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Aging affects the direction selectivity of MT cells in rhesus monkeys

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Abstract

The ability to accurately perceive the direction and speed of moving objects declines during normal aging. This is likely due to functional degradation of cortical neurons. Most neurons in the primate middle temporal area (MT) are direction-selective and their activity is closely linked to the perception of coherent motion. We investigated the mechanisms that underlie this age-related decline by comparing the proportions of direction-selective MT cells in old and young macaque monkeys, using *in vivo* single-cell recording techniques. Our results showed that the proportion of such cells was lower in old than in young monkeys. Moreover, one type of direction-sensitive cells, pattern cells, was especially sensitive to aging and was affected more severely than another class, component cells. We also found that direction selectivity was affected more severely in MT than in V1 of senescent monkeys. Thus, the functional degradation of MT and V1 cells may mediate perceptual decline in visual motion tasks in old primates.

Keywords: Aging; Area MT; Degradation; Direction selectivity; Monkey; Pattern cell

1. Introduction

The ability to accurately perceive the direction and speed of moving objects is critical for survival. Many psychophysical studies (Habak and Faubert, 2000; Kline et al., 2001; Norman et al., 2000, 2003; Snowden and Kavanagh, 2006; Stanford and Pollack, 1984; Tran et al., 1998; Trick and Silverman, 1991; Willis and Anderson, 2000; Wist et al., 2000) have shown that this ability declines in humans during normal aging. This cannot be due to optical changes or changes in the retina alone (Ball and Sekuler, 1986). Therefore, it has been hypothesized that this decline results from functional degradation in central visual areas (Spear, 1993; Spear et al., 1994).

The mechanisms that underlie the visual decline that accompanies aging have been investigated using single-cell recording techniques in different visual areas. Studies have provided evidence that the effects of aging on the dorsal lateral geniculate nucleus (dLGN) are minor, while those in the striate cortex (V1) and extrastriate cortex (V2) are severe (Hua et al., 2006; Schmolesky et al., 2000; Spear et al., 1994; Yu et al., 2006). Both the orientation and direction selectivity of V1 and V2 cells degrade during senescence. These declines are accompanied by hyperactivity and decreased signal-to-noise ratios. Such hyperactivity and decreased selectivity are thought to be due to the degradation of GABA-mediated inhibition within the visual cortex (Schmolesky et al., 2000; Leventhal et al., 2003).

It is known that direction-selective neurons play an important role in motion processing. V1 cells are involved in early stages of motion perception. Motion-sensitive neurons in this area respond to the 'component' motion of moving stimuli (Movshon et al., 1986). These cells signal motion that is orthogonal to their preferred orientations. Recent studies

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(Schmolesky et al., 2000; Yu et al., 2006) have shown that aging reduces the direction selectivity of V1 cells. To date, nothing is known about age-related changes in later stages of motion processing.

The middle temporal area (MT or V5) of the extrastriate cortex has been linked to higher order motion detection. In this area, more than 90% of the neurons are direction-selective (Maunsell and van Essen, 1983). A proportion of MT direction-selective neurons are pattern cells (Albright, 1984; Movshon et al., 1986). These cells can detect the direction of moving objects independently of their particular spatial pattern. Thus, the responses of these cells can be equated with human perception (Movshon et al., 1986). In fact, a population of pattern cells exists in human MT+, and the activity of these neurons is closely linked to the perception of coherent pattern motion (Huk and Heeger, 2002).

We studied the effect of aging upon MT cells in macaque monkeys by comparing the proportion of pattern cells and the degree of direction selectivity of MT cells in young and old monkeys. In order to investigate whether MT cells simply inherit degradation from the primary visual cortex, areas V1 and MT were studied in the same animals.

2. Materials and methods

2.1. Electrophysiology

We recorded extracellularly cells' response in area MT of three young adult (4–6 years old) and four old (23–31 years old) male rhesus monkeys (*Macaca mulatta*). Area V1 was also studied in all three young and two of the four old monkeys. Monkeys were examined ophthalmoscopically prior to recordings, and had no apparent optical or retinal problems that could impair visual function. Retinal blood vessels, lens clarity and the maculae were all within normal limits. Monkeys were prepared for electrophysiological recording using standard techniques consistent with the Society for Neuroscience and National Institute of Health guidelines. The experiments described here were approved by the University of Utah Institutional Animal Care and Use Committee.

The techniques used in our laboratory have been reported in detail elsewhere (Schmolesky et al., 2000). Monkeys were sedated with ketamine HCl (10 mg/kg). Intravenous and tracheal cannulae were inserted. A mixture of D-tubocurarine (0.4 mg/kg/h) and gallamine trithiodide (7 mg/kg/h) was infused intravenously to induce and maintain paralysis. Monkeys were ventilated, and anesthesia was maintained with a mixture of N_2O (75%), O_2 (25%) and halothane (0.25–1.0%) as needed. Expired CO_2 was maintained at approximately 4%. Body temperature was maintained at 38 °C. Heart rate, ECG and cortical electrical activity were monitored throughout the experiment to assess the level of anesthesia.

After the animal was placed on life support, we adjusted the level of anesthesia so that all the vital signs were comparable in young and old animals. For the MT area, a hole with a 4-mm radius was centered 2 mm posterior to the ear bar and 15 mm lateral to the midline. For the V1 area, a hole with a 4-mm radius was centered 3 mm posterior to the ear bar and 2 mm lateral to the midline. Holes were filled with a 4% solution of agar in saline and sealed with Vaseline. The eyes were protected from desiccation with contact lenses. The locations of the optic discs and foveae were determined repeatedly during the course of each recording session. The normality of the optics and retinal vasculature was monitored throughout the experiment. No visible deterioration in optics occurred during the experimental period in either old or young animals. We recorded extracellular action potentials with glass microelectrodes filled with 3 M NaCl solution (impedance, 2–3 MΩ). MT cells were studied at eccentricities ranging from 2 to 40°, but the majority of cells were between 2 and 15°. The electrode was advanced using a hydraulic microdrive (David Kopf Instruments, Tojunga, CA, USA).

2.2. Visual stimulus

We displayed all visual stimuli at a resolution of 1024 × 768 pixels and frame rate of 100 Hz on a 17-in. color monitor Mutiscan G220 (Sony, Japan). The center of the video monitor was placed 57 cm from the animals' eyes. Visual stimulus patterns were drifting sinusoidal gratings (Fig. 1A) and plaids (Fig. 1B) in an oval aperture. Plaids were composed of two overlapping sinusoidal gratings that differed in direction by 120°. The program that generated the stimulus was written in MATLAB, using the extensions provided by the high-level Psychophysics Toolbox (Brainard, 1997) and low-level Video Toolbox (Pelli, 1997). The mean luminance of the display was 38.7 cd/m^2. For stimulus presentation, a blank screen of mean luminance was first presented for 3 s. The stimulus then appeared and started to move. After moving, the stimulus remained on the screen for 0.5 s. After a single unit was isolated, the cell's receptive field was carefully mapped by presenting a series of computer-generated sinusoidal gratings and spots in the preferred direction. The optimal spatial and temporal parameters for the unit were then determined. After the initial characterization of each cell, optimal sinusoidal gratings moving randomly in 24 different directions were used to compile the orientation and direction tuning curves. The contrast of each stimulus was 99%.

2.3. Data collection and analysis

The responses of isolated cells were amplified with a microelectrode amplifier (DAGAN, USA). The signal was then fed into an oscilloscope, audio monitor, and digitized using an acquisition board (National Instruments, USA) controlled by IGOR software (WaveMetrics, USA). The responses of the cells to the drifting stimuli were stored in the computer for later analysis. Baseline firing rates were

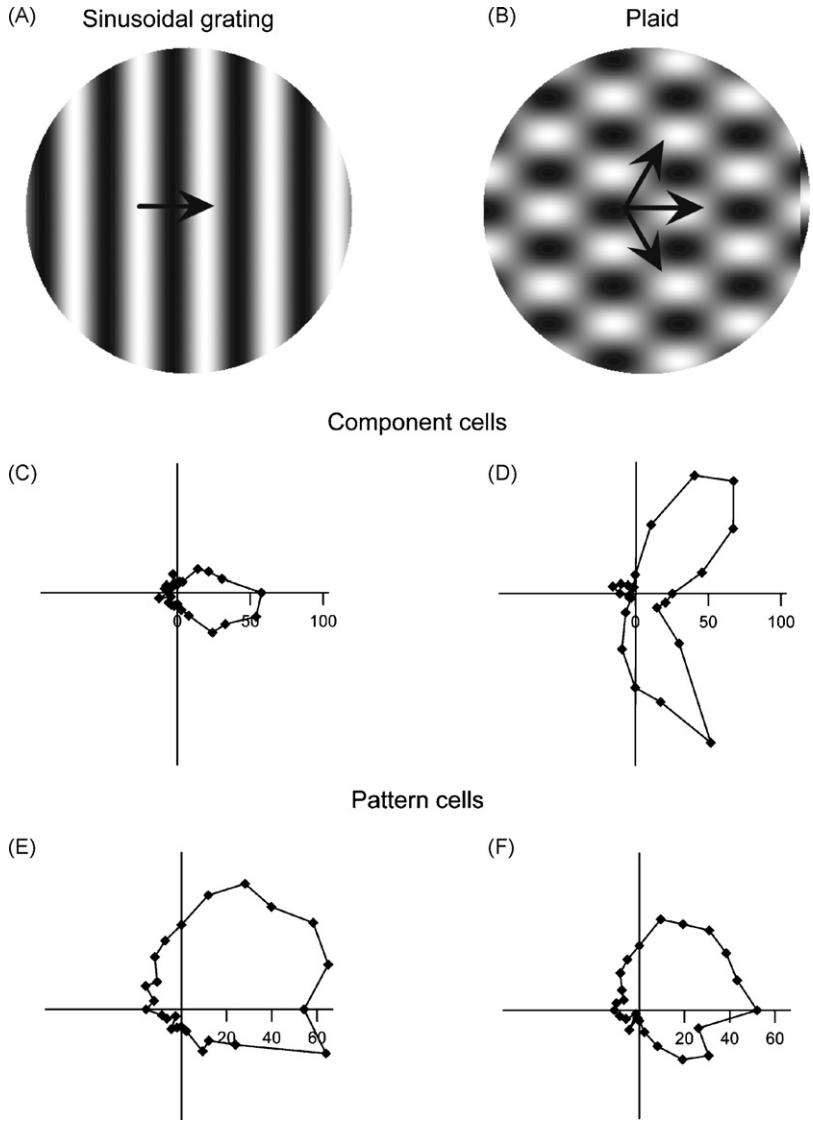

Fig. 1. The sinusoidal grating and plaid patterns used in our experiments are shown in A and B. Most cells in MT were tuned for the direction of drifting gratings. Some MT cells responded selectively to pattern motion, whereas others responded to the motion of stimulus components. MT cells were classified into component and pattern cells based upon their responses. Responses of component and pattern cells to sinusoidal gratings are illustrated in the polar graphs in C and E, respectively. Responses of the component and pattern cells to plaids are shown in D and F, respectively.

obtained during a time window of 0.5–1 s before each stimulus. Spontaneous activity was defined as the mean of the baseline values. Spontaneous activities below 1 spike/s were set equal to 1 spike/s for the signal-to-noise ratio analysis (Schmolesky et al., 2000).

Direction selectivity was calculated for each cell using statistical methods described in detail elsewhere (Leventhal et al., 1995). Briefly, the responses of each cell to the different stimulus directions were stored as a series of vectors. The vectors were added and divided by the sum of the absolute values of the vectors. The angle of the resultant vector gave the preferred direction of the cell. The length of the resultant vector, termed the direction bias, provided a quantitative measure of the direction sensitivity of the cell.

2.4. Analysis of MT pattern and component data

Partial correlations for the pattern and component selectivity were computed using the standard methods of Movshon et al. (1986). For each cell, we used the responses to sinusoidal gratings to determine the direction tuning of pattern and component cells. The direction tuning in response to sinusoidal gratings was used to classify pattern cells. The sum of this same direction tuning rotated 60° clockwise and counterclockwise was used to classify component cells. Partial correlations were carried out to determine whether the actual responses to plaids were consistent with the response predicted for pattern or component cells. Correlations were computed using the pairs of actual and expected responses for all directions of stimulus motion. The equations for partial

correlations were:

$$R_p = \frac{(r_p - r_c r_{pc})}{\sqrt{(1 - r_c^2)(1 - r_{pc}^2)}} \quad (1)$$

and

$$R_c = \frac{(r_c - r_p r_{pc})}{\sqrt{(1 - r_p^2)(1 - r_{pc}^2)}} \quad (2)$$

where r_c and r_p are the correlations of the actual direction tuning for plaids for component and pattern predictions, and r_{pc} is the correlation of the two predictions. Because the distribution of Pearson's r is not normal, Fisher's Z transformation was employed to stabilize the effects of variance in our study (Smith et al., 2005). We converted each value of R_p and R_c to a Z-score using the following equations:

$$Z_p = \frac{\ln\ (1 + R_p/1 - R_p)}{2\sqrt{1/df}} \quad (3)$$

and

$$Z_c = \frac{\ln\ (1 + R_c/1 - R_c)}{2\sqrt{1/df}} \quad (4)$$

where df is the degree of freedom. We used a criterion of 1.28, equivalent to $p = 0.90$, for testing the significance of Z_c and Z_p. If Z_p exceeded the greater of zero and Z_c by 1.28, the cell was judged to be a pattern cell. Similarly, if Z_c exceeded the greater of zero and Z_p by 1.28, the cell was judged to be a component cell. If the cell did not meet either of the foregoing conditions, it was placed in the unclassified group.

2.5. Analysis of half-width at half-height

We also used another measure, half-bandwidth, to determine the degree of direction selectivity. Half-bandwidth is a measure that depends upon the shape of the tuning curve around its peak. It is not sensitive to the overall shape of the curve (Ringach et al., 2002). This measure of selectivity was calculated from the data as follows. The direction tuning curves were first fitted with the von Mises function (a circular approximation to the Gaussian function):

$$R = R_p\, e^{b\cos(\theta - x_c)} \quad (5)$$

where R represents the response of the cell as a function of direction θ, R_p is the value of the function at the preferred orientation x_c, and b is a width parameter. Then, the half-width of the tuning curve at half-height (HWHH) was used to describe the tuning width. It was calculated as follows:

$$\mathrm{HWHH} = ar\cos\left(\frac{\ln 0.5 + b}{b}\right) \quad (6)$$

3. Results

We recorded a total of 84 MT cells from three young monkeys (4–6 years old) and 98 cells from four old monkeys (23–31 years old). All data were collected from three to five penetrations in each monkey. The recording depths and eccentricities of the cells studied were comparable in young and old groups. The length of the penetration and cortical thickness in coronal sections were comparable in old and young monkeys. For each cell, we measured responses to sinusoidal gratings and plaids. Sixty-four young and 70 old MT cells were classified into three types. Twenty cells from young animals and 28 from old animals were excluded because responses to plaids were not measured. In area V1, we measured responses to sinusoidal gratings. The data from 67 V1 cells in all three young monkeys studied and 46 V1 cells in two of the four old monkeys studied were recorded and analyzed. Direction selectivity (known as direction bias or DB) was calculated for each cell using statistical methods described in detail elsewhere (Leventhal et al., 1995).

Drifting sinusoidal gratings and plaids used in the present experiment are illustrated in Fig. 1A and B. Most cells in MT were tuned for the direction of a drifting grating (Fig. 1C and E). When plaid stimuli were presented, some MT cells responded selectively to the motion of stimulus components (Fig. 1D), whereas other cells responded to the pattern motion independently of their particular spatial pattern (Fig. 1F). The former are termed component cells and the latter are called pattern cells. Cells that do not fall into these two categories are defined as unclassified cells.

3.1. Proportions of component, pattern and unclassified cells

Our results provided evidence for a reduced proportion of pattern cells in area MT of old monkeys. The distribution of component, pattern and unclassified cells in young and old monkeys is shown in Fig. 4E. The class boundaries separated the MT cells into component, pattern and unclassified cells. The diamonds, squares and circles represent component, pattern and unclassified cells, respectively. Different colors were used to discriminate the age groups (see legend to Fig. 4E for details).

Table 1 shows the proportions of component, pattern and unclassified cells in young and old monkeys. Contingency tables and χ^2 testing for statistical evaluation were used to determine the age-related changes in the properties of these types of cells. Notice that the percentage of pattern cells was decreased in old monkeys (11.4%; 8 of 70) compared with young controls (28.1%; 18 of 64; χ^2 test, $p < 0.05$). The percentage of component cells in old monkeys (22.9%; 16 of 70) was the same as that in young controls (23.4%; 15 of 64; χ^2 test, $p = 0.94$). The percentage of unclassified cells in old monkeys was higher but the difference was not significant (31 of 64 in young monkeys, 46 of 70 in old monkeys; χ^2 test, $p = 0.10$).

Table 1
Proportions of component, pattern and unclassified cells in old and young monkeys

	Pattern cells	Component cells	Unclassified cells
Young ($n=64$)	18 (28.1%)	15 (23.4%)	31 (48.4%)
Old ($n=70$)	8 (11.4%)	16 (22.9%)	46 (65.7%)
p value	$p=0.015$	$p=0.94$	$p=0.10$

Percentages of different types of cells in area MT of old and young monkeys. The percentage of pattern cells decreased in old monkeys (11.4%; 8 of 70) compared with young controls (28.1%; 18 of 64; χ^2 test, $p<0.05$). The proportions of component cells did not show age-related changes. The percentage of unclassified cells increased in old monkeys but did not reach statistical significance ($p=0.10$). These results provide evidence for a significant decrease in the percentage of pattern cells in area MT in old monkeys.

The foregoing results provided evidence for a significant decrease in the proportion of pattern cells in MT cells of old monkeys. It was notable that the proportions of component and pattern cells were 23.4 and 28.1%, respectively, in the young group. This is consistent with previous studies (Movshon et al., 1986; Priebe et al., 2003). In order to investigate this, a lower criterion of 1.04, equivalent to $p=0.85$, was used for testing significance. Consistent with the criterion of 1.28, the proportion of pattern cells in old MT area also showed a significant decrease (19 of 64 in young monkeys, 9 of 70 in old monkeys; χ^2 test, $p=0.017$) relative to that in young controls.

3.2. Direction selectivity

Most neurons in young area MT exhibit strong direction selectivity and play an important role in motion processing (Albright, 1984; Britten et al., 1992; Movshon et al., 1986; Newsome and Pare, 1988). Fig. 2 illustrates the direction-selective visual responses of typical MT neurons recorded from young and old monkeys. The tuning curves and corresponding polar plots obtained from old monkeys (Fig. 2A–C) were much broader than those obtained from young monkeys (Fig. 2D and E). Thus, direction selectivity was weaker in old than in young monkeys.

DBs were calculated for 84 young and 98 old monkey MT cells. Direction selectivities of young and old monkey cells are shown in Table 2, Figs. 2 and 3D. The percentage of MT neurons showing strong direction selectivity (DB ≥ 0.2) was smaller in old monkeys (40.8%; 40 of 98) than in young controls (90.5%; 76 of 84; χ^2 test, $p \ll 0.001$). The percentage of cells that were very strongly biased for direction (DB ≥ 0.4) was affected by aging even more severely. The percentage of such cells was decreased in old animals (8.2%; 8 of 98) compared with young controls (50.0%; 42 of 84; χ^2 test, $p \ll 0.001$). We also analyzed the distribution of DBs of cells in old and young monkeys. This is shown in Fig. 3D. We found that MT cells in old monkeys exhibited significantly lower DB (0.19 ± 0.12, $n=98$) than in young monkeys (0.40 ± 0.13, $n=84$; t test, $p \ll 0.001$). In order to provide a second measure of direction tuning, we studied direction half-width in old and young monkeys. This is shown in Table 2, Figs. 2 and 3E. MT cells in old monkeys exhibited significantly broader half-widths at half-height ($98.71 \pm 60.01^\circ$, $n=98$) than do cells in young monkeys ($55.21 \pm 23.13^\circ$, $n=84$; Mann–Whitney test, $p \ll 0.001$). In summary, old monkey MT cells displayed lower DBs and broader half-widths than young monkey cells did, which confirmed that age dramatically reduced direction selectivity.

We also studied the effects of age upon different types of direction-sensitive cells in MT. MT cells were classified into component, pattern and unclassified cells. Fig. 4 illustrates the distribution of DB for these three types of MT cells. The DB of component cells in old monkeys declined to 0.25 ± 0.16 ($n=16$) compared with young controls (0.40 ± 0.12, $n=15$; t test, $p<0.01$). The DB of pattern cells in old monkeys declined to 0.25 ± 0.14 ($n=8$) compared with cells in young controls (0.45 ± 0.12, $n=18$; t test, $p<0.001$). The DB of unclassified cells in old monkeys declined to 0.18 ± 0.11 ($n=46$) compared with young controls (0.40 ± 0.13, $n=31$; t test, $p \ll 0.001$). In short, all types of MT cells in old monkeys showed a significant decrease in direction selectivity compared with young controls (shown in Table 2, Fig. 4D).

Area MT receives projections from V1 (Anderson et al., 1998; Anderson and Martin, 2002; Felleman and Van Essen, 1991; Maunsell and van Essen, 1983; Rockland, 1989, 1995), as well as from other areas. We have shown that the receptive field properties of cells in area V1 degrade during aging (Hua et al., 2006; Leventhal et al., 2003; Schmolesky et al., 2000; Wang et al., 2006, 2005; Yu et al., 2006). It is not surprising, therefore, that we observed decreased direction selectivity in MT. In order to investigate whether MT cells simply inherit such degradation from the primary visual cortex, cells in area V1 were also investigated in the present study. Sixty-seven V1 cells in young monkeys and 46 cells in old monkeys were recorded and analyzed. V1 and MT cells were recorded from the same animals. The percentage of V1 neurons showing significant DBs (>0.1) in old monkeys (19.6%, 9 of 46) was less than that in young monkeys (58.2%, 39 of 67, χ^2 test, $p<0.001$). The percentage of cells showing strong DBs (>0.2) in old monkeys (8.7%, 4 of 46) was also less than that in young monkeys (32.8%, 22 of 67, χ^2 test, $p \ll 0.001$). The overall direction selectivity of V1 cells was also analyzed (Fig. 5). The mean DB of V1 cells was lower in old monkeys (0.08 ± 0.07; $n=46$) than in young controls (0.20 ± 0.18; $n=67$; Mann–Whitney, $p \ll 0.001$). These results confirm our previous studies (Schmolesky et al., 2000; Yu et al., 2006).

The distribution plots of DB values for V1 and MT are shown in Fig. 5. The decrease in mean DB in young and old V1 and MT was 0.12 and 0.21, respectively (Table 2). A larger decrease (increasing from 0.12 to 0.21) was found in MT area. To further examine this result, two-way ANOVA was applied to the dataset obtained from V1 and MT in old and young animals. The results revealed effects of brain area ($F_{1,226}=49.22$, $p \ll 0.001$) as well as age ($F_{1,226}=97.65$,

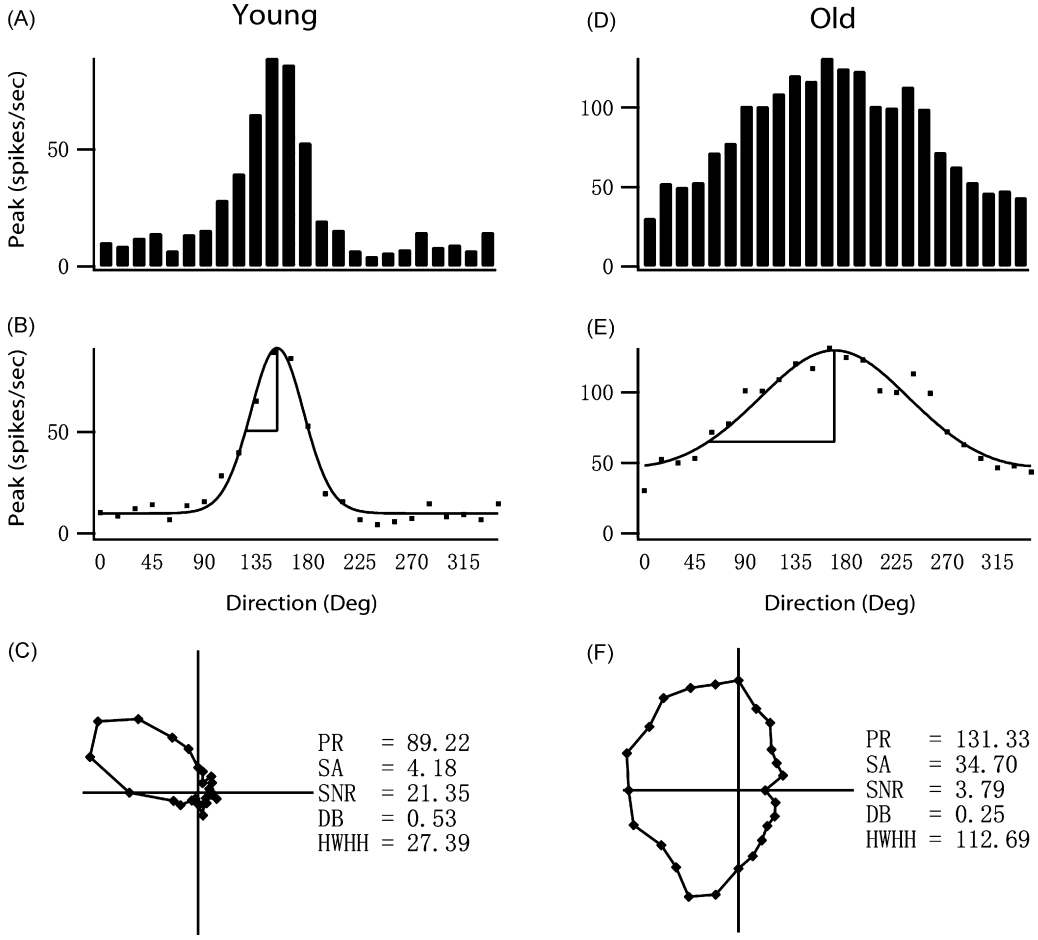

Fig. 2. Tuning curves and corresponding polar plots obtained from young monkeys (A–C) and old monkeys (D–F). The stimuli were drifting sinusoidal gratings, randomly varied in 24 directions, which ranged from 0 to 360° in 15° steps. Each point in the polar and curve-fitting graph represents the response to the stimulus moving in the indicated direction. The peak response (PR), spontaneous activity (SA), signal–noise ratio (SNR), DB and HWHH are shown. HWHH was determined by fitting the tuning curves with a circular Gaussian function. MT cells in old monkeys exhibited reduced SNRs and DBs, as well as increased PRs and SA.

$p \ll 0.001$) on direction selectivity. More importantly, the interaction of age and brain area ($F_{1,226} = 13.77$, $p \ll 0.001$) demonstrated that the decline in MT was more than in V1. To minimize the effects of individual variation, we excluded the monkeys for which we only had data for V1 or MT. Therefore, 67 young V1 cells and 84 young MT cells, as well as 46 old V1 cells and 33 old MT cells, were analyzed using two-way ANOVA. This analysis confirmed that MT cells were affected by age more severely than V1 cells. Therefore, it is reasonable to conclude that the functional changes in MT

Table 2
Descriptive statistics of visual response properties of MT cells in young and old monkeys

Properties	YM cells	OM cells	Statistical test	p value
Peak response (spikes/s)	85.70 ± 31.1	114.0 ± 34.2	Two-sample t test	$p \ll 0.001$
Spontaneous (spikes/s)	10.20 ± 5.0	25.6 ± 13.0	Two-sample t test	$p \ll 0.001$
Signal–noise ratio	10.10 ± 5.46	5.81 ± 3.93	Mann–Whitney	$p \ll 0.001$
HWHH (°)	55.21 ± 23.13	98.71 ± 60.01	Mann–Whitney	$p \ll 0.001$
DB	0.40 ± 0.13	0.19 ± 0.12	Two-sample t test	$p \ll 0.001$
DB (pattern cells)	0.45 ± 0.12	0.25 ± 0.14	Two-sample t test	$p < 0.001$
DB (component cells)	0.40 ± 0.12	0.25 ± 0.16	Two-sample t test	$p < 0.01$
DB (unclassified cells)	0.40 ± 0.13	0.18 ± 0.11	Two-sample t test	$p \ll 0.001$
DB (V1)	0.20 ± 0.18	0.08 ± 0.07	Mann–Whitney	$p \ll 0.001$

Two group comparisons of peak response, spontaneous, signal–noise ratio, HWHH and DB of cells in area MT (unless noted in parentheses) in young and old monkey. Independent sample t test or Mann–Whitney test were used depending upon the normality of sample. Data are presented as mean ± S.D. YM, OM: young monkeys and old monkeys, respectively.

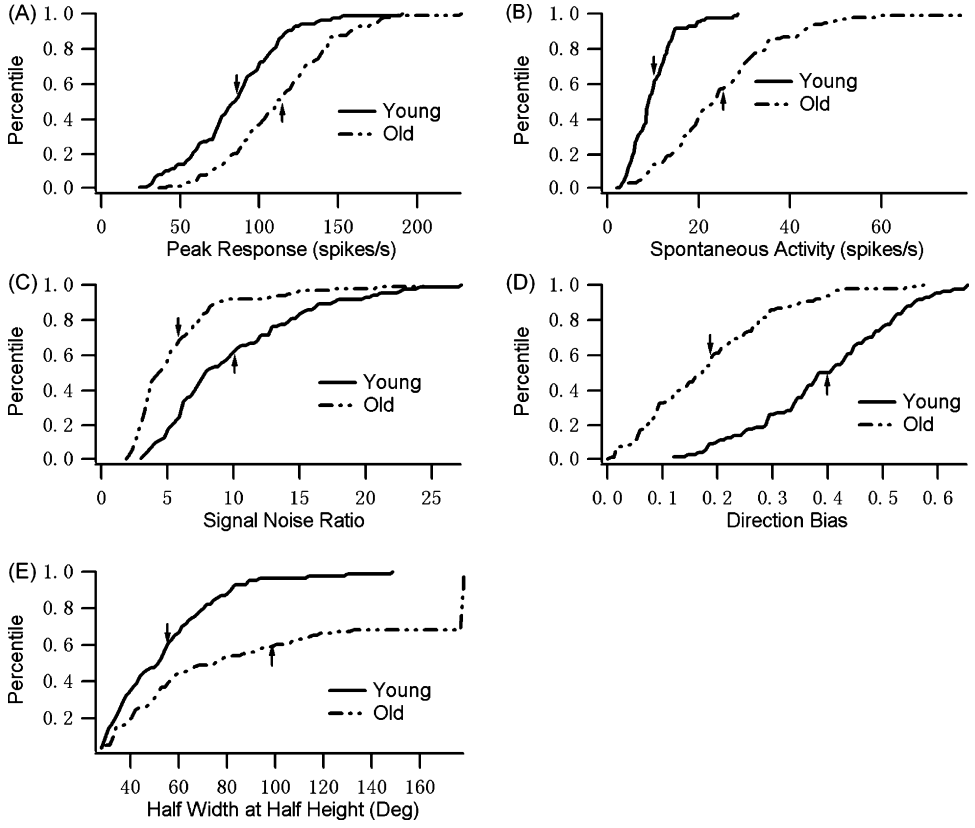

Fig. 3. Cumulative distribution of PR, SA, SNR, DB and HWHH in young and old monkey MT cells. The percentage of young ($n = 84$) and old ($n = 98$) monkey cells with any given PR (A), SA (B), SNR (C), DB (D) and HWHH (E) is shown in cumulative distribution plots. Solid and dashed lines represent the data for young and old monkeys, respectively. The arrow on the line indicates the mean value. Old monkey cells showed increased SA and PR, and decreased SNR and DB values compared with young monkey cells. Cells in old monkeys also exhibited much wider HWHH values.

cells may have been the result of both V1 inputs and changes within MT.

3.3. Peak response, baseline activity and signal–noise ratio

In order to investigate the relationship between the decrease in direction selectivity and age-related changes in neuronal responsiveness, we analyzed the spontaneous and visually evoked (peak) responses of all recorded MT cells. In line with our previous findings (Hua et al., 2006; Leventhal et al., 1995, 2003; Schmolesky et al., 2000; Wang et al., 2005; Yu et al., 2006), MT cells in old monkeys showed significantly increased spontaneous and peak responses compared with young monkey cells (Table 2, Figs. 2 and 3A–C). Spontaneous response was affected more severely than peak response. Ninety-five percent of cells in young monkeys showed spontaneous responses less than 20 spikes/s. In contrast, only 37.8% of cells in old monkeys exhibited spontaneous responses less than 20 spikes/s. Overall, old monkey cells increased their spontaneous response by 151%. The peak responses of old cells increased only by 33.0%. The greater increase in spontaneous responses results in a dramatic decrease in signal-to-noise ratio in old monkeys.

4. Discussion

In the present study, we examined the effects of aging upon the response properties of cells in areas MT and V1 in macaque monkeys. The results show that the proportion of pattern cells in MT decreases in old macaques. A comparison of direction selectivity of areas V1 and MT in old and young monkeys provides evidence that DB in cells in both areas decrease in old monkeys. MT cells showed a larger decrease than V1 cells did. These age-related changes were accompanied by increases in peak response and spontaneous activity, as well as a decrease in signal-to-noise ratio. Taken together, our results indicate that functional degradation occurs in both areas of MT and V1 during normal aging, and that area MT is affected by aging more severely than the striate cortex is. Such functional degradation in area MT may contribute to the decline in perception of moving objects during normal aging.

4.1. Age-related proportional changes of pattern cells

Our results show that the proportion of pattern cells in MT decreases in old monkeys. Two hypotheses might explain this. The first is that a selective loss of pattern cells, but

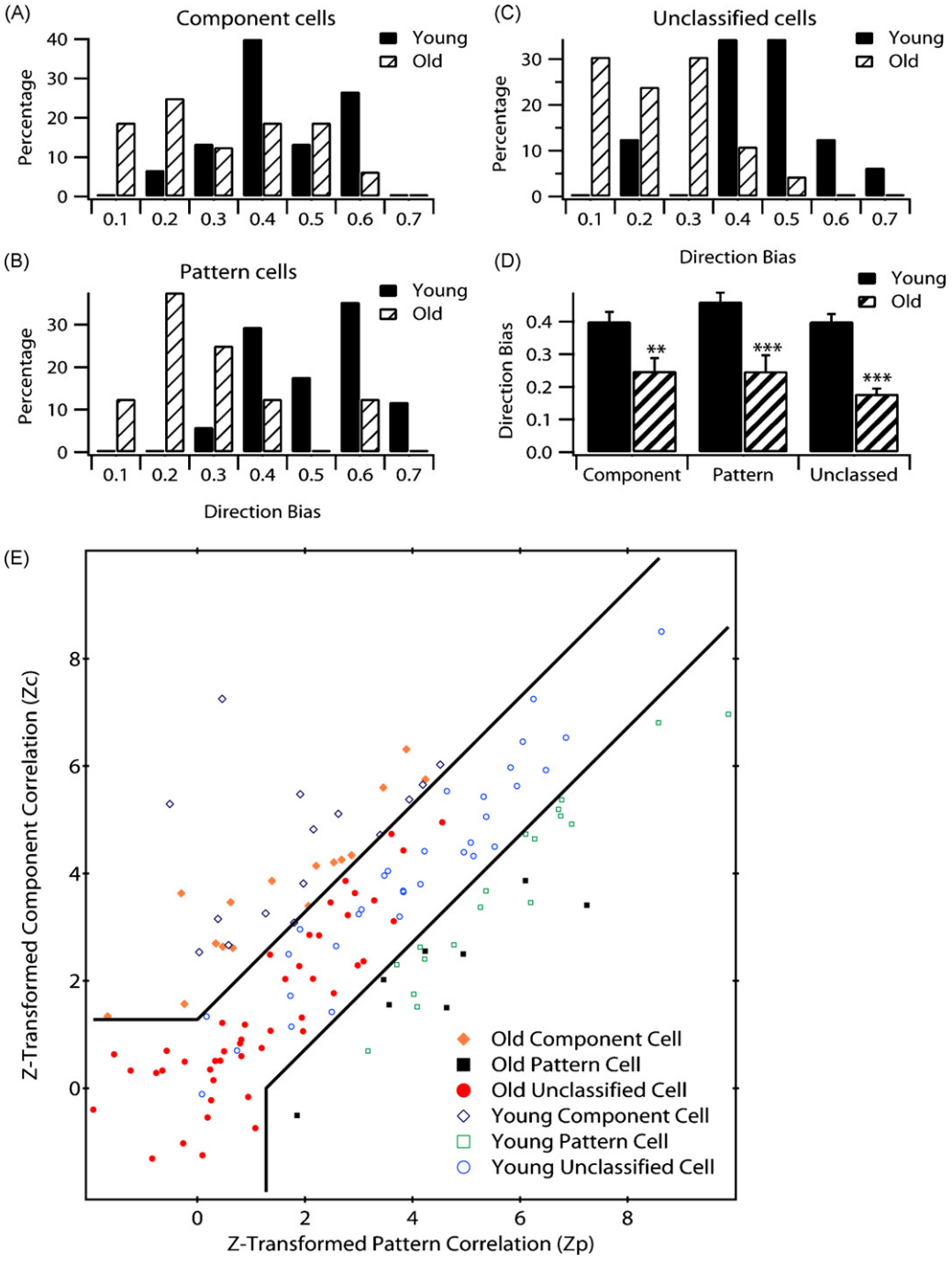

Fig. 4. The percentages of cells with different DB in old and young monkeys. Component, pattern and unclassified cells are shown in separate histograms (A–C). The histograms for the three types of cells in old monkeys were shifted leftward relative to those for young monkeys. This indicates that direction selectivity decreased for all types of cells in old monkeys. D shows comparisons for young and old monkeys for the three types of cells. All types of old MT cells showed significant decreases in direction selectivity compared with young controls. Scatter plot E illustrates the distribution of component, pattern, and unclassified cells in young and old monkeys. The class boundaries represent differences between Z_p versus Z_c values that have a 0.1 probability of arising by chance. The scatter plots represent different cell types and age groups.

not other cell types, occurs in old MT. However, evidence from neuronal counts has shown that cell number is minimally changed in the aging cortex (Morrison and Hof, 1997; Peters et al., 1998; Rapp and Gallagher, 1996). This evidence seems to argue against the foregoing hypothesis. The second hypothesis involves functional degradation of MT cells during aging. It has been suggested that motion processing in the visual cortex occurs in at least two stages (Adelson and Movshon, 1982). In the first stage, the motion of 1D patterns appears to be analyzed by component cells in V1 and MT. In the second stage, pattern cells combine inputs from component cells to compute the true direction of 2D patterns.

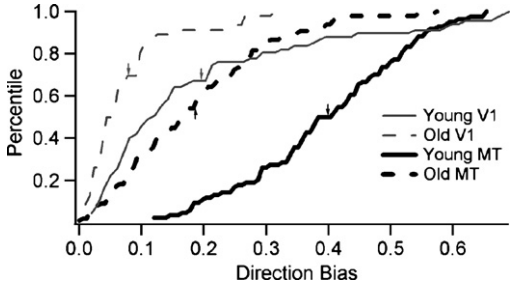

Fig. 5. The percentages of cells with any given DB in areas V1 and MT are shown in the cumulative distribution plots. Solid and dashed lines represent the data for young and old monkeys, respectively. Gray and black lines represent the data for areas V1 and MT, respectively. The arrows indicate mean values. Two-way ANOVA tests were applied to the dataset for areas V1 and MT using age and brain area as variables. The results revealed a significant affect of brain area ($F_{1,226} = 49.22$, $p \ll 0.001$), as well as age ($F_{1,226} = 97.65$, $p \ll 0.001$) on direction selectivity. The results ($F_{1,226} = 13.77$, $p < 0.001$) demonstrate that MT was affected more severely than V1.

Functional degradation of one of the stages, especially the second, obstructs pattern cells from computing the direction of moving plaids. To put it another way, such degradation causes pattern cells to be classified into unclassified cells, even component cells. As a result, the number and proportion of pattern cells decrease in old monkeys. Consistent with this hypothesis, we found component and pattern cells exhibited degraded direction selectivity, which was affected more severely in area MT than in area V1. In summary, it is reasonable to conclude that pattern cells degrade into other cell types in old MT.

4.2. Mechanistic considerations

The age-associated degradation reported here might be a consequence of age-associated cellular alterations. Although other work has proposed that cognitive decline arises from widespread and substantial loss of cortical neurons in old brains, recent evidence suggests that the number of cortical neurons is largely preserved in aged macaque monkeys and humans (Morrison and Hof, 1997, 2007; Peters et al., 1998, 1996; Wong, 2002). In particular, studies in the superior temporal sulcus (STS) have failed to detect an age-related loss in humans and macaques (Duan et al., 2003; Morrison and Hof, 2007). MT is a small, elliptically shaped area on the posterior bank of the STS, which furnishes corticocortical projections that have long, complex dendritic arbors and massive spines to prefrontal area 46. MT neurons can be identified by retrograde transport from prefrontal area 46. Retrogradely labeled neurons show statistically significant age-related decreases in spine numbers and density of both apical and basal dendritic arbors (Duan et al., 2003). Abnormalities in these pre- and post-synaptic structures might have contributed to the functional degradation of MT cells presented here.

Neurochemical changes may also be involved in the degradation of senescent visual cortex. Our results show that MT cells in old monkeys exhibit increases in peak response and spontaneous activity, as well as decreased direction selectivity. This suggests that degradation of inhibitory intracortical circuits may occur in old animals. Schmolesky et al. (2000) have suggested that degradation of inhibitory intracortical circuits in old monkey cortex may account for hyperactivity and many of the functional changes that they found in V1. Furthermore, administration of GABA and its agonists can suppress hyperactivity in old brains and improve neural function in old monkeys (Leventhal et al., 2003). Studies of human visual cortex have shown that L-glutamic acid decarboxylase, an enzyme needed to synthesize the inhibiting transmitter GABA, is reduced during aging (McGeer and McGeer, 1976). Recent psychophysical work has also suggested decreased inhibitory function in old humans (Betts et al., 2005; Butler and Zacks, 2006). It has been reported that GABAergic interneurons are widely distributed in macaque MT (Thiele et al., 2004). Therefore, the functional degradation of MT cells that we observed was also likely to have been due to decreased GABAergic inhibition.

The visual system combines motion signals from multiple component cells to compute pattern motion. A model has been proposed to understand the computations performed by pattern cells in MT (Rust et al., 2005, 2006). It is suggested that strongly tuned inhibition suppresses the response of pattern cells to the individual plaid components. This suppression results in tuning for the direction of plaid motion. In component cells, however, such suppression is weak or absent. Given that inhibition appears to be weak in the old brain, it is reasonable to expect that old pattern cells should be weakly tuned for the direction of moving plaids. Thus, the percentage of pattern cells should be reduced. In line with this prediction, we observed that the direction selectivity of pattern cells was weaker and their proportion decreased in old MT.

Motion direction sensitivity and discrimination are degraded in old people (Habak and Faubert, 2000; Tran et al., 1998; Trick and Silverman, 1991; Willis and Anderson, 2000). These functions are likely to rely upon the competence of direction-selective cells. The functional degradation of old monkey MT cells that we observed here provides a possible explanation for these declines in motion perception. Furthermore, the loss of pattern cells in old MT also suggests that the ability to accurately perceive the direction of moving objects is impaired in old primates. Specifically, pattern cells, which also exist in human MT+ (Huk and Heeger, 2002), are closely linked to perception of coherent motion (Albright and Stoner, 1995). The functional degradation of V1 and MT cells may mediate perceptual declines in visual motion tasks in old primates.

Disclosure statement

There are no apparent or potential conflicts of interest including any financial or other relationship with other peo-

ple or organizations that could have influenced this work in an inappropriate manner.

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