020 ± 0.002; Old: 0.015 ± 0.002), but it was marginal ($P = 0.091$; Mann–Whitney U test). A mixed repeated-measures ANOVA on log-transformed DC($\delta\theta$) revealed significant Age $\times$ $\delta\theta$ interaction ($F = 8.08$, $P = 0.005$), also significant main effects of Age ($F = 4.03$, $p = 0.046$) and $\delta\theta$ ($F = 2.23 \times 10^4$, $P < 0.0001$). The significant decrease of Chernoff distance in smaller $\delta\theta$ and age $\times$ $\delta\theta$ interaction means a severely declined neuronal fine coding of orientation information than the coarse coding in the aged V1 area.

Effects of aging on SNR and noise correlation

In order to further research the relationship between the changes in information coding and neuronal activities, we analyzed the maximum induced response (R_{max}), spontaneous response (R_{spon}) and SNR. As shown in Fig. 4, the R_{max} of aged V1 neurons was increased as compared with neurons in young V1 (33.986 ± 1.402 *versus* 30.639 ± 2.203; Mann-Whitney U test; $P = 0.006$; Fig. 4A and Table 2). Also, the R_{spon} of aged V1 neurons was increased as compared with neurons in young V1 (21.681 ± 1.100 *versus* 16.952 ± 1.604; Mann-Whitney U test; $P = 0.0002$; Fig. 4B and Table 2). Moreover, the effect size for R_{spon} (0.336) was greater than for R_{max} (0.160). As a result, the SNR of aged V1 neurons was significantly lower than young V1 neurons (2.343 ± 0.227 *versus* 3.282 ± 0.727; Mann-Whitney U test; $P < 0.0001$; Fig. 4C and Table 2). These changes in neuronal activities were similar to previous studies (Schmolesky et al., 2000; Liang et al., 2010; Wang et al., 2014; Yuan et al., 2014).

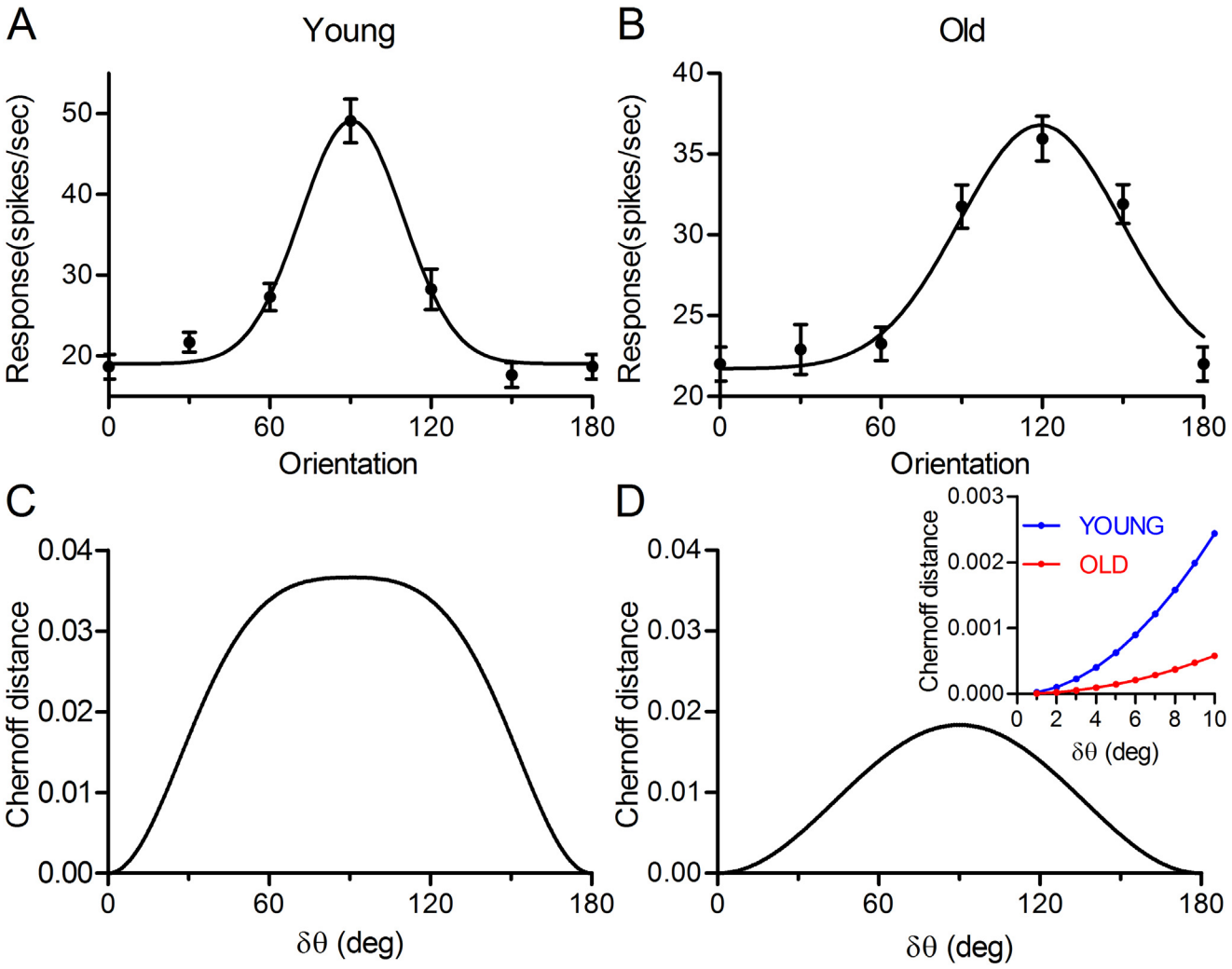

Fig. 2. Two example neurons in the young and old V1 area. **(A)** and **(B)** Responses (black dots) to stimuli with different orientations and the response tuning curves (black line) of neurons from the young and old monkey V1 area, respectively. **(C)** and **(D)** The information curves of Chernoff distance for the two example neurons, which is also unimodal like the response tuning curve. The inset plot in (D) is the Chernoff distance for $\delta\theta$ from 1° to 10°.

Also, we analyzed the signal and noise correlation (r_{signal} and r_{SC}) for young and aged V1 neurons because previous studies have shown that signal and noise correlation together control information coding (Averbeck et al., 2006; Kohn et al., 2016). We measured the signal and noise correlation by pairing neurons which were recorded simultaneously in one penetration. In total, we coupled 620 and 1326 paired neurons in the young and old groups, respectively. The distance between paired neurons was defined as the distance between record sites. We firstly analyzed the distances for two groups because the noise correlation was related to the distance between two paired neurons (Huang and Lisberger, 2009; Wang et al., 2019). The Mann–Whitney *U* test showed that there was no significant difference in the distances ($P = 0.160$; Mann–Whitney *U* test; Fig. 5A and Table 3). We then directly compared the r_{signal} and r_{sc} without adjusting the distance. Both young and aged monkeys showed positive mean r_{signal} across all of the pairs, and increased significantly from young to aged monkeys (0.176±0.019 *versus* 0.364±0.014; Mann–Whitney *U* test; $P < 0.0001$; Fig. 5B and Table 3). The average noise correlation across all of the pairs in the young V1 area was 0.152, which remained at the same level as reported in previous studies (Gutnisky and Dragoi, 2008; Smith and Kohn, 2008; Kohn et al., 2016). For aged monkeys, the average of r_{SC} increased significantly to 0.295 (Mann–Whitney *U* test; $P < 0.0001$; Fig. 5C and Table 3).

DISCUSSION

In the present study, we examined the effects of aging on neuronal fine and coarse coding of orientation information in the V1 area of young and old rhesus monkeys. The results showed a clear decline in the information encoded for the small orientation difference but not for the large orientation difference. In addition, V1 neurons in aged monkeys showed increased maximum induced and spontaneous responses and decreased signal-to-

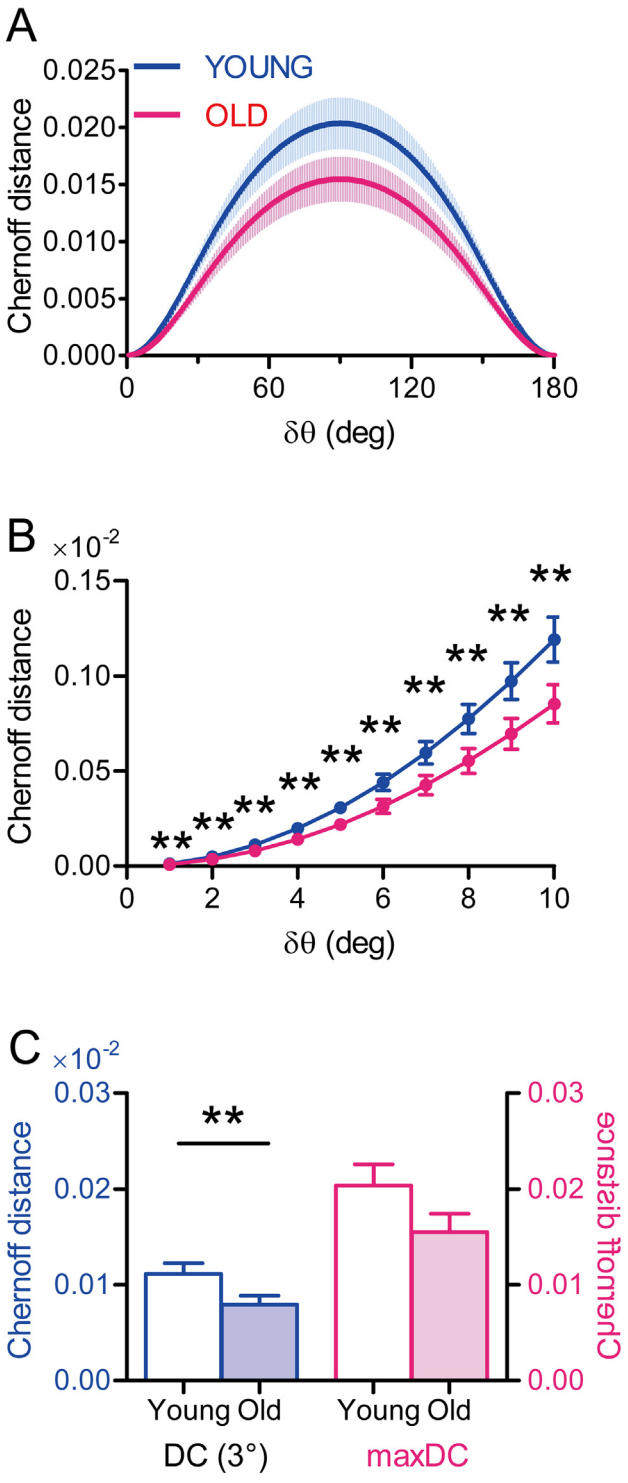

Fig. 3. The Chernoff distance of neurons in the young and old V1 areas. **(A)** Mean Chernoff distance at $\delta\theta$ from 1° to 180° for all neurons in young (blue) and old group (red). Shadows are error bars. **(B)** The Chernoff distance at $\delta\theta$ from 1° to 10°, which is significantly decreased from young to old group. **(C)** Comparison of the Chernoff distance between young and old groups. The DC(3°) (scaled as left *Y*-axis, in blue) shows a significant age-related decline. The DC(90°) (scaled as right *Y*-axis, in red) also shows a decline, but it is negligible. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

noise ratio, which is consistent with previous studies. Also, the changes in information coding during aging was accompanied by increased signal and noise correlation.

Previous psychophysical studies have reported that the ability of orientation, direction and speed perception decreases in the elderly population (Norman et al., 2003; Snowden and Kavanagh, 2006; Owsley, 2011). Using Gabor patterns, Delahunt et al. showed significantly increased orientation discrimination thresholds in the elderly population (Delahunt et al., 2008). And consistently, Tam also found the increase of orientation discrimination threshold (Tam, 2015). These findings are consistent with those of Betts et al. for low contrast stimuli (Betts et al., 2007). However, Roudaia et al. (2011), Betts, et al. (2007) and Govenlock et al. (2009a,b) both reported that the performance between young and old groups at high contrast levels was similar. It is still not clear now why the results of these studies differ in higher contrast, and further work may be required to resolve this issue. Meanwhile, we noticed that Betts found a significantly higher orientation threshold in older than younger subjects with low external noise, but not with high external noise (Betts et al., 2007). This finding was consistent with physiological studies that found elevated spontaneous activity (Hua et al., 2006), and the low external noise is similar to our living conditions. Although there was conflict, generally, these studies indicated impairment in the orientation perception for the old population such as extracting orientation information from low contrast stimuli or certain level of external noise. Moreover, the decrement of discrimination performance was significant for small orientation separations (fine discrimination) rather than larger separations (coarse discrimination) (Ball and Sekuler, 1986; Bennett et al., 2007; Betts et al., 2007; Govenlock et al., 2009a,b; Owsley, 2011).

However, the potential neuronal mechanism still remains unclear. Using the Chernoff distance, we investigated neuronal fine and coarse coding for orientation information in the primary visual cortex of old and young animals. Most measurements in study neuronal orientation property, e.g., OB and OSI are global measures of the responses to various orientations and are supposed to ignore local changes. As to tuning width, which might further considered the local property, however, it has been shown that its description of the shape of the tuning curve crest is still not sufficiently refined (Ringach et al., 2002). Thus, the ability of a single neuron in discriminating small stimuli differences cannot be described using these measures. Using Chernoff distance, we are able to exactly calculate the information encoded in every orientation difference, and thus compare the fine and coarse coding between young and aged groups simultaneously. The Chernoff distance is also directly related to Fisher information, which are widely used in neuroscience. Especially, as different from Fisher information, the Chernoff distance has not been restricted only in fine coding. Thus, it is more suitable to study the neuronal orientation discrimination (Kang et al., 2004; Jacob et al., 2016).

Table 1. Summary of DC(3°) and DC(90°) for neurons in young and aged V1 areas

Properties	Young (n = 128)	Old (n = 161)	Test	P value	Effect size
DC(3°) ($\times 10^{-2}$)	0.011 ± 0.001	0.008 ± 0.001	Mann–Whitney	0.007	0.261
DC(90°)	0.020 ± 0.002	0.015 ± 0.002	Mann–Whitney	0.091	0.198

Data for each group are shown as the mean value ± SEM. We statistically analyzed the comparisons between young and aged V1 neurons using the Mann–Whitney U test. The P values and effect sizes are shown.

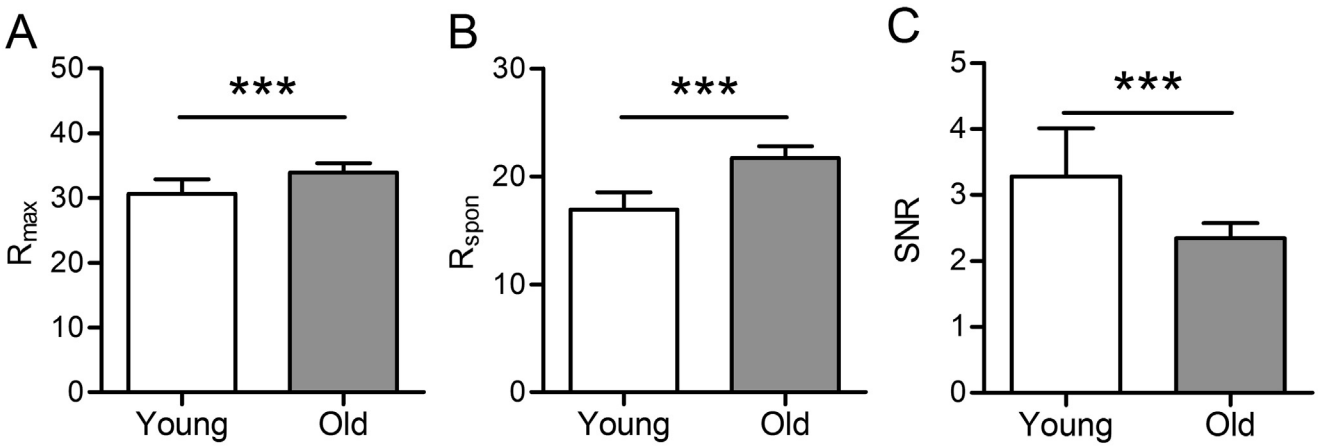

Fig. 4. Neuronal response properties for young and old monkeys. **(A)** Distribution of R_{max}. The R_{max} in the old monkeys increases significantly compared with the young monkeys. **(B)** Comparison of R_{spon} between the young and old monkeys. The R_{spon} in the old monkeys increases significantly compared with the young monkeys. **(C)** Comparison of the SNR in the young and old monkeys. The SNR in the old monkeys shows a clear decrease compared with the young monkeys.

Table 2. Summary of R_{max}, R_{spon} and SNR in young and aged V1 areas

Properties	Young	Old	Test	P value	Effect size
R_{max}	30.639±2.203	33.986±1.402	Mann–Whitney	0.006	0.160
R_{spon}	16.952±1.604	21.681±1.100	Mann–Whitney	0.0002	0.336
SNR	3.282±0.727	2.343±0.227	Mann–Whitney	< 0.0001	0.157

Data for each group are shown as the mean value ± SEM. We statistically analyzed the comparisons between young and aged V1 areas using Mann–Whitney U test. The P values and effect sizes are shown.

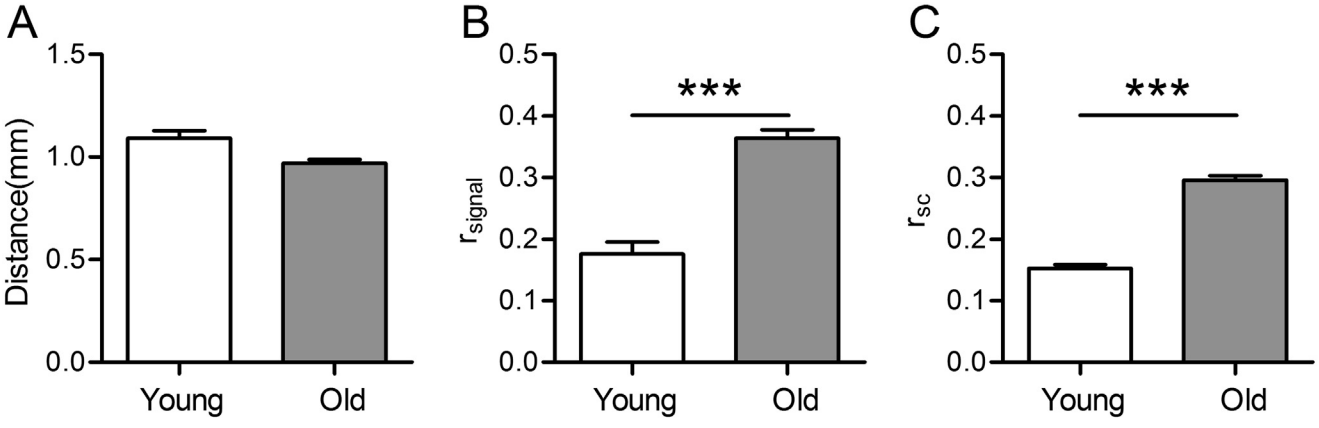

Fig. 5. Signal and noise correlation for young and old monkeys. **(A)** Comparison of the distances between paired neurons. The distance for the young and old groups does not have a significant difference. **(B)** Comparison of the r_{singal} between the young and old monkeys. The r_{singal} is positive for both the young and old monkeys and significantly increased from young to old. **(C)** Comparison of the r_{sc} in the young and old monkeys. The r_{sc} in the old monkeys shows a clear increase compared with the young monkeys.

By comparing the fine and coarse orientation information coding in the V1 area of young and old monkeys, we firstly found significantly decreased information in fine coding during normal aging. However, the coarse coding of single neurons in old monkey is comparable to that in young monkeys. Previous studies

Table 3. Summary of distance, r_{signal} and r_{SC} in young and aged V1 areas

Properties	Young	Old	Test	*P* value	Effect size
Distance (mm)	1.092±0.035	0.968±0.020	Mann–Whitney	0.160	0.158
r_{signal}	0.176±0.019	0.364±0.014	Mann–Whitney	< 0.0001	0.372
r_{SC}	0.152±0.007	0.295±0.010	Mann–Whitney	< 0.0001	0.564

Data for each group are shown as the mean value ± SEM. We statistically analyzed the comparisons between young and aged V1 areas using Mann–Whitney *U* test. The *P* values and effect sizes are shown.

have shown that senescence was accompanied by hyperactivity which is manifested by significant increased spontaneous activity and evoked response. It has been proposed that the cortical inhibitory system is damaged and result to the adverse changes in neuronal properties (Leventhal et al., 2003; Li et al., 2008; Liang et al., 2010; Wang et al., 2014). Indeed, through local administration of the GABAa receptor antagonist bicuculline, Leventhal et al. found a much weaker effect on neuronal responses in old than in young monkeys, which indicated a decline for GABAergic inhibition. While the neuronal response was decreased and neuronal function (orientation and direction selectivity) was improved after administration of GABA and the GABAa receptor agonist muscimol (Leventhal et al., 2003). Consistent with this, Hua et al. reported that the density of GABAergic neurons and the ratio of GABAergic neurons to total neurons in the V1 area of old cats were decreased significantly than young cats (Hua et al., 2008). In this study, we also found abnormally increased spontaneous response, maximum induced response and decreased signal-to-noise ratio. The attenuated cortical inhibition might be a potential reason for declined neuronal fine coding of orientation information.

It is well known that the nervous system represents the outside world using a large population of neurons, rather than single neurons (Georgopoulos et al., 1986; Sompolinsky et al., 2001; Kohn et al., 2016). To unravel the neuronal mechanism underlying the decline of visual function during normal aging, it is crucial to pay attention to the alteration of population coding, especially, the noise and signal correlation of neuronal responses. According to the computational model, if the response variability of neurons in a population was correlated, i.e., have high noise correlation, the information encoded by the population will decrease dramatically (Zohary et al., 1994; Panzeri et al., 1999; Averbeck et al., 2006; Kohn et al., 2016). In this study of V1 neurons, the signal and noise correlation are both positive and significantly increased in the aged monkeys. These confirmed our recent research found that the noise correlation increased in aging (Wang et al., 2019). Moreover, previous studies pointed out that fine coding depends more on neuronal interactions in a population (Samonds et al., 2003; Samonds and Bonds, 2004). Thus we think that a more seriously damaged fine coding than coarse coding in aging we observed there is because of the increases noise correlation. And it may further relate to the deteriorated behavior performance of old people in the fine orientation discrimination task.

Bair and colleagues divided the noise correlation into short-term (r_{ST}) and long-term (r_{LT}) components. They found that the noise correlation was predominantly r_{ST} (Bair et al., 2001). The comparable timescale of r_{ST} (10–100 ms) with the transient period in the transient-sustained firing pattern of neurons in the visual cortex reminded us of their implicit relationship (Kulikowski et al., 1979; Nelson, 1991; Priebe et al., 2002). The noise correlation we computed in this study was directly based on the spike rate between stimulus onset and end [total experimental time (TET)], with no divide of r_{ST} and r_{LT}. We believe, however, it was still meaningful to describe changes between young and aged V1 areas. In addition, the auto-correlations were responsible for long-term fluctuations. The long-term fluctuations, however, was uncorrelated between neurons. Moreover, the timescale of TET in our experiments (1 s) was not long enough to match the r_{LT} (many seconds to minutes) (Bair et al., 2001).

In summary, this study quantified the information of fine and coarse coding of neurons in aged V1 area using Chernoff distance, and revealed a significant decline in the fine coding, but not coarse coding. Together with the observation of enhanced noise correlation, these results may provide a neuronal substrate for the perceptual decline in the fine orientation discrimination task. As mentioned above, the GABAergic inhibitory circuit shows a deficit in the aging visual system and increasing the level of GABA could to some extent restore neuronal properties (at least, orientation selectivity). It shed light on the possibility to improve the performance of old people through enhancement of the inhibitory system.

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