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RESEARCH ARTICLE

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Age-related performance of human subjects on saccadic eye movement tasks

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Abstract We measured saccadic eye movements in 168 normal human subjects, ranging in age from 5 to 79 years, to determine age-related changes in saccadic task performance. Subjects were instructed to look either toward (pro-saccade task) or away from (anti-saccade task) an eccentric target under different conditions of fixation. We quantified the percentage of direction errors, the time to onset of the eye movement (saccadic reaction time: SRT), and the metrics and dynamics of the movement itself (amplitude, peak velocity, duration) for subjects in different age groups. Young children (5–8 years of age) had slow SRTs, great intra-subject variance in SRT, and the most direction errors in the anti-saccade task. Young adults (20–30 years of age) typically had the fastest SRTs and lowest intra-subject variance in SRT. Elderly subjects (60–79 years of age) had slower SRTs and longer duration saccades than other subject groups. These results demonstrate very strong age-related effects in subject performance, which may reflect different stages of normal development and degeneration in the nervous system. We attribute the dramatic improvement in performance in the anti-saccade task that occurs between the ages of 5–15 years to delayed maturation of the frontal lobes.

Key words Saccade · Visual fixation · Anti-saccade · Reaction times · Express saccade · Frontal cortex · Aging · Senescence

Introduction

Recent neurophysiological, neuroanatomical, and neuroimaging studies in humans and nonhuman primates have revealed a number of brain areas that are involved in the control of saccadic eye movements and visual fixation. The areas include the posterior parietal and frontal cortices, basal ganglia, thalamus, superior colliculus, cerebellum, and brain-stem reticular formation (Wurtz and Goldberg 1989; Leigh and Zee 1991). Because these areas span almost the entire neuraxis, there is considerable likelihood that neurological immaturity, degeneration, or malfunction may influence saccade performance. Indeed several neurological and psychiatric disorders are frequently accompanied by disturbances in the control of saccadic eye movements. This study attempts to create a foundation from which to study such possible relationships by providing important normative information across age groups.

Several studies have investigated the effects of senescence on reaction times and the metrics and dynamics of saccadic eye movements (Spooner et al. 1980; Abel et al. 1983; Warabi et al. 1984; Sharpe and Zackon 1987; Wilson et al. 1993; Moschner and Baloh 1994; Bono et al. 1996; Fischer et al. 1997; Pratt et al. 1997). To date, very few studies have investigated age-related performance in saccadic tasks during different states of visual fixation (Pratt et al. 1997) or the ability to suppress reflexive saccades and generate voluntary saccades in the absence of a visual target (Fischer et al. 1997). The main goal of our study is to create a more comprehensive pool of data describing the influence of age on saccade suppression, saccade initiation, and saccade metrics and dynamics. The tasks we employ are frequently used in oculomotor studies: they can be combined with cell-recording studies in non-human primates, and they are being explored for their possible clinical relevance.

Saccadic reaction times are dependent on the state of fixation at the time of target appearance. Reaction times are increased when the initial fixation point remains illuminated during the appearance of the new saccade target (overlap task; Fig. 1A) and reduced when the initial fixation point disappears some time prior to target appearance (gap task; Fig. 1B) (Saslow 1967; Kalesnykas and Hallett 1987; Fischer and Weber 1993; Munoz and Corneil 1995). A gap of 200 ms allows for the fastest responses to a target, likely related to the drop in fixation activity, which has been observed in the superior colliculus of

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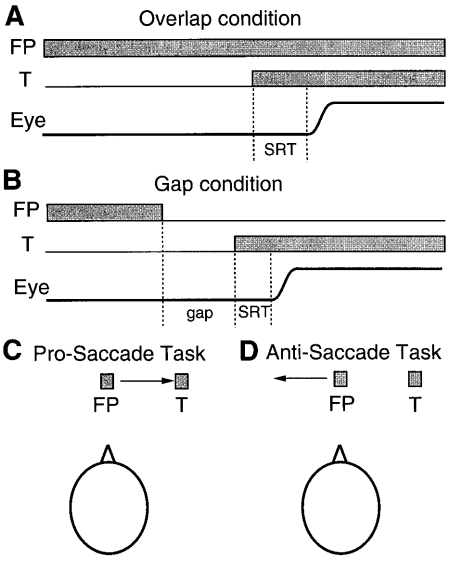

Fig. 1A–D Schema showing the different behavioral paradigms used. In the overlap condition (**A**), the central fixation point (*FP*) remained illuminated when an eccentric target (*T*) appeared. In the gap condition (**B**), the FP disappeared 200 ms before the appearance of the eccentric T. Within a block of trials, subjects were instructed to either look from the FP to the T (**C** *Pro-saccade Task*) or from the FP to the opposite side of the vertical meridian of the T (**D** *Anti-saccade Task*)

monkeys during the gap period (Dorris and Munoz 1995). This difference in saccadic reaction time (SRT) between the gap and overlap conditions is termed the gap effect. In some experimental conditions, SRTs can be reduced to a minimum of about 100 ms (Fischer and Rampsberger 1984; Fischer and Weber 1993). It has been suggested that subjects generating an abundance of these short-latency *express saccades*, especially in the overlap condition, may have some underlying pathology (Biscaldi et al. 1996; Cavegn and Biscaldi 1996).

The anti-saccade task (Fig. 1D) probes the ability of a subject to generate a voluntary saccade after first suppressing a reflexive saccade (Hallett 1978; Hallett and Adams 1980). In this task, subjects are required to look away from an eccentric visual target that suddenly appears, rather than look towards it. It is supposed that, in order to perform this task correctly, the subject must first suppress a reflexive movement to the target and then generate a voluntary movement in the opposite direction to a location in the visual field in which no stimulus was presented.

A number of parameters can be measured in the tasks and conditions illustrated in Fig. 1. Analysis of SRT distributions in the gap and overlap conditions yield insight into the influences of visual fixation. The distribution of SRTs from correct and incorrect responses in the pro- and anti-saccade tasks may be an indicator of the degree of reflexive versus voluntary control exerted during saccade-generation and thus can measure the inability of subjects to override reflexive behaviors. Amplitude, velocity, and duration measures of saccades provide an indication of the efficacy of the brainstem saccade generating circuitry in generating a saccade. We describe the age-related changes in these parameters measured in normal human subjects from age 5 to 79 years. The data correlate with the delayed maturation of frontal lobe function. Some of these data have been presented in abstract form (Munoz et al. 1996).

Materials and methods

All experimental procedures were reviewed and approved by the Queen's University Human Research Ethics Board. One hundred sixty-eight subjects between the ages of 5 and 79 years were recruited from the greater Kingston area with local newspaper advertisements and by word-of-mouth. All subjects were informed of the nature of the study and consented to participate. Parents provided informed consent for minors (<18 years of age). Participants in the study were reimbursed $10.00 per recording session. All subjects reported no known visual, neurological, or psychiatric disorders other than refractive errors, and none was taking any psychoactive medication. Subjects were able to wear their prescription lenses during the recording sessions.

Subjects were seated upright in a dental chair equipped with a head rest, which could be adjusted for height, so that they faced the center of a translucent visual screen, 100 cm away. The experiments were performed in darkness and silence except for the controlled presentation of visual stimuli, which consisted of red light-emitting diodes (LEDs; international chromaticity coordinates: CIEx=0.73, CIEy=0.26). One LED (2.0 cd/m^2) was back projected onto the center of the translucent screen and served as a central fixation point (FP) to start all trials. Eccentric target LEDs (5.0 cd/m^2) were mounted into small boxes on portable stands that were positioned 20° to the left and right of the central FP. Between trials, the screen was diffusely illuminated (1.0 cd/m^2) with background slides to reduce dark adaptation and boredom. Each recording session lasted not more than 40 min, and there were breaks between blocks of trials, during which participants were provided with snacks and drinks to maintain alertness.

In the pro-saccade task (Fig. 1C), subjects were instructed to look from the FP to an eccentric target that appeared randomly either 20° to the left or right. Each trial began when the background illumination was turned off. After a 250-ms period of darkness, the FP appeared. After 1000 ms, one of two events occurred. In the overlap condition (Fig. 1A), the FP remained illuminated while the eccentric target appeared. In the gap condition (Fig. 1B), the FP disappeared and, after a gap period of 200 ms, the eccentric target appeared. The target remained illuminated for 1000 ms, after which all LEDs were turned off and the background illumination came on for 500 ms to signify the end of the trial. Target location (20° right or left) and fixation condition (gap or overlap) were randomly interleaved within a block of trials.

In the anti-saccade task (Fig. 1D), the presentation of stimuli was identical to the pro-saccade task. Subjects were instructed to look at the FP, but then, after the appearance of the eccentric target, they were asked to look to the opposite side of the vertical meridian. Once again, target location (20° right or left) and fixation conditions (gap or overlap) were randomly interleaved within a block of trials.

Each subject was tested on only one day. We always ran one block (30 trials of each location and condition, 120 trials total) of pro-saccade trials followed by two blocks of anti-saccade trials. Subjects were not given any practice prior to data collection. However, in the case of the anti-saccade task, subjects were asked to repeat the instructions to the experimenter prior to the initiation of data collection. Eye position was monitored on-line and we verified that each subject understood the instructions by observing either correct anti-saccades or error corrections after incorrect pro-saccades. Additional anti-saccade trials were collected to ensure an adequate number of correct responses for statistical purposes, because direction errors occurred on a number of these trials.

Horizontal eye movements were measured using DC electrooculography (EOG). Ag-AgCl skin electrodes were placed on the outer canthus between each eye and the temple to record horizontal eye position. A ground electrode was placed just above the eyebrows in the center of the forehead. The EOG signal was amplified and low-pass filtered with a Grass P18 amplifier rated for human use. To minimize EOG drift, subjects wore the electrodes for approximately 10 min before the onset of calibration and recording.

The experimental paradigms, visual displays, and storage of eye-movement data were under the control of a 486 computer running a real-time data-acquisition system (REX; Hays et al. 1982). Horizontal eye position was digitized at a rate of 500 Hz. Digitized data were stored on a hard disk, and subsequent off-line analysis was performed on a Sun Sparc 2 workstation. Horizontal eye velocity was computed from the position traces by applying software differentiation (finite impulse response filter; –3 dB cut-off frequency was 45.9 Hz). The onset and termination of each saccade was determined when eye velocity increased or decreased, respectively, beyond 30°/s. Saccades were scored as correct if the first movement after target appearance was in the correct direction (i.e., toward the target in the pro-saccade task; away from the target in the anti-saccade task). Saccades were scored as incorrect if the first saccade after target appearance was in the wrong direction (i.e., away from the target in the pro-saccade task; toward the target in the anti-saccade task). Reaction latencies were measured from target onset to the onset of the first saccade. Mean SRTs were computed from trials with reaction latencies between 90 and 1000 ms after target appearance. Movements were classified as anticipatory and were excluded from analysis if they were initiated less than 90 ms after target appearance. This anticipatory cutoff was obtained from viewing the reaction-time distributions for correct and incorrect movements in the pro-saccade task: saccades that were initiated less than 90 ms after target appearance were correct about 50% of the time, whereas saccades initiated more than 90 ms after target appearance were correct more than 95% of the time. SRTs of up to 1000 ms were included so as not to miss responses of slower subject groups.

From the data of each subject, we computed the following values in the eight experimental conditions representing the factorial combination of saccade task (anti vs. pro), fixation condition (gap vs. overlap), and target direction (right vs. left): the mean saccadic reaction time (SRT) for correct trials; the coefficient of variation of SRT for correct trials [(CV=standard deviation/mean)*100]; the percentage of express saccades (latency: 90–140 ms; Fischer et al. 1993); and the percentage of direction errors (saccades away from the target in the pro-saccade task; saccades toward the target in the anti-saccade task). We also computed the *gap effect* (overlap SRT – gap SRT) in the pro-saccade and anti-saccade tasks, and the *anti-effect* (anti-saccade SRT – pro-saccade SRT) in the gap and overlap conditions. For all correct movements in the pro-saccade task with latencies between 90 and 1000 ms, we computed the mean amplitude of the first saccade following target appearance. For saccades with amplitudes between 18° and 21°, we also computed the mean peak velocity and duration. Pro-saccade amplitudes were calculated based on the assumption that the subject's final eye position was at the eccentric target. Subjects were not provided any feedback regarding the accuracy of their anti-saccades, so that variability in the amplitude of these movements between subjects of all age groups was assumed to be considerable. Thus, anti-saccade amplitudes and velocities were not considered.

Data were pooled into one of 11 bins based upon subject age, with a concentration on children's bins, to reveal rapid developmental changes at these ages. Table 1 provides the range of ages in each bin and the number of male and female subjects that comprised each age bin.

Table 1 Composition of the age-related groups

Age range (years)	Mean age (± SD)	Number of Subjects	Female	Male
5–8	7.0±0.8	14	4	10
9–11	9.9±0.9	16	6	10
12–14	12.9±0.8	22	10	12
15–17	15.7±0.9	12	6	6
18–22	20.9±1.2	20	8	12
23–29	25.5±2.2	14	8	6
30–39	35.5±3.7	11	8	3
40–49	44.0±3.0	28	14	14
50–59	55.0±3.1	9	6	3
60–69	65.2±2.5	14	8	6
70–79	75.3±3.1	8	5	3
Total		168	83	85

Results

Saccadic reaction times

Table 2 shows the mean SRTs for correct responses as a function of saccade task (anti vs. pro), fixation condition (gap vs. overlap), and target direction (right vs. left). A three-way analysis of variance was collapsed across groups and revealed an interaction among the factors. Age was excluded from this analysis because of the high variability across groups and unequal number of subjects in each age bin (see Table 1). The results of this analysis are consistent with previous reports in the literature. The gap condition (mean SRT: 266 ms) produced shorter SRTs than the overlap condition (mean SRT: 319 ms) [$F(1, 167)=877.30$, $P<0.001$]. Pro-saccade reaction times (mean SRT: 252 ms) were faster than the anti-saccade reaction times (mean SRT: 332 ms) [$F(1, 167)=446.40$, $P<0.001$]. Rightward saccades (mean SRT: 290 ms) had shorter SRTs than leftward saccades (mean SRT: 295 ms) [$F(1, 167)=9.10$, $P<0.01$].

Subject age influenced the shape of the distributions of SRTs. Figure 2 shows the distribution of SRTs in the pro-saccade and anti-saccade tasks for the 11 different age groups studied. In the pro-saccade task (Fig. 2A), SRTs ranged from 90 ms to more than 600 ms. Saccades initiated between 90 and 400 ms after target appearance were distributed into at least two modes and possibly more. Express saccades, with latencies between 90 and 140 ms, comprised the first mode and were most evident in the gap condition. Responses comprising this first mode in the gap condition were reduced among the older subject groups. In the overlap condition, the percentage of express saccades was reduced for all age groups. Among the longer latency responses (i.e., SRT>140 ms), there was a gradual and continuous shift in the peak of the distribution toward longer latencies for subjects older than

Table 2 Mean saccadic reaction times (ms) from all subjects in the eight conditions (saccade task: anti vs. pro; gap condition: gap vs. overlap; saccade direction: left vs. right)

	Anti-saccade		Pro-saccade	
	Left	Right	Left	Right
Gap	310.90	303.38	223.24	226.18
Overlap	360.69	354.85	283.60	276.42

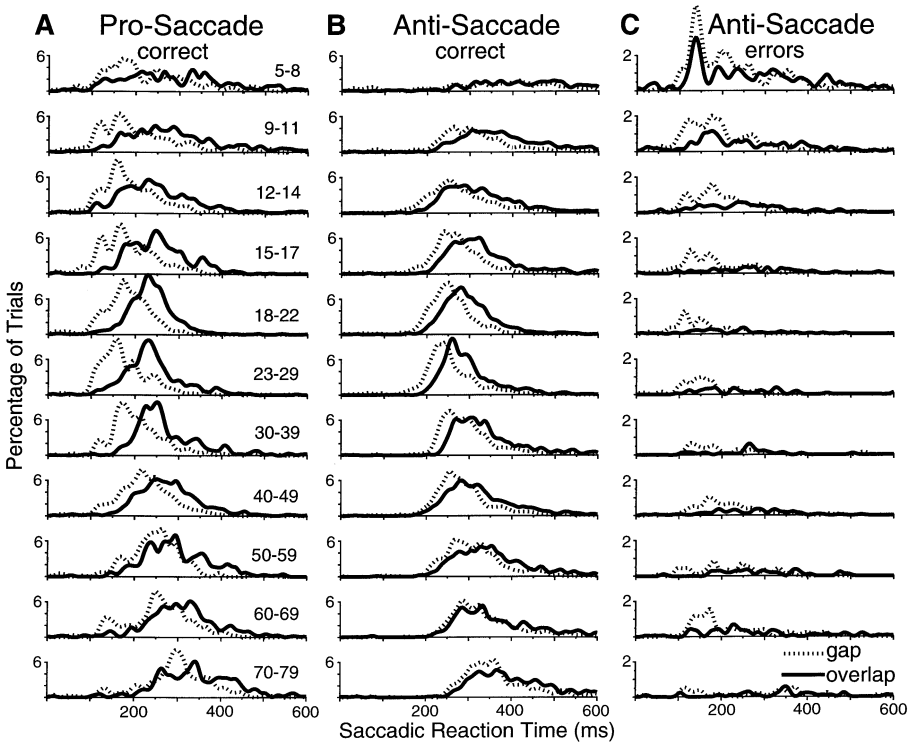

Fig. 2 Distribution of latencies of correct responses in the pro-saccade task (**A**), correct responses in the anti-saccade task (**B**), and direction errors in the anti-saccade task (**C**) for all subjects comprising the 11 different age groups (ages listed in **A**). Data shown for both the gap (*dotted lines*) and overlap (*solid lines*) conditions. The distribution of reaction times varied systematically as a function of subject age and condition. To generate the curves, the responses were first collected into bins, which were 10 ms in width. We then fit a cubic spline function through the discrete bin values of reaction times to produce the continuous functions

40 years of age. The data obtained from the two youngest age bins (ages 5–8 and 9–11 years) and the oldest age bin (ages 70–79 years) in both the gap and overlap conditions revealed the greatest number of SRTs above 300 ms and the broadest distribution of SRTs.

In the anti-saccade task, the distribution of both correct and incorrect responses also varied systematically with age. Most correct saccades (i.e., saccades away from the target) were initiated between 200 and 500 ms after target appearance (Fig. 2B). Once again, the youngest (ages 5–8) and oldest (ages 70–79) age groups had the broadest distribution in responses.

Most of the incorrect responses in the anti-saccade task (i.e., saccades toward the target) were triggered 100–200 ms after target appearance, and the distribution of incorrect saccade SRTs was multimodal (Fig. 2C), especially in the gap condition. An express saccade mode (SRTs: 90–140 ms) and a second mode were present in all age groups in the gap condition. The range of SRTs among incorrect anti-saccades (Fig. 2C) was similar to that observed for correct pro-saccades (Fig. 2A). The young children (ages 5–8) had the most direction errors (top panel, Fig. 2C). Both the variance in SRTs and number of direction errors decreased with increasing age up to about 20 years. For all older groups, the distribution of SRTs in responses with direction errors remained relatively constant.

Subject age was a significant factor in influencing mean SRT (Figs. 3A,B and 4A). The plots of age versus SRT produced an asymmetric "U" shaped function in all conditions. Figure 4A illustrates the distribution of individual-subject mean SRTs and group mean SRTs (± standard error) as a function of age in the anti-gap condition for correct saccades to the left. This distribution is typical of all conditions tested. From the group mean data (Fig. 3A,B), it is apparent that the group between 18 and 22 years of age consistently produced the shortest SRTs. Younger and older subjects were slower to initiate saccades than young adults in all conditions tested. A non-parametric Kruskal-Wallis test demonstrated that mean SRT differed significantly across the 11 age groups [$H(10)=71.35$, $P<0.005$].

For all age groups, the distribution of SRTs obtained in the gap condition (dotted traces in Fig. 2) was shifted toward shorter latencies than the distribution of SRTs obtained in the overlap condition (solid traces in Fig. 2). The gap effect on saccade latency (overlap SRT – gap SRT) is plotted for the different age groups in the pro-saccade and anti-saccade tasks for right and left targets in Fig. 5A. There was a consistent difference between the gap and overlap mean SRTs for all age groups. Within each age group, the gap effect was remarkably constant across task and direction. For ages of 18 years and above, the gap effect ranged from about 40 to 60 ms. For the youngest age group (ages 5–8), the gap effect ranged from 70 to 100 ms, a difference shown to be reliable by a Kruskal-Wallis non-parametric test [$H(10)=25.04$, $P<0.01$].

As noted above, mean SRT was significantly longer in the anti-saccade than in the pro-saccade task. This anti-effect (correct mean anti-SRT – correct mean pro-SRT) is plotted for all age groups in all conditions in Fig. 5B. The anti-effect was not identical across the age bins [$H(10)=43.43$, $P<0.001$]; it was greatest in young children (~150 ms) and was reduced to between 50 and 80 ms for subjects older than 15 years of age. Note that

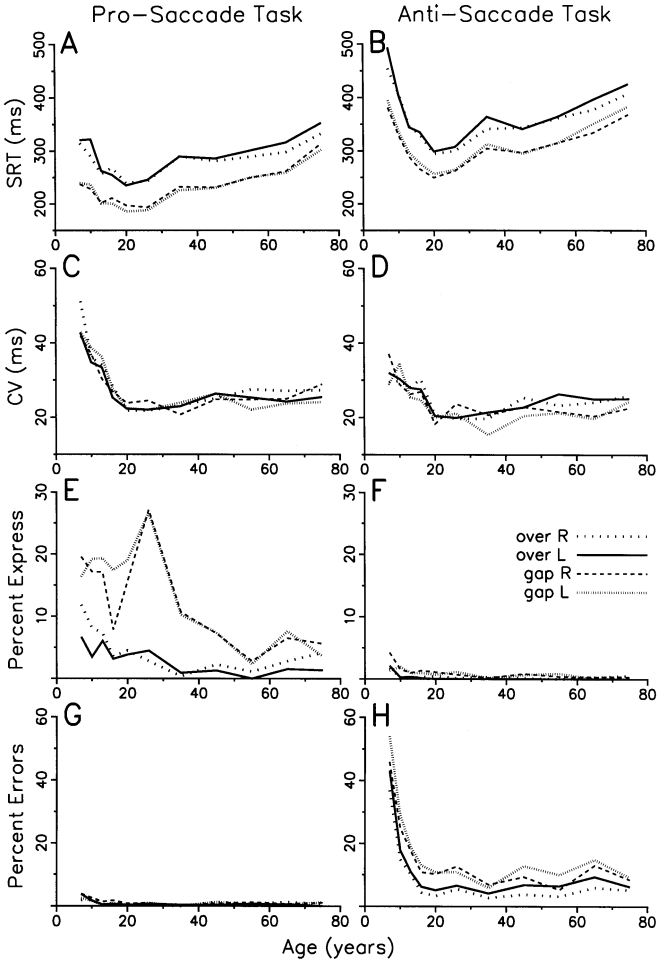

Fig. 3A–H Age-related effects in the pro-saccade task (*left column*) and anti-saccade task (*right column*) for gap and overlap conditions to the left and right (direction refers to correct saccade direction). **A, B** Saccadic reaction times (*SRT*s). **C, D** Coefficient of variation (*CV*) in SRT. **E, F** Percentage of expressed saccades. **G, H** Percentage of direction errors

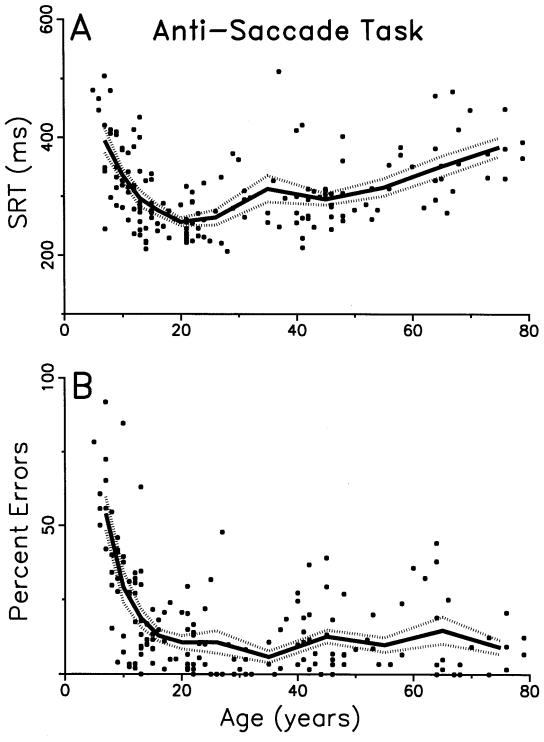

Fig. 4A, B Representative data from the 168 subjects in the anti-gap condition with the target located on the right side and the correct saccades generated to the left side. The *solid line* links the group means, and the *dotted lines* provide the standard error of the mean. **A** Mean saccadic reaction times (*SRT*) versus subject age. **B** Percentage direction errors versus age

the anti-effect was similar for both the gap and overlap conditions and for target-left and -right conditions.

Intra-subject variance in SRT was affected by task and fixation condition. To ensure that the measure of variance was not biased by variations in mean SRTs between age groups, we used the coefficient of variation (CV). The CV was lower in the gap condition (mean CV: 26.1) than in the overlap condition (mean CV: 27.1) [$F(1, 167)=5.85$, $P<0.05$]. The CV was lower in the anti-saccade task (mean CV: 24.7) than in the pro-saccade task (mean CV: 28.6) [$F(1, 167)=51.90$, $P<0.0001$], due in part to a reduced express mode leading to a tighter anti-SRT distribution. Age also influenced intra-subject variance in SRT (Fig. 3C,D). The CV was greatest for young children and decreased with increasing age until about age 20 years, thereafter remaining constant. A non-parametric Kruskal-Wallis test demonstrated that the age differences in CV were significant [$H(10)=78.21$, $P<0.005$].

Express saccades

We also quantified the percentage of express saccades (latency; 90–140 ms) generated by subjects in all age groups (Fig. 3E,F). Express saccades were generated in all age groups in the pro-saccade task (mean: 8.8%) and were virtually non-existent in the anti-saccade task (mean: 0.6%). In the pro-saccade task, there was a significant difference in the percentage of express saccades between gap (mean: 13.8%) and overlap (mean: 3.9%) conditions [$F(1, 167) =118.00$, $P<0.0001$]. In general, young subjects (<40 years) made more express saccades than older subjects (>40 years). A Kruskal-Wallis assessment of means showed that in the pro-saccade task, group mean express-saccade rates were different across age groups [$H(10)=48.63$, $P<0.01$]. The youngest subject group (ages 5–8) generated the greatest percentage of express saccades in the overlap condition (mean: 9.3%). The subject group comprising ages 23–29 generated the highest percentage of express saccades in the gap condition (mean 26.9%). There were, however, subjects in all age groups who failed to generate any express saccades, even in the pro-gap condition. The percentage of express saccades among individual subjects varied from 0 to 79% in the gap condition and from 0 to 35% in the overlap condition.

Direction errors

Direction errors also changed as a function of subject age. Figure 4B illustrates the percentage of direction errors for individual subjects and the group mean (± standard error) in the anti-gap condition with the target presented to the right, requiring a correct leftward saccade. Direction errors were quantified for all conditions (Fig. 3G,H). Direction errors were negligible in the pro-saccade task (mean: 1.1%) compared with the anti-saccade task (mean: 13.0%) [$F(1, 167)=138.51$, $P<0.0001$]. The distribution of direction errors among individual subjects in all anti-saccade conditions was comparable to that shown in Fig. 4B. There were fewer direction errors in the overlap condition (mean: 9.8%) than in the gap condition (mean: 16.3%) [$F(1, 167)=109.41$, $P<0.0001$]. There were fewer errors when subjects were required to look right (mean: 11.8%) than when they were required to look left (mean: 14.2%) [$F(1, 167)=11.67$, $P<0.001$]. That is, in the anti-saccade task, subjects made fewer errors when the target appeared on the left side.

The ability to perform the anti-saccade task accurately varied greatly with subject age (Fig. 3H). A Kruskal-Wallis assessment of means among age groups showed that group means differed significantly [$H(10)=65.36$, $P<0.01$]. The percentage of direction errors (i.e., initial saccade directed toward the target) was greatest in young children (5–8 years). There was a dramatic improvement in task performance, such that by age 15–17 years, the error rate was reduced to around 10%, where it remained for all older age groups.

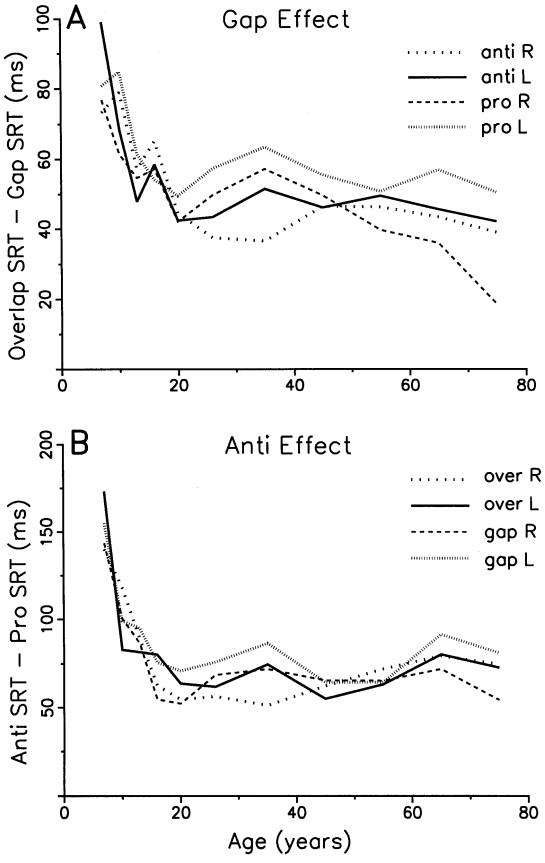

Fig. 5 **A** The gap effect [*overlap* saccadic reaction times (*SRT*) – *gap SRT*) plotted for all condition. **B** The anti effect (anti-saccade SRT – pro-saccade SRT) plotted for all conditions

Metrics and dynamics

The metrics and dynamics of saccadic eye movements in the pro-saccade task were analyzed for age effects. Figure 6 shows the amplitude, peak velocity, and duration of primary saccades in the gap and overlap conditions for targets located on the right and left side at 20°. Overall, mean amplitude of the first correct-direction saccade after target appearance was greater in the overlap condition (mean: 19.5°) than in the gap condition (mean: 19.3°) [$F(1, 167)=27.05$, $P<0.001$]. Saccadic amplitude was not affected by the direction of the target. Saccadic amplitude varied systematically across age groups, as confirmed by a Kruskal-Wallis test [$H(10)=21.13$, $P<0.05$]. The greatest amount of hypometria was observed among the youngest (ages 5–8 years).

We quantified the peak velocity and duration of primary saccades in the pro-saccade task that were between 18° and 21° in amplitude. Peak saccadic velocity (Fig. 6B) was only influenced by target direction. Saccades to the right (mean peak velocity: 389°/s) were modestly slower than saccades to the left (mean peak velocity: 396°/s) [$F(1, 167)=4.54$, $P<0.05$]. Gap condition did not influence peak saccadic velocity, nor did age across the subject groups [Kruskal-Wallis test; $H(10)=11.07$, $P>0.25$]. Saccadic duration was longer in the overlap condition (mean: 73.7 ms) than in the gap condition (mean: 73.0 ms) [$F(1, 167)=7.71$, $P<0.01$] and was also longer for leftward saccades (mean: 74.7 ms) than for rightward saccades (mean: 72.1 ms) [$F(1, 167)=25.24$, $P<0.001$]. The Kruskal-Wallis test revealed that duration increased significantly across age groups [$H(10)=30.96$, $P<0.01$]. The longest duration saccades were produced by the oldest subjects (Fig. 5C).

Discussion

The purpose of this study was to establish normative, age-related parameters of performance in the pro-saccade and anti-saccade tasks. We demonstrated strong age-related influences upon several characteristics of saccadic eye movements: (1) the distribution of SRTs (Figs. 2, 3A,B, 4A); (2) the magnitude of the gap effect (Fig. 5A); (3) the magnitude of the anti-effect (Fig. 5B); (4) intra-subject variance in SRT (Fig. 3C,D); (5) the percentage of express saccades in the pro-saccade task (Fig. 3E); (6) the percentage of direction errors in the anti-saccade task (Fig. 3H, 4B); (7) the amplitude of the primary saccade in the pro-saccade task (Fig. 6A); and (8) the duration of the primary saccade (Fig. 6C). There are three main findings in the data that we wish to focus the discussion upon.

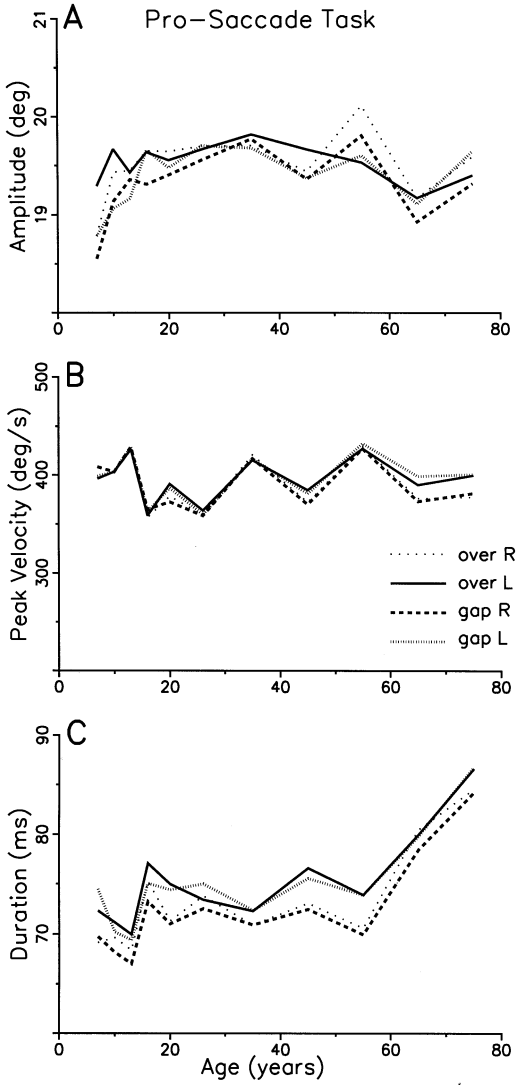

Fig. 6 Influence of age on the amplitude (**A**), peak velocity (**B**), and duration (**C**) of saccadic eye movements in the pro-saccade task. Amplitude corresponds to the size of the first saccade after target appearance. Peak velocity and duration were computed from saccades that were between 18° and 21° in amplitude

First, the distribution of SRTs varied systematically with age (Fig. 3A,B). Second, the frequency of direction errors in the anti-saccade task decreased dramatically with increasing age (Fig. 3H). Third, the metrics and dynamics of the saccades in the pro-saccade task varied little with subject age (Fig. 6). We discuss our results in relation to previous studies describing the effects of aging upon saccade parameters and speculate on possible changes in the brain, in both normal development and normal degeneration, that may account for these findings.

Saccadic reaction time

Several studies have described significant increases in mean SRT in pro-saccade tasks with senescence (Spooner et al. 1980; Warabi et al. 1984; Sharpe and Zackon 1987; Tedechi et al. 1989; Moschner and Baloh 1994; Bono et al. 1996; Fischer et al. 1997; Pratt et al. 1997). In these studies, elderly subjects (usually between 60 and 80 years of age) tended to have greater mean SRTs and greater intrasubject variance than young adult subjects (usually between 20 and 40 years of age). In addition, some studies have also described increased mean SRTs among younger children. Bono and coworkers (1996) studied subjects from ages 5 to 90 years in a pro-overlap task and found the fastest SRTs among subjects aged 16–30; younger and older subjects had longer mean SRTs. Fischer and coworkers (1997) studied SRTs in normal subjects from ages 8 to 70 years in two tasks, the pro-overlap and anti-gap tasks, and found that, for both, the shortest mean SRTs were obtained from teenagers and young adults (ages 13–31 years); mean SRTs were longer among both young children and older adult subjects. The effects of age on mean SRT, which we described in the gap and overlap conditions of both the pro-saccade (Fig. 3A) and the anti-saccade (Fig. 3B) tasks, are comparable with these previous studies. We found that SRT-versus-age plots (Fig. 3A,B) produced an asymmetric "U"-shaped function: subjects aged 18–22 years generated the shortest mean SRTs in all conditions; younger and older subjects had longer mean SRTs. We attribute this "U"-shaped function to two separate processes: a developmental process in the children and normal degeneration in adults (see below).

The difference in mean SRT between the overlap and gap conditions, the gap effect, was equivalent in both the pro-saccade and anti-saccade tasks (Fig. 5A). In addition, it was constant (~50 ms) across all age groups except for young children (<12 years), when it was enhanced (~80 ms). In contrast to our results, Pratt and coworkers (1997) described a significant increase in the magnitude of the gap effect in the elderly, which they believed existed only as an artifact of longer proportional reaction times in general. The gap effect may be the result of several factors (Csibra et al. 1997), including the disengagement of visual fixation prior to target appearance afforded by the gap period (Fischer and Weber 1993; Fischer et al. 1993; Dorris and Munoz 1995; Paré and Munoz 1996; Dorris et al. 1997). In the overlap task, fixation is actively engaged at the time of target appearance, leading to increased SRTs.

Normally, SRTs exceed the conduction time of the shortest neural pathways from the retina to the extraocular muscles; that is, the minimal time required for information to travel from the photoreceptors to the extraocular muscle motoneurons via the shortest possible route (Carpenter 1981). Express saccades have RTs that approach these minimal afferent and efferent conduction times, and they usually form a distinct mode in the SRT distribution (Fischer and Weber 1993; Fischer et al. 1993; Paré and Munoz 1996). These saccades were most often seen in gap conditions (Fig. 3E). Although express saccades were generated in all age groups, each group had at least one subject that failed to generate any express saccades. Express saccades were far less common among subjects older than 40 years (see

Fig. 3E). It has been suggested that an above average frequency of express saccades in the pro-saccade overlap condition may be a reflection of some underlying pathology in the system controlling visual fixation (Biscaldi et al. 1996; Cavegn and Biscaldi 1996), and thus it is important to note that older adults normally generate very few express saccades. The youngest age group (ages 5–8) in our study generated the greatest percentage of express saccades in overlap conditions (Fig. 3E), yet also had the largest gap effect (Fig. 5A) and the most variable SRTs (Figs. 2, 3C,D). These observations suggest that young children have poor control over visual fixation, leading to the generation of either reflexive express saccades or abnormally long-latency saccades. Fixation ability improves as a function of increasing age, and both the frequency of express saccades in overlap conditions and the variance in SRTs diminishes.

Suppression of reflexive saccades

During the early stages of human development, movements are often triggered reflexively in response to sensory stimuli. The ability to guide behaviors by internalized knowledge emerges only later in development. To correctly perform the anti-saccade task, subjects must first suppress a reflexive movement to the target and then generate a voluntary movement in the opposite direction to a location in the visual field in which no stimulus was presented. One of the most striking age-related effects we observed was the reduction in the error rate in the anti-saccade task among children (Fig. 3H). Error rates were near 50% among young children (ages 5–8 years) and this decreased to around 10% by the age of 15 years. Performance improved considerably among teenagers and the fewest direction errors were generated by subjects 20 years of age and older. The difference in SRT between correct anti-saccade and correct pro-saccade trials, the anti-effect (Fig. 5B), was also dramatically elevated in young children, likely in response to the more demanding nature of the task. It should be noted that most incorrect anti-saccades were eventually completed correctly. All subjects corrected at least some of their errors, so we knew that all subjects were capable of generating voluntary saccades and understood the instructions of the task. Our results show, that although all subjects were capable of generating the voluntary anti-saccades, children had greater difficulty suppressing the short-latency reflexive pro-saccades. As observed previously (Fischer and Weber 1992), most of the direction errors were short-latency reflexive saccades, triggered 100–200 ms after stimulus appearance (see Fig. 2C), and many were in the range of express saccades.

Fischer and coworkers (1997) also described considerable age-related improvements in performance of the anti-gap saccade task. In their study, error rates were the highest among children under 11 years of age. This age-related improvement in task performance is similar to that found by Paus and coworkers (1990), who employed a task that required maintenance of steady fixation in the presence of distracting visual stimuli. These authors described dramatic improvement in the ability to suppress reflexive saccades between the ages of 9–10.

Dynamics and metrics of saccadic eye movements

The modest influences of age on the duration of saccades in the pro-saccade task that we described (Fig. 6C) are consistent with previous studies describing age-related changes in saccade metrics and dynamics among subjects older than 60 years of age. Many studies have also described modest reductions in peak velocity among elderly subjects (Spooner et al. 1980; Warabi et al. 1984; Sharpe and Zackon 1987; Tedeschi et al. 1989; Wilson et al. 1993; Moschner and Baloh 1994; Bono et al. 1996). These reductions in peak velocity were most evident with larger amplitude saccades, usually to targets beyond 20° eccentricity. We failed to reveal any significant reductions in peak velocity among our older subjects. It was noted, however, that elderly subjects did not sustain peak/near-peak velocities for as long as younger subjects. Evidence of this can be seen in Fig. 6B and C, in which saccade duration increased in the oldest age groups without an accompanying drop in peak velocity. The target eccentricities used in our study were limited to 20°. Perhaps testing with greater eccentricities would have revealed an age-related reduction in peak velocity among our oldest group of subjects.

While some studies have reported that elderly subjects display a significant increase in the percentage of hypometric saccades (Sharpe and Zackon 1987; Tedeschi et al 1989), other studies have reported that elderly subjects do not perform any differently than younger adult subjects (Warabi et al. 1984; Moschner and Baloh 1994). We failed to reveal any evidence for dysmetria among the elderly subjects in our study (Fig. 6A). To our knowledge, the modest hypometria we found among young children (Fig. 6A) has not been reported previously. We did not analyze the metrics and dynamics of correct anti-saccades because of the assumed variability of these movements between subjects.

Possible brain areas involved in age-related changes

Imaging studies have shown that several areas of the human cerebral cortex are activated during pro-saccade and anti-saccade tasks (Anderson et al. 1994; O'Driscoll et al. 1995; Petit et al. 1995, 1996; Sweeney et al. 1996; Doricchi et al. 1997). These areas include striate and extrastriate cortex, posterior parietal cortex, the frontal eye fields (FEF), supplementary motor area, and dorsolateral prefrontal cortex. Human subjects with discrete lesions have abnormal SRTs following damage to the frontal cortex (Guitton et al. 1985; Pierrot-Deseilligny et al. 1991a; Braun et al. 1992; Rivaud et al. 1994), posterior parietal cortex (Pierrot-Deseilligny et al. 1991a; Braun et al. 1992), and the superior colliculus (Pierrot-Deseilligny

et al. 1991b). During normal aging, there is selective wide-spread atrophy of both gray and white matter in the cerebral cortex (Creasey and Rapoport 1985). The increase in mean SRTs that accompanies senescence may therefore be the result of neuronal degeneration in several of the eye-movement areas of the cerebral cortex. Because atrophy continues with aging, the mean SRTs should continue to rise throughout life.

The frontal eye fields and the superior colliculus provide the major descending input to the brainstem saccadic-burst generator (Wurtz and Goldberg 1989; Leigh and Zee 1991). The peak velocity and duration of the saccade are a function of the properties of the burst generator and are not under voluntary control. In our study, peak velocity (Fig. 6B) and duration (Fig. 6C) were relatively constant from ages of 5 to 59 years and the amplitudes of these movements were constant from the ages of 12 to 79 year (Fig. 6A). This suggests that the saccadic-burst generator and the nuclei of the extraocular muscle motoneurons remain relatively unchanged across the age groups we studied. In support of this conclusion, histological examination of senescent brains has failed to identify neuronal degeneration in the brainstem reticular formation (Brody and Vijayashankar 1977), which houses the saccadic-burst generator circuitry.

Our data suggest that young children had considerable difficulty controlling visual fixation. They had a greater gap effect, generated more express saccades in the pro-saccade overlap condition, and generated the greatest percentage of direction errors in the anti-saccade task. The ability to control visual fixation improved considerably with subject age up to the age of 15. The relatively poor control over visual fixation present in young children may reflect underdeveloped frontal and prefrontal cortices.

Maturation of cortex has been studied in numerous ways. General cortical development is fueled by a significantly higher cerebral blood flow (CBF) to the grey matter of children than adults (Ogawa et al. 1989), and areas of high activity require larger blood flow. Notably, rCBF in the frontal lobes of children does not show the normal adult pattern until age 10. At this age, several researchers have found the beginnings of a spurt in frontal lobe development. Yakovlev and Lecours (1967) showed that frontal association areas become fully myelinated around adolescence. EEG coherence and phase-network analysis define cortical maturation as an increase in numbers of synchronously oscillating cell assemblies. Anokhin and coworkers (1996) found that the greatest increase in numbers of these functional assemblies occurred during puberty. Additionally, they found that, between the ages of 7 and 25 years, the maximal increases occur over frontal association cortex. Although frontal cortex was shown to develop connections with ipsilateral temporal and occipital areas in earlier childhood, the peak in *bilateral frontal* connectivity begins at age 11 (Thatcher et al. 1987). Peak frontal development is reached around 15 years of age, after which point rCBF (Ogawa et al. 1989) and coherence of functional units (Thatcher et al. 1987; Anokhin et al. 1996) have reached adult levels. It has been found that young children (~5 years) generated the largest amplitude short-latency-evoked potential over frontal and central scalp locations following the sudden appearance of a visual stimulus (Dustman and Shearer 1987). It was suggested that these large early potentials, whose magnitudes decrease throughout childhood, reflect reduced cortical inhibition, which may be necessary for higher cognitive processing of visual inputs. Therefore, maturation of cortico-cortical connections involving regions of the frontal lobe probably provides the neuroanatomic correlate for the improved control of visual fixation we observed. This timetable of development has also been observed in several cognitive tasks believed to engage the frontal cortex (reviewed in Fuster 1997).

Development and localization of function may also play a role in left/right asymmetries in saccadic responses. In our study, SRTs were significantly faster to the right than to the left in all but the pro-gap condition (Table 2). This difference was accentuated in the youngest age group, where the percentage of express saccades was higher to the right, especially in the pro-overlap condition (Fig. 3E). In addition, the percentage of direction errors in the anti-saccade task was greatest when the stimulus appeared on the right side (Fig. 3H). Fischer and coworkers (1997) described similar left/right asymmetries, in which SRTs were faster for rightward saccades. They found that subjects produced faster SRT's for pro-overlap saccades to the right, a higher percentage of express saccades to the right, and more errors to the right stimulus in the anti-saccade gap condition.

The reduced SRTs generated by the left hemisphere may have a basis in cortical development. EEG coherence and phase network analysis has revealed that left fronto-occipital and left fronto-temporal coupling occurs between the ages of 4 and 6 years (Thatcher et al. 1987). At this age, the right hemisphere is poorly developed, showing only very localized frontal-pole pairings on the EEG coherence trace. Only later in development (ages 8–10) do right fronto-temporal/occipital couplings become evident (followed lastly by bilateral frontal coupling after age 11). The delay in right-hemisphere development may lead to some preferential saccade-generating abilities in the left hemisphere, because asymmetries seem to continue into adulthood.

In conclusion, we have described the age-related changes in performance of normal human subjects in both pro- and anti-saccade tasks. Understanding these normative data may provide important insights into normal development. In addition, these data can be used to contrast with performance of individuals with various neurological or psychiatric disorders. Performance in the anti-saccade task in particular may serve as a useful marker of normal frontal-lobe development and dysfunction.

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