

Age-related trends in saccade characteristics among the elderly

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Abstract

Eye movement recordings are useful for assessing neurological disorders, the prevalence of which increases with age. However, there is little rigorous quantitative data on describing oculomotor changes that occur during healthy aging. Here, we measured the ability of 81 normal elderly subjects (60–85 years) to perform two saccadic eye movement tasks: a pro-saccade task, requiring an automatic response to look towards a stimulus and an anti-saccade task, requiring inhibition of the automatic response to instead initiate a voluntary saccade away from the stimulus. Saccadic ability decreased with age: the oldest subjects were slower to initiate saccades and they made more direction errors (i.e., erroneous pro-saccades) in the anti-saccade task. Intra-subject variability in reaction time also correlated positively with age in both saccade tasks. Voluntary saccade control, as assessed by the anti-saccade task, was far more affected by aging than automatic control, as assessed by the pro-saccade task, suggesting that the mechanisms driving voluntary and automatic saccade performance deteriorate at different rates in the aging brain, and therefore likely involves different neural substrates. Our data provide insight into deficits due to normal brain changes in aging as well as a baseline to evaluate deficits caused by neurological disorders common in this age range.

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1. Introduction

The proportion of elderly individuals in society is increasing dramatically (Turcotte and Schellenberg, 2006), leading to an increase in the prevalence of age-related neurological disorders that affect the function of the frontal lobes and overall movement control (Gavrilov and Heuveline, 2003). In order to study these disorders most effectively, cognitive deficits due to normal brain changes in healthy aging first need to be understood. The eye movement system is an excellent model to assess brain function (Leigh and Kennard, 2004; Munoz et al., 2007; Ramat et al., 2007). The circuitry controlling saccadic eye movements is well understood and involves

areas of the frontal and parietal lobes, basal ganglia, thalamus, visual cortex, superior colliculus, cerebellum, and brainstem reticular formation (Hikosaka et al., 2006; Leigh and Zee, 2006; Moschovakis et al., 1996; Munoz and Everling, 2004; Scudder et al., 2002; Wurtz and Goldberg, 1989). These structures contribute to specific components of saccadic behaviors, and altered saccade performance often gives insight into the etiology of various clinical disorders. Because there is overlap in the frontal cortical areas controlling the production of saccades and the areas involved in controlling various aspects of cognition, measuring saccadic eye movements can provide an important tool to assess cognitive functions subserved by the frontal lobes. These same areas are frequently degenerating as people age (Creasey and Rapoport, 1985; Kramer et al., 2007).

Saccadic eye movement tasks can be designed to probe simple sensory-motor processes as well as higher cognitive functions. Eye movement tasks can be used to dissect differ-

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ent components of the system. In a pro-saccade task, subjects are instructed to look towards an eccentric visual stimulus when it appears. This task has high stimulus-response compatibility and requires a simple, automatic response (Munoz and Everling, 2004). In the anti-saccade task (Hallett, 1978), subjects are instructed to look away from the eccentric stimulus in the opposite direction. The location of the stimulus and the saccade goal are dissociated in this task. Successful completion of the anti-saccade task requires additional stages of processing: suppression of the automatic pro-saccade to the stimulus, followed by voluntary initiation of the anti-saccade away from the stimulus (Munoz and Everling, 2004). The difference between pro- and anti-saccade latencies, the anti-effect, provides a measure of the time it takes for these additional processes. Fixation state can also be manipulated by introducing a gap period between disappearance of the fixation spot and the appearance of the stimulus (Saslow, 1967), which serves to reduce reaction times. A subset of these short-latency stimulus-driven saccades have latencies that approach the minimal afferent and efferent conduction times in the oculomotor system and have been called “express” saccades (for review, see Dorris et al., 1997; Fischer and Weber, 1993). Express saccades have been identified as the first peak in a multimodal distribution of SRTs (Fischer and Boch, 1983; Fischer et al., 1997) and are often reported as minimal or absent in the elderly (Klein et al., 2000; Munoz et al., 1998). Here, we investigate in greater detail the occurrence of these short-latency stimulus-driven saccades in the elderly.

Our knowledge of the neural pathways underlying pro- and anti-saccade generation is under continual debate as new findings emerge. However, studies of patients with frontal lobe lesions (Gaymard et al., 1998; Guitton et al., 1985; Pierrot-Deseilligny et al., 1991; Rivaud et al., 1994) and recent neuroimaging studies of normal individuals (Connolly et al., 2002; Ettinger et al., 2005; Ford et al., 2005; O’Driscoll et al., 1995; Sweeney et al., 1996) have identified specific frontal regions (e.g., dorsolateral prefrontal cortex, frontal and supplementary eye fields) that are involved in voluntary saccade control. For example, lesions to the frontal eye fields (FEF) lead to increased anti-saccade latencies (Gaymard et al., 1998; Rivaud et al., 1994). Lesions to the dorsolateral prefrontal cortex (DLPFC) lead to difficulties in saccade suppression (Gaymard et al., 1998; Guitton et al., 1985; Pierrot-Deseilligny et al., 1991). These lesions do not typically affect pro-saccade generation. Instead, lesions to the posterior parietal cortex and supplementary motor area influence the accuracy and timing of pro-saccade reaction times, respectively (Heide and Kömpf, 1998; Pierrot-Deseilligny et al., 1991). Therefore, contrasting performance on these tasks provides measures of frontal lobe function that can be applied to the elderly.

Numerous studies have described the effects of senescence on saccadic eye movement performance, but their conclusions are inconsistent. Many studies suggest saccade parameters such as reaction times, error rates, and metrics are corre-

lated with aging (Abel and Douglas, 2007; Klein et al., 2000; Munoz et al., 1998; Olincy et al., 1997; Shafiq-Antonacci et al., 1999), whereas others have shown no differences between elderly and younger subjects (Eenshuistra et al., 2004; Pratt et al., 2006). However, there is one broad consensus: the more automatic parameters such as pro-saccades latencies are at best, minimally influenced by aging (Abrams et al., 1998; Kaneko et al., 2004; Munoz et al., 1998; Pratt et al., 2006), whereas more cognitively complex aspects of saccadic performance such as suppression and voluntary initiation of a goal-directed saccade (e.g., anti-saccades) are more strongly influenced by aging (Olincy et al., 1997; Shafiq-Antonacci et al., 1999). This suggests that the neural structures in the oculomotor system responsible for generating pro-saccades such as visual occipital cortex, parietal cortex, the brainstem burst generator, reticular formation, and superior colliculus (Munoz and Everling, 2004) may remain relatively uncompromised as people age compared to structures in the frontal and parietal cortices that are involved in complex cognitive function required in the anti-saccade task (Curtis and D’Esposito, 2003; Pierrot-Deseilligny et al., 2003).

The purpose of this study is to determine the rate at which various saccade parameters change between the ages of 60 and 85 years as assessed with pro- and anti-saccade tasks. If automatic processes are affected by aging, then pro-saccade latencies, and the gap effect, including proportion of express saccades, should be altered. Alternatively, if voluntary processes are primarily affected with aging, then anti-saccade latencies, direction errors, and the anti-effect should be altered. It is hypothesized that performance decrements in the healthy aging will reflect the natural cognitive slowing and cerebral atrophy (Aizenstein et al., 2004; Creasey and Rapoport, 1985; Kramer et al., 2007) that occur over time. Elucidating the patterns of eye movement deficits in aging will help to determine both the feasibility of eye movement testing to evaluate the aging process and the aspects of the saccade system that are most resilient to the aging process.

2. Methods

2.1. Subjects

All experimental procedures were reviewed and approved by the Queen’s University Human Research Ethics Board. Eighty-one subjects ranging between 60 and 85 years of age were recruited into this study (Table 1). Subjects reported no known visual, neurological or psychiatric symptoms, and had normal or corrected to normal vision. All subjects provided informed consent and were compensated for their participation.

2.2. Experimental paradigm

The experiment was conducted in one 40-min session in which subjects performed one block of a pro-saccade task

Table 1
Composition of age-related groups.

Age range (years)	Mean age (\pm S.D.)	Number of subjects	Female	Male
60–64	61.9 \pm 1.4	16	10	6
65–69	67.0 \pm 1.3	19	11	8
70–74	72.5 \pm 1.6	19	13	6
75–79	77.2 \pm 1.5	13	8	5
80–85	81.9 \pm 1.7	14	10	4
Total		81	52	29

(120 trials; Fig. 1A), and two blocks of an anti-saccade task (120 trials per block; Fig. 1B). Subjects were seated alone in a dark room 100 cm away from a translucent visual screen. Visual stimuli consisted of red light emitting diodes (LEDs; central fixation point = 2.0 cd/m²; peripheral stimuli = 5.0 cd/m²). Between trials, the screen was diffusely illuminated (1.0 cd/m²) to reduce dark adaptation. Each trial began when the background illumination was turned off and after 250 ms of complete darkness, the fixation point (FP) appeared. After 1000 ms, one of two events occurred depending on the trial condition. In an ‘overlap’ condition, the FP remained illuminated while a peripheral stimulus appeared 20° to the left or right, and in a ‘gap’ condition, the FP disappeared for 200 ms before the peripheral stimulus appeared. In both conditions the stimulus remained illuminated for 1000 ms, after which all three LEDs were turned off and the background illumination came on for 500 ms. Stimulus location (left and right) and fixation condition (gap and overlap)

were randomly interleaved within a block of trials. During the pro-saccade block (Fig. 1A), subjects were instructed to look towards the peripheral stimulus as soon as it appeared. During the blocks of anti-saccade trials (Fig. 1B), subjects were instructed to look in the opposite direction of the stimulus as soon as it appeared.

2.3. Recording and apparatus

Horizontal eye movements were measured using direct current electrooculography (EOG) to obtain a continuous measure of eye position. The EOG signal was amplified (Grass P18 Amplifier) and low-pass filtered (50 Hz). Horizontal eye position was digitized at a rate of 1 kHz using REX, Ver 5.4 (Hays et al., 1982). Subjects were asked to direct their eyes between left/right peripheral and central stimulus locations in order to calibrate the signal. We then set the EOG amplification to 1 V = 10°. Within this range (\pm 20°) the horizontal eye position signal was linear (Goldring et al., 1996) and the noise was <2° in position and <15°/s in velocity (e.g., see traces in Fig. 1). Digitized data were stored on a hard disk, and analyzed off-line on a Sun Ultra 60 Spark station.

2.4. Data analysis

The onset and termination of each saccade was determined when eye velocity exceeded 30°/s. Trials were scored

Fig. 1. Left column, saccade paradigm: pro-saccade task (A) and anti-saccade task (B), including individual saccade traces and reaction time distributions (C–D) in the gap condition for a representative 67-year old. Right column, individual saccade traces (E and F) and reaction time distributions (G and H) for a representative 80-year old.

as correct if the first saccade after stimulus appearance was in the correct direction. Trials were classified as direction errors if the first saccade after stimulus appearance was in the wrong direction. Saccadic reaction time (SRT) was measured from stimulus appearance to onset of the first saccade.

For each subject, the following values were computed for the pro- and anti-saccade task from correct trials with latencies up to 1000 ms (broken down for both gap and overlap conditions): mean SRT for correct trials, coefficient of variation of SRT (S.D./mean \times 100) for correct trials, percentage of direction errors, and percentage of express saccades. Pro- and anti-saccades from 0 to 110 ms occurred at a 50% chance level (correct:incorrect), so saccades with SRTs < 110 ms were classified as anticipatory and were not included in measures of correct mean SRT (see Section 3; Fig. 2). Because saccadic latencies, including latency of express saccades, depend on stimulus intensity, size, and contrast (Bell et al., 2006; Carpenter, 2004; White et al., 2006), we used anti-saccade direction error latencies (erroneous stimulus-driven pro-saccades) in combination with correct pro-saccade latencies to help identify the latency range wherein express saccades occurred. The first mode in the distribution of anti-saccade error latencies corresponded to both a decrease in correct anti-saccades, and the first mode in the distribution of pro-saccades, reflecting the earliest stimulus-driven saccades that were no longer anticipatory. A binomial sign test determined the start and end of this stimulus-driven epoch (shaded grey boxes in Fig. 2) by measuring when the proportion of anti-saccade error trials (in 10 ms bins) significantly exceeded that of correct anti-saccade trials, for each age category (Fig. 2F–G, black bars on negative ordinate). Then, the proportion of correct pro-saccades occurring during this epoch specific to each age category (i.e., express saccades) was measured for each age group.

2.5. Statistical analysis

For all tasks, statistical corrections for heterogeneity (Levene's) and sphericity of variance (Greenhouse-Geisser) were made as needed, and outliers $> \pm 3$ standard deviations of mean of each age category were removed (1–3 outliers per measurement for all age categories). Correlations were measured by pairing oculomotor parameters with age as a continuous variable where statistical significance was based on *t*-tests different from zero. To analyze differences with increasing age, the population was stratified into five groups by age as follows: 60–64, 65–69, 70–74, 75–79, and 80–85 (see Table 1 for group composition). Repeated measures ANOVAs were also used to evaluate the results from all elderly age groups. The independent variable used to carry out the ANOVAs was age (categorized into 5-year age increments; Table 1), and the repeated measures were experimental task (pro-saccade vs. anti-saccade), and fixation condition (gap vs. overlap). Values for right and left stimulus positions were not significantly different (paired *t*-test; $p > .05$), allowing the data to be collapsed across direction for each task.

3. Results

The results of this study can be summarized by four main points: (1) Saccadic reaction times (SRTs) increased with age; (2) intra-subject variability in SRT increased with age; (3) the proportion of direction errors increased with age; and (4) express saccades did not decrease with age (in contrast to previous literature).

3.1. Saccadic reaction time (SRT)

Fig. 1 shows individual saccade traces in the gap condition for both pro-saccades (Fig. 1A and E) and anti-saccades (Fig. 1B and F) for a representative 67-year old (Fig. 1A–D) and an 80-year old (Fig. 1E–H). Reaction time distributions reveal that for these sample subjects, mean gap and overlap SRTs are greater in the 80-year old (Fig. 1G–H) than in the 67-year old (Fig. 1C–D). Individually, anti-saccade SRTs differed significantly from pro-saccade SRTs (anti-effect; anti-SRT–pro-SRT) in 89% of the subjects in the gap condition, and 77% in the overlap condition. Gap condition SRTs and overlap condition SRTs (gap effect; overlap SRT – gap SRT) differed significantly in 77% of subjects in the anti-saccade task, and 79% of subjects in the pro-saccade task. Subsequently, subjects were divided into five age groups (see Section 2).

Fig. 2 shows the distribution of correct and error pro-saccade and anti-saccade latencies in the gap condition for the five different age groups studied. A change in both correct and incorrect latency distributions occurred between the eldest subjects (80–85 years) and the youngest subjects (60–64 and 65–69 years), i.e., the distribution broadened, where an increased proportion of errors were seen as older subjects became slower to initiate correct anti-saccades. This same pattern held true in the overlap condition (not shown). The proportion of errors in relation to the proportion of correct anti-saccades can be examined further to determine the occurrence of express saccades in the elderly.

The grey shaded boxes in Fig. 2 show the range of express saccades (short-latency pro-saccades) for each age group based on the binomial sign test between correct vs. direction error anti-saccade latencies (see Section 2). Surprisingly, the shortest SRTs in the error distribution (epoch onset) remained relatively fixed across age group (60–64: 120 ms; 65–69: 140 ms; 70–74: 130 ms; 75–79: 110 ms; 80–85: 130 ms), whereas the longest SRTs with more errors than correct responses changed with age group (epoch end; 60–64: 180 ms; 65–69: 180 ms; 70–74: 210 ms; 75–79: 210 ms; 80–85: 240 ms ($r = .945$, $p = .015$; Fig. 3)). This was consistent with a delay in the shortest SRTs for correct anti-saccades (Fig. 2F–J, upper histograms). Express saccade production is influenced by multiple factors and do not appear to be time-locked at the 90–135 ms reported in previous literature (Fischer and Weber, 1993; Munoz et al., 1998), so we used the epoch onset to epoch end latency range (grey shaded regions in Fig. 2) to determine the mean proportion of pro-

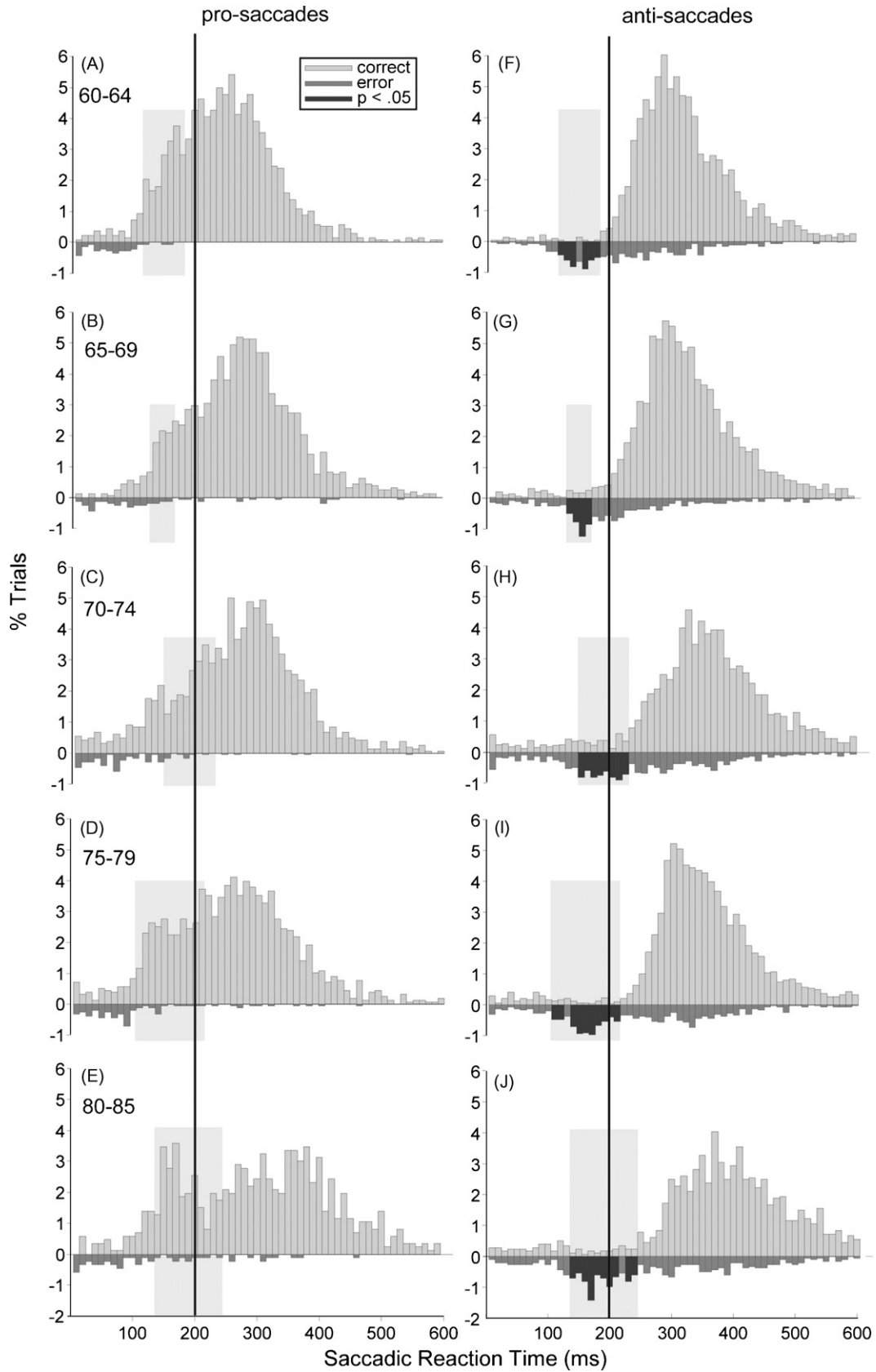


Fig. 2. (A–E) Distribution of SRT in pro-saccade gap trials for each age category (correct responses on positive ordinate (light grey); incorrect responses on negative ordinate (medium grey)). (F–J) Distribution of SRT in anti-saccade gap trials. Darkened black bars on the negative ordinate represent 10 ms error bins statistically different from correct bins. Grey shaded boxes represent calculated express saccade epoch based on the error latencies (see Section 2).

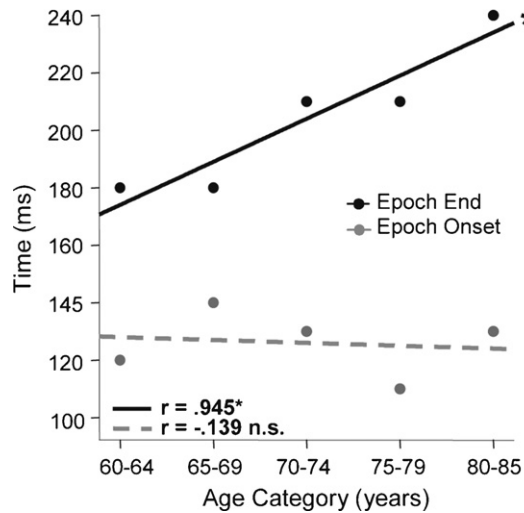


Fig. 3. Onset of express saccade epoch (grey) vs. end of epoch (black) for each age category. *Pearson correlation across age category, $p < .05$.

saccades falling within these latencies (express saccades) for each age category (60–64 = 18%; 65–69 = 7%; 70–74 = 17%; 75–79 = 30%; 80–85 = 25%), which did not correlate with increasing age group. The express epoch onset did not change systematically across the ages of 60–85, but the epoch end did (Fig. 3). Furthermore, the proportion of fast, automatic saccades occurring per bin did not increase with aging (Fig. 2F–J, lower histograms). Therefore, advancing age appears to differentially influence voluntary vs. automatic processes.

Correlation analyses were then performed to determine the rate at which pro- and anti-saccade latencies changed with age. SRTs increased with age in all four conditions: pro-gap ($r = .283$, $p = .011$); pro-overlap ($r = .222$, $p = .048$); anti-gap ($r = .501$, $p < .001$); and anti-overlap ($r = .420$, $p < .001$). However, age was a much stronger predictor of anti-saccade reaction times than of pro-saccade reaction times (Fig. 4A and B). Furthermore, the rates (determined using a linear regression analysis) at which pro- and anti-SRTs changed with age also differed. Pro-SRTs increased at a rate of 2.0 ms/year for gap, and 1.9 ms/year for overlap conditions, whereas anti-SRTs increased at a rate of 5.0 ms/year for gap and 4.7 ms/year for overlap conditions. The anti-effect also correlated significantly with age for both gap ($r = .274$, $p = .014$) and overlap conditions ($r = .240$, $p = .032$). Conversely, the gap effect did not correlate with age either for pro- or anti-saccades (Fig. 5). The slope of the linear regression for the anti-effect (2.9 ms/year for gap, 2.8 ms/year for overlap) differed significantly from that of the gap effect (–.07 ms/year for pro, –.06 ms/year for anti-). These results suggest that the difference between pro- and anti-saccade latencies increases as people age, whereas the gap effect does not.

Data was then grouped into five age categories to determine if age differences were specific to certain age ranges. A three-way ANOVA (age group \times task (anti/pro) \times condition (gap/overlap)) revealed significant differences between saccade tasks (anti-saccade vs. pro-saccade) and fixation

conditions (gap vs. overlap) (Fig. 4A and B). Pro-saccade reaction times were faster than correct anti-saccade reaction times in both gap and overlap conditions (the anti-effect; $F(1,75) = 130.05$, $p < .01$). The gap condition produced shorter SRTs than the overlap condition in both pro- and anti-saccade tasks (the gap effect; $F(1,75) = 263.36$, $p < .01$). Furthermore, SRT increased with group age for all tasks ($F(1,4) = 5.57$, $p < .01$). Specifically, group differences were most robust in the anti-saccade task, whereas in the pro-saccade task, only the eldest subjects (80–85 years) differed from the youngest subjects (60–64 years; see post hoc comparisons, Table 2). The anti-effect increased for older age groups (Fig. 5) who became even slower to initiate voluntary anti-saccades than automatic pro-saccades ($F(1,4) = 2.85$, $p < .05$). A trend analysis revealed that although there was a significant linear trend ($p < .001$) for SRT increasing with age in all conditions, there was also a significant non-linear trend ($p = .007$), indicating that the most severe decrement in performance occurred after the age of 70 years.

3.2. Intra-subject variability in SRT

To measure intra-subject variability for each of the four saccade conditions we computed coefficient of variation (CV) of SRT, the relative standard deviation expressed as a unitless proportion of each subject mean (see Section 2). The amount of intra-subject variability was correlated positively with advancing age in all conditions; pro-gap ($r = .455$, $p < .001$); pro-overlap ($r = .396$, $p < .001$); anti-gap ($r = .314$, $p = .005$); and anti-overlap ($r = .242$, $p = .031$) (Fig. 4C and D). Intra-subject variability increased in the pro-saccade task at a rate of 0.6 ms/year for gap, 0.5 ms/year for overlap, and 0.2 ms/year for both gap and overlap conditions in the anti-saccade task. A three-way ANOVA was performed to further investigate the pattern of increased variability across age groups. As age categories increased, intra-subject variability in SRT also increased ($F(1,4) = 6.845$; $p < .001$). The CV was lower in the gap condition (22 ± 6) than in the overlap condition (25 ± 5) for the anti-saccade task ($F(1,73) = 16.62$, $p < .01$). The CV was also higher in the pro-saccade task (29 ± 9) compared with the anti-saccade task (24 ± 6) ($F(1,74) = 40.21$, $p < .01$), likely due to shorter reaction times in the pro-saccade task. A trend analysis indicated that the CV increased ($p < .001$) with group age, and post hoc analysis (Tukey HSD) showed that the CVs of most age categories differed from those of others, especially in the pro-saccade task (see Table 2 for post hoc comparisons).

3.3. Direction errors

As individuals aged, the percentage of direction errors increased significantly in the anti-overlap ($r = .342$, $p = .002$) and approached significance in the anti-gap ($r = .219$, $p = .051$) conditions (Fig. 4F). A non-parametric correlation also showed that pro-gap direction errors also increased with age ($r = .286$, $p = .011$; Fig. 4E). The anti-overlap errors

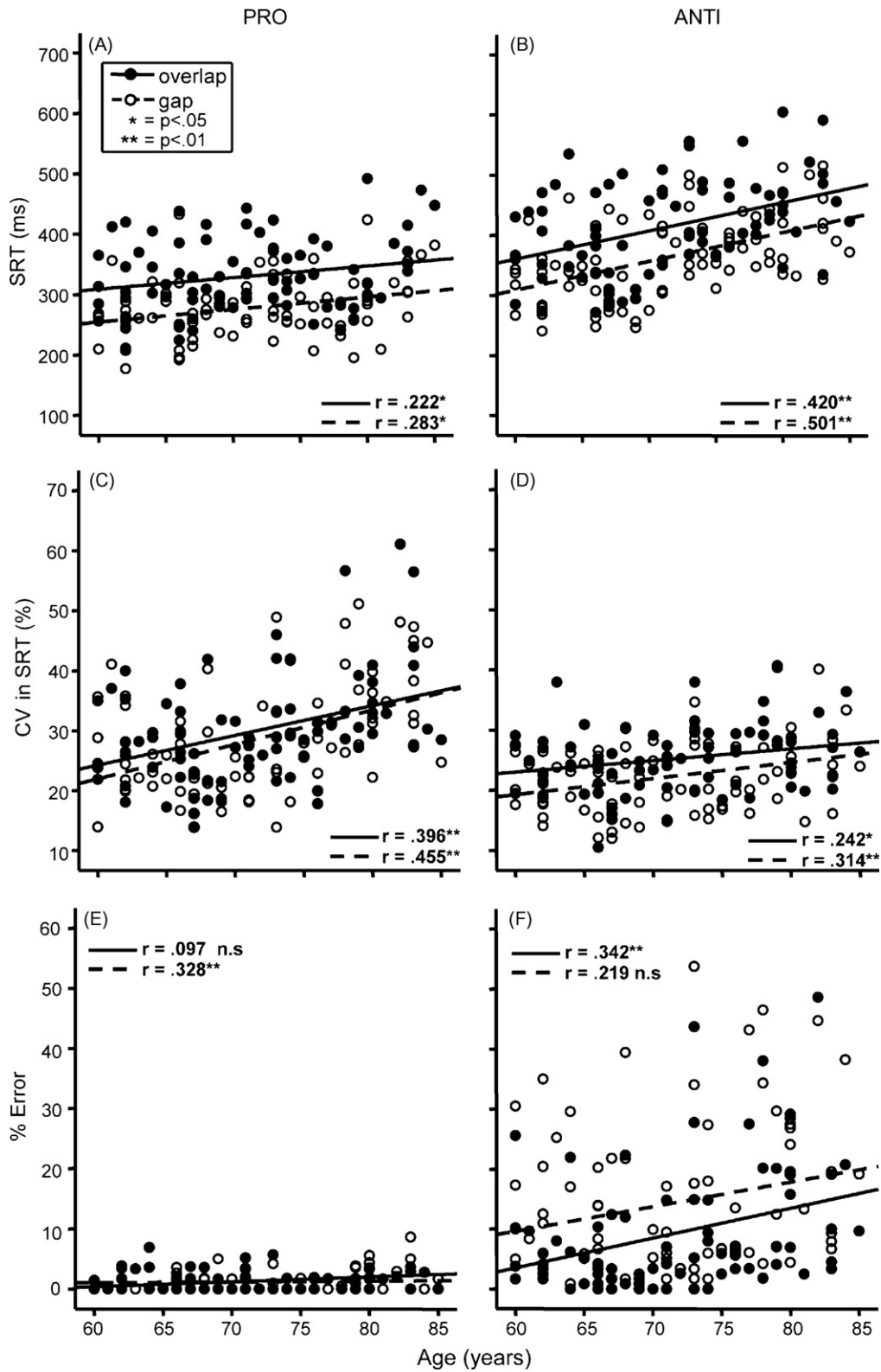


Fig. 4. Pro- and anti-saccade results for both gap (open-faced circles) and overlap (solid circles) conditions, individually plotted (horizontal line = Pearson correlation, * $p < .05$) across age: (A and B) saccadic reaction time (SRT); (C–D) coefficient of variation (CV) of SRT (standard deviation/mean $\times 100$); (E and F) Percent direction errors (erroneous pro-saccades). Correlation across age, * $p < .05$, ** $p < .01$. Outliers ± 3 standard deviations from the mean have been removed.

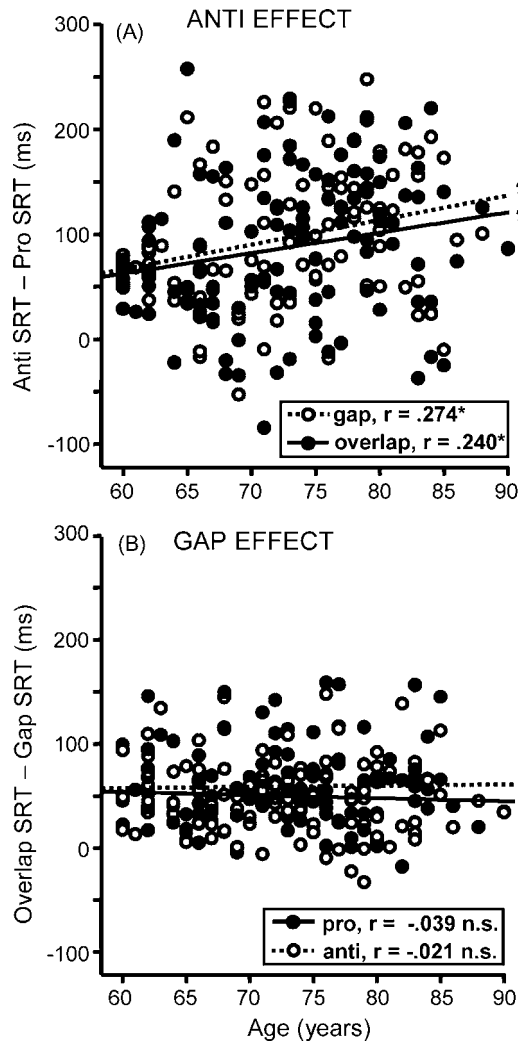


Fig. 5. Gap effect and anti-effect individually plotted across age (horizontal line = Pearson correlation, $*p < .05$): (A) anti-effect = anti-SRT – pro-SRT for both gap (open-faced circles) and overlap (solid circles). (B) Gap effect = overlap SRT – gap SRT for both pro-saccade (solid circles) and anti-saccade (open-faced circles). Horizontal line = Pearson correlation, $*p < .05$.

increased at a rate of 0.5%/year—a considerable increase, considering that over a 20-year period, this would amount to approximately 10% increase in the proportion of anti-saccade direction errors. A three-way ANOVA was performed to investigate how direction errors were influenced for increasing age groups. The proportion of direction errors increased significantly with group age in the anti- but not in the pro-saccade task ($F(1,4) = 107.17, p = .035$). A two-way interaction between task (pro-saccade vs. anti-saccade) and fixation condition (gap vs. overlap) revealed that subjects made more direction errors in the anti-saccade vs. pro-saccade task, and more errors in gap vs. overlap conditions in the anti-saccade task ($F(1,4) = 3.64, p = .01$; Fig. 4E and F). In the anti-saccade task, post hoc comparison revealed a significant difference only between age category 65–69 and age category 80–85 (Table 2). A trend analysis indicated a linear ($p = .015$) relationship between anti-saccade errors and group age.

4. Discussion

This study provides a detailed description of the changes in saccade parameters that occur with healthy aging (60–85 years). Saccadic reaction times, intra-subject variability, the range of express saccades, the “anti-effect” (mean latency difference between pro- and anti-saccades), and the proportion of direction errors were all sensitive to the effects of aging. Specifically, the generation of pro-saccades, a simple sensory-motor process, was minimally influenced by age (revealed by pro-saccade SRT, express saccades, and the gap effect—the mean latency difference between overlap and gap saccades). In contrast, processes required for voluntary saccade initiation (revealed by anti-saccade SRT and the anti-effect) and voluntary saccade suppression (revealed by anti-saccade errors) were more sensitive to aging. The rate at which these parameters changed correlated with age, such that from age 60 to 85 years, correct anti-saccade reaction times increased by about 110 ms, and error rates increased by approximately 11%. This suggests that the mechanisms driv-

Table 2
Post hoc (Tukey) analysis of mean differences between age groups.

Pro				Anti			
Age category	Age category	SRT (Sig.)	CV (Sig.)	Direction error (Sig.)	SRT (Sig.)	CV (Sig.)	Direction error (Sig.)
60–64 vs.	65–69	1.000	.825	.999	.820	.717	.867
	70–74	.526	.995	.963	.106	.945	.986
	75–79	.996	.340	.797	.213	.842	.958
	80–85	.019*	.005*	.181	.006*	.209	.155
65–69 vs.	70–74	.438	.557	.991	.003*	.233	.531
	75–79	.998	.034*	.879	.015*	.172	.481
	80–85	.011*	.000*	.233	.000*	.008*	.011*
70–74 vs.	75–79	.353	.513	.984	1.000	.996	.999
	80–85	.402	.009*	.456	.696	.553	.327
75–79 vs.	80–85	.011*	.486	.839	.699	.831	.553

* The mean difference is significant at the .05 level.

ing anti-saccades vs. pro-saccades degrade at different rates in the elderly, implying that they are subserved by different underlying processes. These data support our hypothesis that the neurological changes related to healthy aging influence saccadic control, such that the ability to initiate voluntary saccades and inhibit automatic responses decreases with age.

4.1. Relation to previous literature

Previous studies on saccadic eye movements in senescence have used pro- and anti-saccade paradigms (Abel and Douglas, 2007; Abrams et al., 1998; Eenshuistra et al., 2004; Kaneko et al., 2004; Klein et al., 2000; Munoz et al., 1998; Olincy et al., 1997; Pratt et al., 2006; Shafiq-Antonacci et al., 1999) and produced conflicting results. Many studies have identified increased error rates and reaction times in the anti-saccade task in the elderly (Abel and Douglas, 2007; Klein et al., 2000; Munoz et al., 1998; Olincy et al., 1997; Shafiq-Antonacci et al., 1999). However, other studies found no differences between young ($M=19$ – 22 years) and old ($M=62$ – 66 years) populations in anti-saccade latencies and error rates (Eenshuistra et al., 2004; Pratt et al., 2006) or pro-saccade latencies (Pratt et al., 2006). These findings could be explained by the relatively young mean age of the elderly populations used in both studies (e.g., 62 years), which does not capture differences that occur later in life. Examining older populations reveals deficits within healthy aging such as slower latencies, increased variability and direction errors, especially between age category 65–69 and age category 80–85 (similar to Klein et al., 2000). A large subject base with many trials from each participant allowed us to clarify many age effects that previously have been masked by the amount of between-subject variability in the elderly. Contrary to Pratt et al. (2006), our results revealed that the anti-effect (the increased time required to inhibit the automatic pro-saccade and initiate the voluntary anti-saccade (Munoz and Everling, 2004; Olincy et al., 1997) correlated with aging (Fig. 5A), revealing that the time it takes to process a voluntary movement lengthens with age.

The gap effect did not correlate with increased aging (Fig. 5B). Controversy remains surrounding the nature of the gap effect. Some studies suggest that the introduction of a gap between fixation removal and stimulus appearance allows attention to disengage before shifting to the new stimulus location (Harwood et al., 2008; Pratt et al., 2006). However, the gap effect has also been linked to low-level warning effects (Ross and Ross, 1980). In our studies, the gap effect was not modulated with task (i.e., consistent across both pro- and anti-saccade tasks), nor was it influenced by aging. Therefore, we speculate that this mechanism of reduced SRT produced by the advanced disappearance of the fixation point is not governed by high-level cognitive processes. Similarly, pro-saccade latencies only changed minimally with age, further suggesting that these more automatic behaviors are subserved by different mechanisms than voluntary saccade

initiation and saccade suppression. The automatic processes are less affected by aging than the voluntary processes.

Short-latency pro-saccades (express saccades) reflect the shortest afferent-to-efferent conduction times in the oculomotor system (Fischer and Weber, 1993; Dorris et al., 1997). Express saccades in humans were reported to range from 75 to 140 (Fischer et al., 1997; Fischer and Ramsperger, 1984; Fischer and Weber, 1993; Munoz et al., 1998). Previously, it has been reported that elderly individuals make significantly fewer express saccades (Klein et al., 2000; Munoz et al., 1998). However, the previous criteria for defining this range did not take into account that SRT can be influenced dramatically by factors such as stimulus intensity (Bell et al., 2006), and are therefore not locked to a specific time. Here, we used the distribution of correct and error SRTs to define the express saccade epoch (see Sections 2 and 3). Using the SRT distributions to calculate express saccade ranges for each age group revealed that the proportion of express saccades occurring in our elderly population was similar to those previously reported in younger populations. Although Klein et al. (2000) reported minimal express saccades in the elderly, the SRT distributions had errors corresponding to bimodal peaks in the pro-SRT distributions occurring at latencies of approximately 110–200 ms. This is very similar to what we have calculated in the present study (Fig. 2F–J). Therefore, it appears that elderly subjects are indeed capable of generating express saccades, but they are delayed in onset. The onset of the range of express saccades in the elderly is delayed from 90 ms to at least 110 ms after stimulus onset. The persistence of short-latency errors in the anti-saccade task up to 200 ms in the elderly suggests that the increase in the duration of this range (grey shaded boxes in Fig. 2) may be due to a weaker voluntary saccade initiation signal which subsequently delays initiation of the correct anti-saccade. Therefore, in addition to a minimal delay in onset of the express saccade epoch, it appears that elderly subjects also require more time to process voluntary initiation signals as reflected by the increase in the end of the express epoch. Although the saccades occurring within this epoch are too slow to fit previous criteria for express saccades (Fischer and Weber, 1993), the onset of the express epoch remained stable across the age groups studied, suggesting that these saccades are subserved by the same mechanism as traditional express saccades, but occur at slightly longer latencies (i.e., the entire distribution is shifted to the right in the elderly). In addition, the minimal changes in pro-saccade latencies suggest that visual and motor processing is not as impaired as cognitive processing in the elderly.

4.2. Saccade circuitry

The dissociation between automatic and voluntary saccade behaviors provides insight into how aging influences the brain circuitry underlying these mechanisms. Lesions studies have demonstrated that frontal areas such as frontal eye fields (FEFs), supplementary eye fields (SEF), and dorsolateral prefrontal cortex (DLPFC) are important for voluntary saccade

initiation and suppression of automatic saccades (Guitton et al., 1985; Pierrot-Deseilligny et al., 1991; Rivaud et al., 1994), whereas the supplementary motor area and the posterior parietal cortex are more important for automatic saccade generation (Heide and Kömpf, 1998; Pierrot-Deseilligny et al., 1991). Electrophysiological studies have also confirmed that neurons in the FEF (Everling and Munoz, 2000), SEF (Schlag-Rey et al., 1997), and DLPFC (Johnston and Everling, 2006) are modulated by task instruction and appear to be selectively recruited for the anti-saccade task. Therefore, we expect that altered input from any one of these areas could influence the oculomotor circuitry downstream, leading to increases in SRT and error rates. Therefore, the ability to initiate movement voluntarily and suppress unwanted or automatic saccades is reflective of good frontal function (Everling and Fischer, 1998; Munoz and Everling, 2004). The stronger correlation between aging and voluntary saccade performance suggested that the structures related to automatic saccade initiation are not as susceptible to age-related declines as those related to voluntary saccade initiation. It is known that the frontal cortex is more susceptible to natural neural degeneration that occurs in the cerebral cortex with age (Buckner et al., 2000; Creasey and Rapoport, 1985; Kramer et al., 2007; Raemaekers et al., 2006). The fact that aging minimally influenced pro-saccade performance and the gap effect, but systematically increased voluntary saccade latencies, the anti-effect, and the quantity of direction errors, supports the notion that different underlying mechanisms and structures are responsible for the generation of automatic vs. volitional saccades (Hikosaka et al., 2006; Munoz and Everling, 2004; Raemaekers et al., 2006), and that the structures involved in executing voluntary saccades are less resilient to the aging process.

5. Conclusions

This is the first study to quantify precisely the rate at which saccade control declines across the elderly, and to show that the latency range of express saccades lengthens in the elderly. It appears that aging is selective for specific aspects of the oculomotor circuitry (Shafiq-Antonacci et al., 1999) such that automatic saccade processing declines with age, but at a much slower rate than the voluntary control of saccades. We speculate that the natural neural degeneration that occurs with age influences the input coming from the frontal cortex to the saccade generating system, and is thus responsible for these changes. This corresponds to the age-related decline in cognitive functions associated with these frontal structures, such as focused attention, task switching, and working memory (Eppinger et al., 2007; Grady et al., 2006; Kray et al., 2005). Appreciation of these normative saccade parameters will be useful in assessing age-related frontal lobe function/dysfunction and as a comparison to age-related neurological disorders such as Mild Cognitive Impairment, Alzheimer's disease, and Parkinson's disease.

Disclosure statement

The authors report no actual or potential conflicts of interest.

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