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RESEARCH REPORT

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The effect of age and gender on anti-saccade performance: Results from a large cohort of healthy aging individuals

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Abstract

By 2050, the global population of people aged 65 years or older will triple. While this is accompanied with an increasing burden of age-associated diseases, it also emphasizes the need to understand the effects of healthy aging on cognitive processes. One such effect is a general slowing of processing speed, which is well documented in many domains. The execution of anti-saccades depends on a well-established brain-wide network ranging from various cortical areas and basal ganglia through the superior colliculus down to the brainstem saccade generators. To clarify the consequences of healthy aging as well as gender on the execution of reflexive and voluntary saccades, we measured a large sample of healthy, non-demented individuals ($n = 731$, aged 51–84 years) in the anti-saccade task. Age affected various aspects of saccade performance: The number of valid trials decreased with age. Error rate, saccadic reaction times (SRTs), and variability in saccade accuracy increased with age, whereas anti-saccade costs, accuracy, and peak velocity of anti-saccades and direction errors were not affected by age. Gender affected SRTs independent of age and saccade type with male participants having overall shorter SRTs. Our rigid and solid statistical testing using linear mixed-effect models provide evidence for a uniform slowing of processing speed independent of the actually performed eye movement. Our data do not support the assumption of a specific deterioration of frontal lobe functions with aging.

KEYWORDS

eye movements, eye tracking, gender differences, healthy aging, humans, main sequence, trial history

Abbreviations: ANOVA, analysis of variance; dlPFC, dorsolateral prefrontal cortex; FEF, frontal eye field; PPRF, paramedial pontine reticular formation; riMLF, rostral interstitial medial longitudinal fasciculus; SC, superior colliculus; SEF, supplementary eye field; SRT, saccadic reaction times; TREND, Tübinger evaluation of risk factors for early detection of neurodegeneration.

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1 | INTRODUCTION

1.1 | Age-related changes in brain functions and cognitive processing

Life expectancy is steadily rising all over the world. This leads to a continuous increase in the fraction of elderly people in our society (Vaupel, 2010). Therefore, age-related changes in brain functions, such as cognitive processing as well as motor control, are in the focus of public interest. Such changes are not necessarily pathological. They also occur during normal, healthy aging, particularly in the seventh decade of life. A manifestation of these changes is a general slowing of processing speed (Cerella & Hale, 1994; Salthouse, 2000), often termed cognitive decline (see Lindenberger (2014) for review). In addition, the control of motor actions also declines with age, causing as a deficit in balance, gait, movement speed, and coordination (Seidler et al., 2010). Recently, it was proposed that a decrease in processing speed may act as the common cause for behavioral slowing in cognitive and motor tasks (Sleimen-Malkoun, Temprado, & Berton, 2013). One possible reason for this general slowing is the decreased connectivity in the frontoparietal and default mode networks of the elderly brain (Grady et al., 2010; Koch et al., 2010; Madden et al., 2010). Age also adversely affects memory, another aspect of cognition, through changes in synaptic plasticity of the hippocampus and the prefrontal cortex (Morrison & Baxter, 2012).

1.2 | The anti-saccade task

Many of these age-related changes affect the frontal cortex, which is the last part of the brain to develop during ontogeny (Fuster, 2002). Ironically, it also seems to be the first one to deteriorate later in life. An oculomotor paradigm, which heavily relies on the integrity of cognitive control and therefore on the frontal cortex, is the anti-saccade task (Hallett, 1978). In contrast to the pro-saccade task, where participants execute a visually guided saccade toward a suddenly appearing target, the anti-saccade task requires participants to perform a voluntarily driven anti-saccade opposite to the position of this target. For example, if a target is presented 10° to the right, the task is to generate a 10° saccade to the left. Sometimes participants fail to suppress the erroneous, reflexively driven saccades toward the target, this is called direction error. The frequency of these direction errors (e.g., error rate) can be used as a measure of cognitive control. Intuitively, one would expect that SRTs should be prolonged following the execution of a direction error (Rabbitt, 1966). However, the opposite is true: SRTs decrease and error rates increase after the execution of a direction error (Tatler & Hutton, 2007). When subjects perform blocks of anti-saccades in alteration with blocks of pro-saccades, a prolongation of the SRTs is observed in the first trial after the change of the experimental paradigm (Hodgson, Golding, Molyva, Rosenthal, & Kennard, 2004).

Single-unit recordings in awake rhesus monkeys have revealed that the execution of pro- and anti-saccades depends on the recruitment of several neural processes (Munoz & Everling, 2004). First, the generation of anti-saccades depends on the suppression of the automatic response and vector inversion of the visual input, which is achieved by the frontal and supplementary eye fields (FEF and SEF) together with the basal ganglia. High activity of neurons in the FEF, which project directly to the superior colliculus (SC) and the brainstem, indicates an upcoming anti-saccade (Everling & Munoz, 2000). Originally, it was thought that during the preparation for an anti-saccade, an additional inhibitory signal from the dorsolateral prefrontal cortex (dlPFC) is sent to the SC to suppress any pending pro-saccade (Johnston & Everling, 2006). However, based on experiments using cryogenic inactivation of the dlPFC, the influence of this area on the SC is excitatory (Everling & Johnston, 2013; Johnston, Koval, Lomber, & Everling, 2014). In the same line of evidence, patients with lesions in the dlPFC show a clear increase in the proportion of direction errors in the anti-saccade task (Muri & Nyffeler, 2008). Second, the execution of a pro-saccade as a visual reflexive behavior depends on projections of parietal and occipital areas to the SC: High pre-stimulus activity of SC buildup neurons signals the occurrence of a direction error, for example, an erroneous pro-saccade (Everling, Dorris, & Munoz, 1998). However, the execution of anti- and pro-saccade depends critically on the correct function of the SC (Hanes & Wurtz, 2001).

These separate neuronal processes underlying the execution of pro- and anti-saccades provide the ground for the observation that several saccade parameters differ between pro- and anti-saccades: Anti-saccades have longer saccadic reaction times (SRT) (Evdokimidis et al., 2002; Hallett, 1978) and lower peak velocities (Edelman, Valenzuela, & Barton, 2006; Smit, Van Gisbergen, & Cools, 1987) compared to pro-saccades.

1.3 | Effects of age in the anti-saccade task

Although several studies analyzed the effects of age on eye movements performed in the anti-saccade task, the results are either inconsistent and contradictory or even missing. To summarize the results, we performed a literature survey (see Table 1). We divided the literature into studies that treated age as a categorical factor, for example, adult and elderly participants (grouped comparison), and studies that used a continuous factor for age correlation (correlation analysis). We restricted our survey to the comparison of adult and elderly

TABLE 1 Previous work on the influence of healthy aging on anti-saccade task performance

			Eye movement parameter									
			SRT			SRT variability		Accuracy		Velocity		Error rate
	Participants	Age	AS	PS	Δ	AS	PS	AS	PS	AS	PS	
Grouped comparison												
Abel and Douglas (2007)	A: 27 O: 32	22 ± 4.2 73 ± 5.8	+	+[a]								+
Alichniewicz et al. (2013)	A: 13 O: 23	25 ± 2 59 ± 7	+	+								+[b]
Butler et al. (1999)	A: 16 O: 16	17–23 65–80	+	+	=			=	=			+[b]
Crawford et al. (2005)	A: 17 O: 18	23.8 75.2	+	=								=
Eenshuistra et al. (2004)	A: 21 O: 20	22 ± 1.7 66 ± 4.2	+	+								−
Fujiwara et al. (2010)	A: 22 O: 96	20–29 60–85	+	+		+	+					+
Harsay et al. (2010)	A: 18 O: 18	18–36 64–85	+									=[c]
Olk and Jin (2011)	A: 28 O: 27	18–24 61–78	+	+								+
Sweeney et al. (2001)	A: 28 O: 20	24 ± 4 72 ± 4	+	+					−		−	+
Correlation analysis												
Bonnet et al. (2013)	145	19–82	+	+								+
Klein et al. (2005)	327	9–88	+	+			+					+[d]
Mirsky et al. (2011)	48	48–79	=	=				=	=	=	−	
Munoz et al. (1998)	168	5–79	+	+	=	=	=			=	=	=
Olincy et al. (1997)	42	19–79	+	+	+			=	−			+
Peltsch et al. (2011)	81	60–85	+	+	+	+	+					+[d]
Raemaekers et al. (2006)	31	18–72	+	+								=[b]
Shafiq-Antonacci et al. (1999)	238	44–85	+	+		+	+	=	=	=	=	+

Note: Age-related changes are indicated by symbols (+: increase with age, =: no change with age, −: decrease with age). Accuracy subsumes several measures of the ratio of saccade and target amplitude.

Δ: Anti-saccade costs (difference between AS and PS SRT); A: Adult age group; O: Old age group.

Abbreviations: AS, Anti-saccade; PS, pro-saccade; SRT, Saccadic reaction time.

[a]Reported as memory-guided saccades.

[b]Derived from the reported percentage of correct AS.

[c]Reported as percentage of hits.

[d]Reported as percentage of direction errors.

participants, as the effects of maturation during childhood and adolescence (Luna, Velanova, & Geier, 2008) are not addressed in our study.

There is wide agreement that SRTs increase with age. With the exception of a single study (Mirsky et al., 2011), a conjoint elongation in anti- and pro-SRTs for older participants is reported (Abel & Douglas, 2007; Abel, Troost, & Dell'Osso, 1983; Alichniewicz, Brunner, Klunemann, & Greenlee, 2013; Butler, Zacks, & Henderson, 1999; Eenshuistra, Ridderinkhof, & van der Molen, 2004; Klein, Foerster, Hartnegg, & Fischer, 2005; Olk & Jin, 2011; Raemaekers, Vink, van den Heuvel, Kahn, & Ramsey, 2006; Sweeney, Rosano, Berman, & Luna, 2001). However, the increase was not always equal, but was stronger in anti-SRTs

(Crawford et al., 2005; Fujiwara et al., 2010; Olincy, Ross, Youngd, & Freedman, 1997; Peltsch, Hemraj, Garcia, & Munoz, 2011). This leads inevitably to contradictory results for the anti-saccade costs, which is defined as the difference between anti- and pro-SRTs. Two studies report no age-related changes of the anti-saccade costs (Butler et al., 1999; Munoz, Broughton, Goldring, & Armstrong, 1998), whereas there are other studies reporting increasing costs with age (Crawford et al., 2005; Fujiwara et al., 2010; Olincy et al., 1997; Peltsch et al., 2011).

In addition, there are contradictory results for the effect of age on error rate. It is well established that there is an inverse relationship between SRTs and error rate (Li et al., 2012; Mack & Ilg, 2014). As most studies show an age-related increase in SRTs, one might expect that older participants show a reduced error rate, as actually shown in one study (Eenshuistra et al., 2004). In contrast to this expectation, the majority of reports show an increase of error rates with age (Abel & Douglas, 2007; Alichniewicz et al., 2013; Butler et al., 1999; Klein et al., 2005; Olincy et al., 1997; Peltsch et al., 2011; Shafiq-Antonacci et al., 1999). In addition, there are also experimental results in which error rates are not affected by age at all (Crawford et al., 2005; Munoz et al., 1998; Raemaekers et al., 2006). Finally, we found no reports in the literature about whether age affects the consequences of errors in the subsequent trial.

Therefore, we decided to clarify these disagreements in the literature and missing information by examining anti-saccades in a huge cohort of 731 neurologically healthy adult and elderly participants. In addition to the effect of age, we examined possible gender differences in the parameters of direction errors and anti-saccades. The high number of participants provides the ground to show even small effects of age and gender by statistical testing with either linear mixed-effect models or simple linear models despite the high inter-individual scatter of the specific parameter.

2 | MATERIAL AND METHODS

2.1 | Participants

Participants (n = 731, aged 51–84 years) were recruited within the Tübinger evaluation of Risk factors for Early detection of Neuro-Degeneration (TREND) study (Berg & Eschweiler, 2009). The age distribution is shown in Figure 1. There is a small but significant difference in the mean age of our female (66 years) and male participants (68 years) (ANOVA: F = 19.33, $\boldsymbol{p < .0001}$). For this study, only healthy, non-demented aging individuals were recruited. All participants were pre-screened and excluded if any history of psychiatric diseases, dementia, epilepsy, stroke, multiple

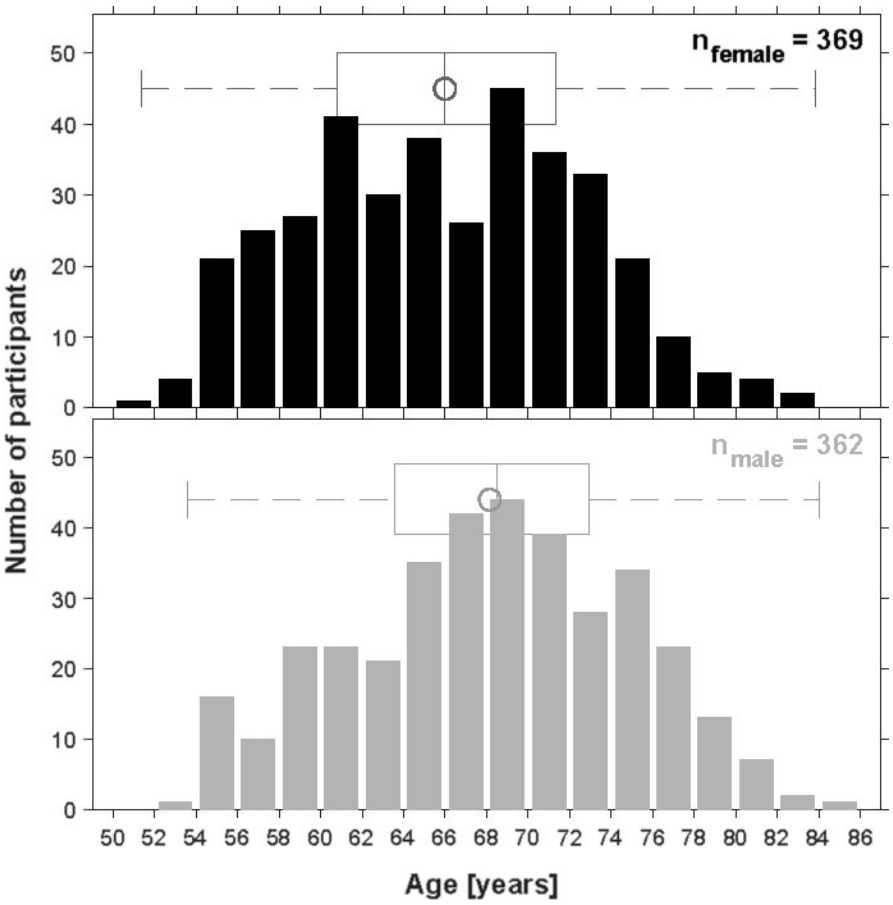

FIGURE 1 Age distribution of the participants grouped by gender (black: females, light gray: males). Boxplots show lower and upper quartiles together with median (box) and whiskers as 1.5 interquartile ranges. Circles depict means. *n*: Number of participants in each group

sclerosis, or encephalitis was reported. Additional exclusion criteria were based on disorders that would have prevented study completion, like paresis, severe sensory dysfunction, or the inability to walk without assistance. For a more detailed description of inclusion/exclusion criteria to the TREND study, see Hobert et al. (2011); Berg (2012). It is important to note that the participants did not only perform our eye movement study. In addition, they contributed to several neurological, behavioral, and mnemonic testing (Berg & Eschweiler, 2009). Therefore, the duration of the oculomotor experiments was limited to 30 min. The experiments were performed in accordance with the Declaration of Helsinki and approved by the Ethic Commission of the Medical Faculty of the University of Tübingen, and all participants gave informed consent.

2.2 | Experimental setup

We measured horizontal eye movements of the left eye with a limbus tracker (Skalar IRIS, Skalar Medical B.V., Delft, Netherlands) (Reulen et al., 1988). The IRIS has a resolution of 2 arcmin, and eye position was digitized at 1 kHz. Stimuli were presented on a 23 " LED screen (Fujitsu P23T-6; 1,920 × 1,080 pixel resolution, 60 Hz refresh rate) and generated using the Psychophysics Toolbox version 3 (Brainard, 1997; Kleiner, Brainard, & Pelli, 2007; Pelli, 1997) under Matlab2008a (The MathWorks Inc., 2008). We used white fixation and saccade targets (luminance 58 cd/m^2) on a black background (luminance ≤ 0.1 cd/m^2). Viewing distance was kept constant at 57 cm through a chin rest and head rest. Participants' heads were gently strapped to the headrest during the entire experiment to reduce possible movement artifacts.

2.3 | The anti-saccade task

Participants were instructed to look at the horizontal mirror position of an appearing square target (size: 10 × 10 arcmin), that is, the position opposite on the horizontal axis. The target appeared randomly at 5° or 10°, respectively, left or right to the initial fixation cross (size: 16 × 16 arcmin) at the center of the screen. The fixation duration was randomly determined from a uniform distribution between 500 and 1,000 ms on a trial-by-trial basis. The saccade target appeared directly afterward and remained on the screen until the end of the trial at 1,500 ms. The next trial started immediately thereafter. In total, 160 trials were conducted (40 repetitions for each of the four target positions as earlier published (Mack & Ilg, 2014)). The experiment was highly standardized by the use of a fixed protocol to avoid differential influences from the experimenter. Because of the already mentioned time restriction within the TREND study, we decided to run only a single block of 160 trials with the anti-saccade instruction. There was no online evaluation of the data during the experiment, so the number of performed anti-saccades and direction errors varied according to the individual error rate.

2.4 | Data processing

Eye position was first low-pass filtered with a 5th-order Butterworth filter (cutoff frequency 45 Hz). Subsequently, velocity and acceleration were obtained by a two-point central difference method. Saccades were detected when eye velocity was larger than 40°/s, peak velocities had to be larger than 80°/s, and peak accelerations had to be larger as 4,000°/s^2. A given trial was rejected if one out of the following six criteria was met:

1. Trial without any saccade: No saccade was detected at all.
2. Eye position changed more than 2.5° in a 250-ms interval before saccade onset.
3. Inaccurate saccade: The saccadic gain (see below) was smaller than 0.4 or larger than 1.6.
4. Preliminary saccade: The SRT was shorter than 90 ms.
5. Exceeded peak velocity: The absolute peak velocity was >1,000°/s.
6. Exceeded peak acceleration: The absolute acceleration/deceleration peak was >100,000°/s^2.

In an accepted trial, a saccade was classified as anti-saccade if its end position was horizontally opposite to the target position; otherwise, it was classified as direction error. To quantify how many valid saccades of either type were recorded for a participant, we computed the percentage of accepted trials as

$$\frac{n_{\text{Anti}} + n_{\text{Err}}}{160} * 100, \tag{1}$$

where 160 is the total number of trials per participant and n_{Anti} and n_{Err} are the numbers of valid anti-saccades and direction errors. The error rate was calculated by

$$\frac{n_{\text{Err}}}{n_{\text{Anti}} + n_{\text{Err}}} * 100. \tag{2}$$

If a participant made less than seven valid saccades of either type in total, the according parameters (see next section) of this type were excluded from the analysis. This exclusion criterion was chosen to be saccade-type specific, because removal of all data of a participant would have artificially

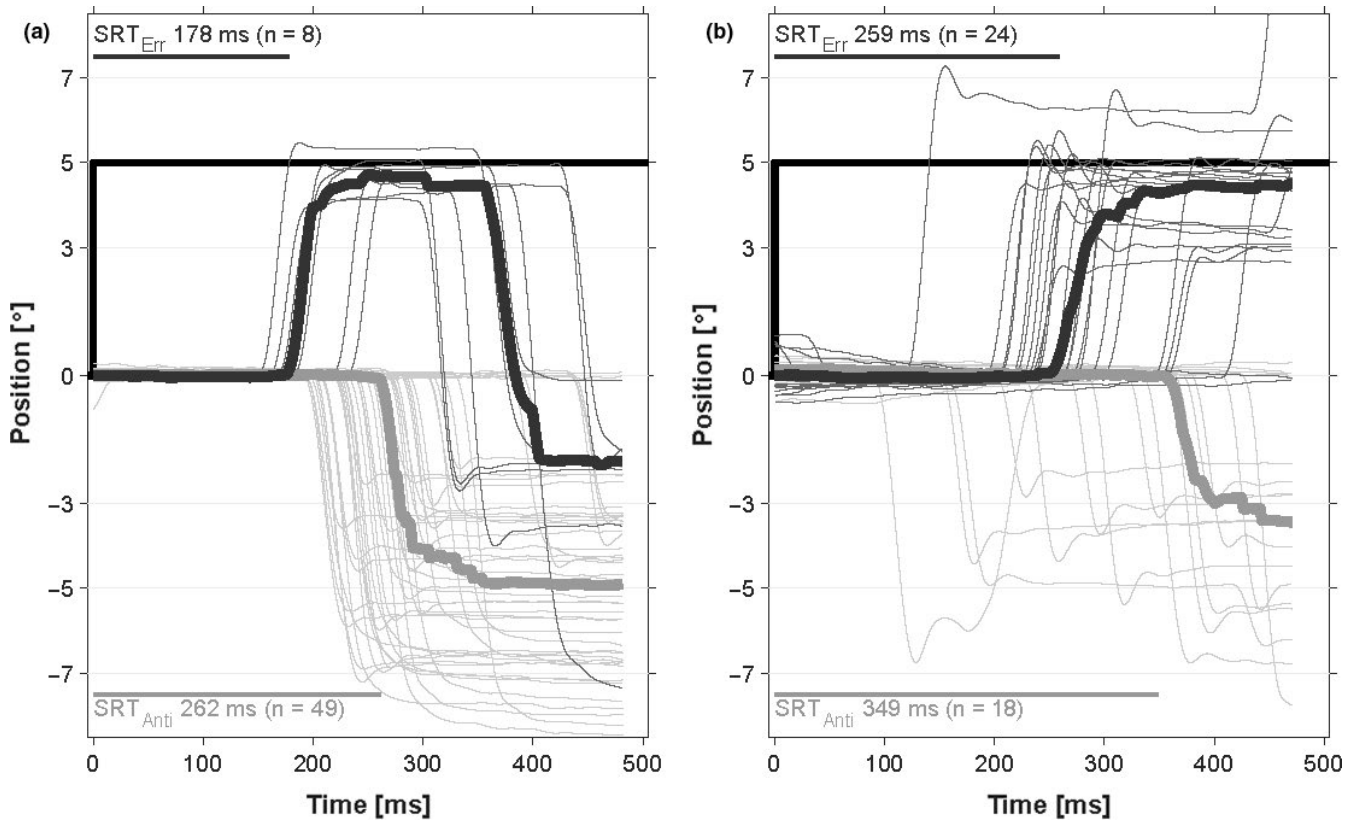

FIGURE 2 Single trial eye position traces for all trials of two typical male participants (a) 54 years, number of accepted trials 74%, error rate 13%; and (b) 82 years, number of accepted trials 46%, error rate 70%. The target appeared at 5° (leftward trials were inverted), and only valid trials are shown. Trials in which the participants performed anti-saccades are shown in light gray, trials with direction errors are presented in dark gray. Bold lines represent median eye position across all traces. The black horizontal line shows target position. *n*, Number of valid saccades; SRT, Saccadic reaction time in each condition

narrowed the distribution of error rates; for example, perfect performance with no direction errors at all may then also have been removed from the analysis. In total, eight participants (1.1%) were removed from the direction error analysis, 46 (6.3%) were removed from the anti-saccade analysis, and one participant (0.1%) was excluded from the entire analysis because he failed to produce enough valid saccades of either type. The data related to the various exclusion criteria as well as the results of the linear models are shown in the supplement (Figure S1 and Table S1–S6) together with the descriptive statistics (Table S7).

2.5 | Statistics and saccade parameter computation

For each valid saccade, the following parameters were determined:

1. saccadic reaction time (SRT) as time from target presentation to saccade onset,
2. saccade amplitude as difference between start and end position of the saccade,
3. gain as saccade amplitude divided by target eccentricity,
4. saccadic peak velocity as the maximum velocity between start and end of the saccade.

We pooled data for all four target positions. To obtain the SRTs and gains for each saccade type and each individual, the median was computed from all valid saccades and used for the further analysis. We decided to report medians as SRTs tend to have especially skewed distributions (see Figure 5).

In addition, we computed the anti-saccades cost. In contrast to the original definition as the difference between SRT of anti- and pro-saccades (Munoz et al., 1998; Peltsch et al., 2011), we calculated the difference between anti-saccades and direction errors. As direction errors have slightly longer SRTs as pro-saccades (unpublished observation) (Noorani & Carpenter, 2014), our anti-saccade costs are rather underestimated compared to the literature. The intra-individual variability of SRT and gain was quantified with the standard deviation (*SD*) of the respective values.

Peak velocity of a saccade depends on the saccade amplitude, and this relationship is called main sequence (Bahill, Clark, & Stark, 1975; Baloh, Sills, Kumley, & Honrubia, 1975). We calculated a robust linear regression (Holland & Welsch, 1977) of

the amplitude and peak velocity of each detected saccade for each participant and saccade type separately. To further analyze the data statistically, we computed the peak velocity of a saccade with the amplitude of 10° from the fitted linear regression

$$\text{peak velocity} = 10 * b1 + b0, \quad (3)$$

where $b0$ and $b1$ are the resulting coefficients.

For the analysis of the influence of age and gender on gain, SRTs, and peak velocities as well as their respective variabilities, we calculated random slope and intercept linear mixed-effect (LME) models (Baayen, Davidson, & Bates, 2008; Luke, 2017) using the function fitlme in the Statistic Toolbox in Matlab2016a. Age of participants in years (not mean centered), gender (0 for female and 1 for male), and saccade type (0 for anti-saccades and 1 for direction errors) were used as fixed factors. Subject was chosen as random factor to control for the interdependences between the aforementioned saccade type measures. For error rate, anti-saccade costs, and the number of valid trials, simple linear models (LM) were applied. Throughout the entire manuscript, results of statistical tests are considered significant at an alpha level of 0.05 and printed bold. In all figures, the results of the LM and LME models, respectively, are visualized. Significant effects of gender are shown by solid regression lines, whereas non-significant effects are indicated by dashed regression lines. Effects of age are indicated by filled (significant) or empty (non-significant) triangles added to the ordinate. The triangles inform about the mean of the median age split (≤67 and >67) of the actual parameter (only for visualization). Differences between saccade type (anti-saccades and direction error) are indicated by solid (significant) abscissa and dashed (non-significant) abscissa. In addition, vertical lines represent the median age and horizontal lines inform about the median of the y-values in each diagram.

Finally, for the examination of the saccade-type history on SRT and error rate, we sorted these values according to the saccade type in the previous trial (anti-saccade or direction error). In addition, we performed a median split of the data according to the age of the participants and calculated two-factorial ANOVAs with the factors previous saccade type and age. All statistical analyses were performed in Matlab2016a.

3 | RESULTS

Figure 2 depicts single eye position traces of an adult (54 years) and an older participant (82 years). The older participant produced more direction errors and had longer and more variable SRTs for both saccade types compared to the adult participant. The number of accepted trials was substantially decreased for the older participant (42 saccades out of 80 trials) compared to the adult participant (57 saccades out of 80 trials).

The direction errors of the adult participant are corrected around 400 ms, whereas the direction errors of the older participant occurred much later. We did not address the properties of the subsequent error correction in our study.

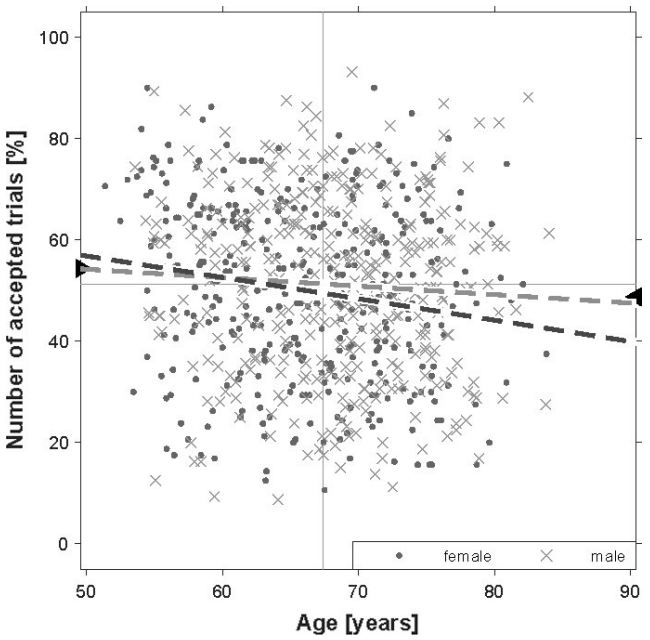

FIGURE 3 Number of accepted trials. Gray lines show the median of the age distribution (vertical; 67 years) and the number of accepted trials (horizontal; 51.2%). Dashed black (female) and gray lines (male) represent the result of the linear model dependency of age and gender. Filled triangles give the age median split of the number of accepted trials. Results of linear model are given in Table 2

3.1 | Number of accepted trials

Figure 3 gives the results of the number of accepted trials, and Table 2 informs about the parameters of the calculated linear model. We found a significant correlation between age and the number of accepted trials. On average, the number decreased at a rate of 0.4% per year (**$p < .001$**). In contrast, gender had no influence ($p = .24$).

TABLE 2 Linear model table on number of accepted trials

Number of accepted trials ~ Age * Gender			
Model: LM			
Model Stats: R^2 .0162, Intercept 77.9 (**$p < .001$**)			
	Estimate	T	p
Age	−0.4	−3.1	**<.001**
Gender	−15.4	−1.2	.24
Age x Gender	0.3	1.3	.19

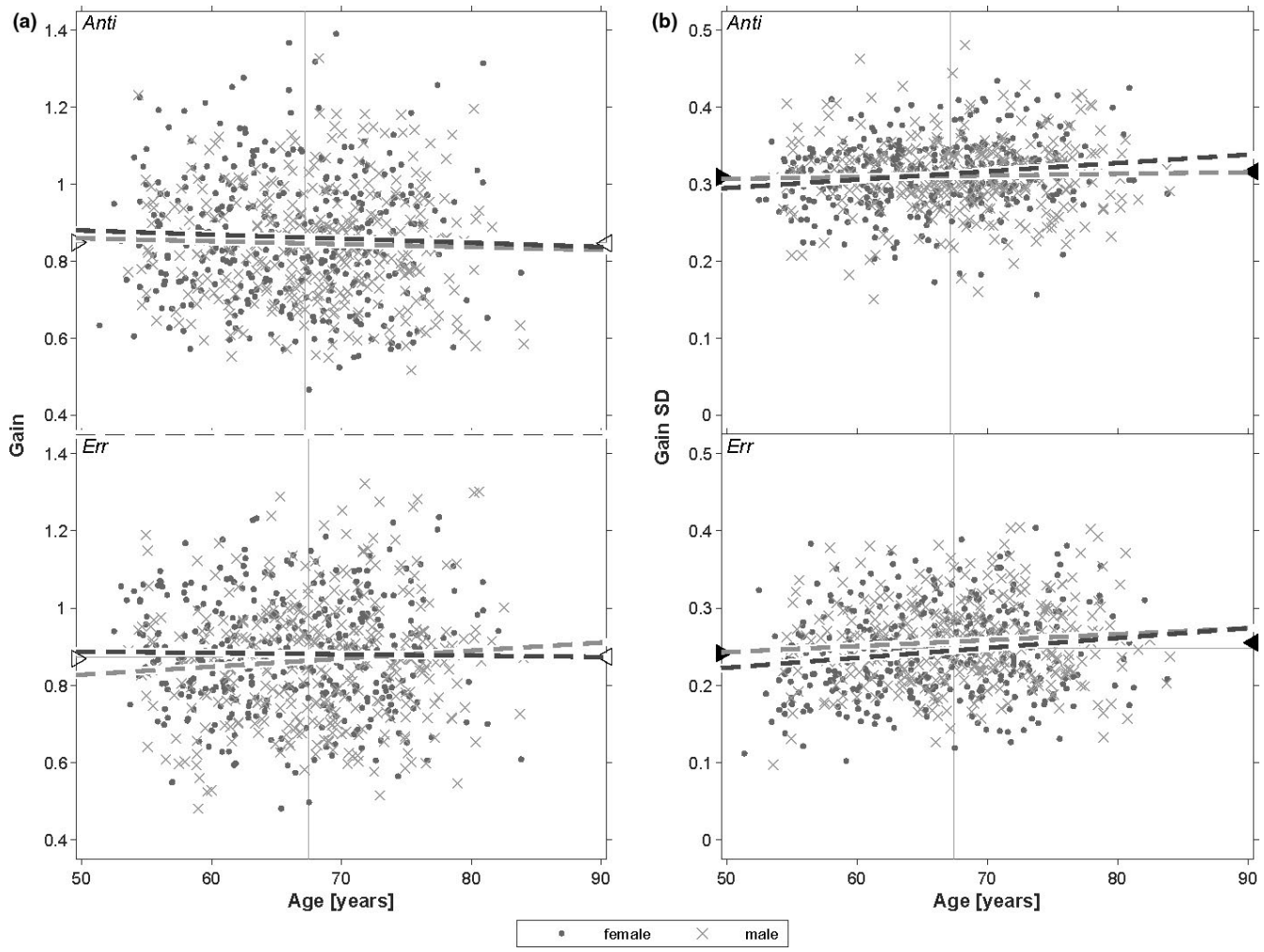

FIGURE 4 Dependency of (a) gain and (b) intra-individual standard deviation of the gain on age, gender, and saccade type. Vertical lines give median age, and horizontal lines give median gain and standard deviation of gain, respectively. Dashed lines represent non-significant effect of gender, whereas solid lines represent significant gender effects (black for female, gray for male regression lines). Empty triangles inform about the age median split with a non-significant age effect, and filled rectangles inform about age median split with significant age effect. Solid abscissa informs about a significant effect of saccade type, and dashed abscissa informs about non-significant effect of saccade type. Results of the linear mixed-effect models are given in Tables 3 and 4

The high amount of invalid trials urged us to analyze in detail why trials were not accepted according to our six criteria (see method section). Inaccurate saccade was the most frequent criterion for an invalid trial. Interestingly, only the number of trials without any saccades and with preliminary saccades revealed a significant correlation with age. Gender did not influence any exclusion criteria (see Figure S1 and Tables S1–S7).

3.2 | Saccade accuracy

The data of our typical participants shown in Figure 2 indicate that the accuracy of saccades seems to be independent of saccade type and age. The analysis of saccade gain as a measure of saccade accuracy with the linear mixed-effect model revealed that it neither depended on age ($p = .39$), nor gender ($p = .76$), nor saccade type ($p = .75$) as shown in Figure 4a and Table 3. In contrast, the intra-individual variability of the gain increased slightly with age as shown in Figure 4b and Table 4 (***p* = .01**). This variability was larger in anti-saccades than in direction errors (***p* = .01**). There was no significant effect of gender upon the variability ($p = .17$).

3.3 | Saccadic reaction time (SRT)

Figure 5 shows a histogram of the reaction times of all obtained saccades separated for anti-saccades and direction errors from all participants in our study. Direction errors had shorter SRTs compared to anti-saccades.

As a first step, we applied a general linear mixed-effect model with the factors target position, saccade type, gender,

TABLE 3 Linear mixed-effect model on saccade gain

Gain ~ Age*Gender*SaccType + (Age | ID)			
Model: LME (ML), Fixed effect *df* 1,400			
Model Stats: R^2 .363, Intercept 0.933 (**$p < .001$**)			
Fixed effects			
Name	Estimate	tStat	*p*-value
Age	−0.001	−0.9	.39
Gender	−0.035	−0.3	.76
SaccType	−0.028	−0.3	.75
Age:Gender	0.003	0.2	.86
Age:SaccType	0.007	0.5	.6
Gender:SaccType	−0.145	−1.1	.27
Age:Gender:SaccType	0.021	1.1	.28

TABLE 4 Linear mixed-effect model on saccade gain variability

GainSD ~ Age*Gender*SaccType + (Age | ID)			
Model: LME (ML), Fixed effect *df* 1,400			
Model Stats: R^2 .433, Intercept 0.241 (**$p < .001$**)			
Fixed effects			
Name	Estimate	tStat	*p*-value
Age	0.00108	2.6	**.01**
Gender	0.05545	1.4	.17
SaccType	−0.08210	−2.4	**.01**
Age:Gender	−0.00086	−1.4	.15
Age:SaccType	0.00019	0.4	.7
Gender:SaccType	−0.00982	−0.2	.84
Age:Gender:SaccType	0.00036	0.5	.62

and age on SRT (see Table 5). Target position did not affect SRT significantly ($p = .48$). Therefore, it is acceptable to pool the data across the four possible target positions (5 and 10° to the left and right).

Figure 6a and Table 6 show the result of the analysis of SRTs. Direction errors had approximately 150 ms shorter SRTs than anti-saccades (**$p = .0001$**). SRTs increased on average 1.1 ms per year (**$p = .01$**). SRTs of our male subjects were approximately 85 ms shorter compared to female subjects (**$p = .03$**). However, the interaction between age and gender was not significant ($p = .06$).

With respect to the intra-individual variability of SRTs shown in Figure 6b and Table 7, only the effect of age reached significance (**$p = .01$**).

So far, our data demonstrate that age influences SRTs of direction errors and anti-saccades in a similar way. In accordance with these results, we also did not find any significant effects of age or gender (see Figure 7a and Table S8) on the anti-saccade costs.

3.4 | Error rate

Inspection of Figure 2 already suggests that older participants express a higher error rate. Figure 7b and Table 8 give the error rates for all participants for age and gender. The linear model shows that the error rate increases significantly (**$p = .01$**) with 0.5% per year. There was no significant effect of gender on the error rate ($p = .16$).

3.5 | Saccade peak velocity

We determined the age dependency of the peak velocity of saccades as described earlier. Figure 8 and Table 9 show the saccadic peak velocity for anti-saccades and direction errors for a 10° saccade, respectively. The linear mixed-effect model revealed that neither age ($p = .05$) nor gender ($p = .07$) had a significant influence on saccade peak velocity. As expected, there was a pronounced difference in the peak velocity of direction errors and anti-saccades: Direction errors with an amplitude of 10° reached approximately 50°/s higher peak velocities compared to 10° anti-saccades. However, this difference was not significant ($p = .05$).

3.6 | Descriptive statistics

Independent of the statistical analysis performed so far, Table 10 informs about the descriptive statistics of our complete data set.

3.7 | Saccade type history

We separated our data set depending on the executed saccade type in the previous trial and analyzed saccadic reaction times and error rates independently. SRTs of anti-saccades did not change with the saccade type in the previous trial (see Figure 9a) ($F = 0.281$, $p = .596$ 2-factorial ANOVA, factor previous saccade type). As already shown before, participants above the median age had generally higher anti-SRTs compared to participants below the median age ($F = 4.658$, **$p = .031$**, 2-factorial ANOVA, factor age).

With respect to the SRTs of direction errors, there was a significant influence of the previous saccade type (see Figure 9b): The error-SRT was longer if the participant produced a correct anti-saccade in the previous trial and shorter if a direction error was previously generated ($F = 6.926$, **$p = .008$**, 2-factorial ANOVA, factor previous saccade type). This finding was true for both age groups—older participants showed longer SRTs for direction errors compared to the adult participants ($F = 20.307$, **$p < .001$**, 2-factorial ANOVA, factor age), similar as for anti-saccades.

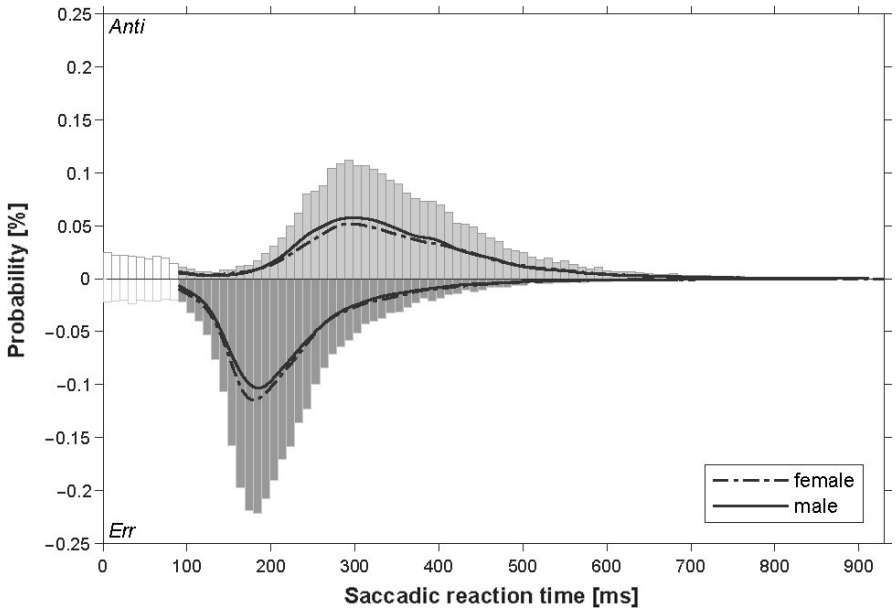

FIGURE 5 Histogram of SRTs over all participants ($n_{Anti} = 28{,}701$, $n_{Err} = 34{,}560$). In addition, the distributions of female and male participants are shown. All saccades in the area below 90 ms were excluded as preliminary saccades ($n_{Anti} = 2{,}001$, $n_{Err} = 2{,}051$, see Supporting information)

TABLE 5 Linear mixed-effect model on SRT on individual saccades

SRT ~ Age*Sex*SaccType*TargetPosition + (Age|ID)			
Number of observation:	58,886		
Fixed effects coefficients:	16		
Random effects coefficients	1,434		
Covariance parameters	4		
Name	Estimate	tStat	*p*-value
Intercept	289	13.278	**<.0001**
Target Position	0.7392	0.7025	.4823
SaccType	−162	−12.751	**<.0001**
Gender	−81	−2.5473	**.0108**
Age	0.994	2.9865	**.0028**

Finally, the error rate was higher if the previous trial was a direction error (see Figure 9c) ($F = 94.397$, $\boldsymbol{p < .001}$, 2-factorial ANOVA, factor previous saccade type), which was true for both age groups. Older participants revealed higher error rates ($F = 6.929$, $\boldsymbol{p = .008}$, 2-factorial ANOVA, factor age). It is important to note that there is no significant interaction between the factors previous saccade type and age for anti-SRT, direction error SRT and error rate, respectively. The consequence of the previous saccade type on SRT and error rate is not changed with age.

4 | DISCUSSION

A very general finding of our study is that the ability to perform anti-saccades or direction errors, expressed as number of accepted trials, decreases with age. Others (Butler et al., 1999; Faust & Balota, 1997; Gottlob, Fillmore, & Abroms, 2007) have also reported a similar decline. The common denominator of these studies is that older participants have more problems with maintaining fixation and suppressing unwanted eye movements. This is in line with our finding of an age-related increase in preliminary saccades. The decrease in number of accepted trials in older participants resulting from an increase of fixation errors might be explained by the increased sensitivity for distractors. Older participants are more sensitive to distractors especially in the visual domain (Guerreiro, Murphy, & Van Gerven, 2010). So if eye movement parameters of elderly participants are reported, the number of accepted trials has to be monitored carefully in order to avoid artifacts resulting from low trial numbers.

We are convinced that the reported effects of age do not result from general effects of age such as decreased head stability, increased body tremor or presbyopia. First, we performed fast Fourier transforms of all eye movement records in our data sample and did not observe an increasing amount of tremor with age. Second, we did not observe increasing age-related deficits monitored by the other tests of the TREND study. So, we are convinced that the observed effect in our study cannot be attributed to general, unspecific age-related factors.

4.1 | Saccadic reaction times and their variance might indicate slowing of processing speed

In line with previous findings, we found that SRTs increased with age (Abel et al., 1983; Bonnet et al., 2013; Bono

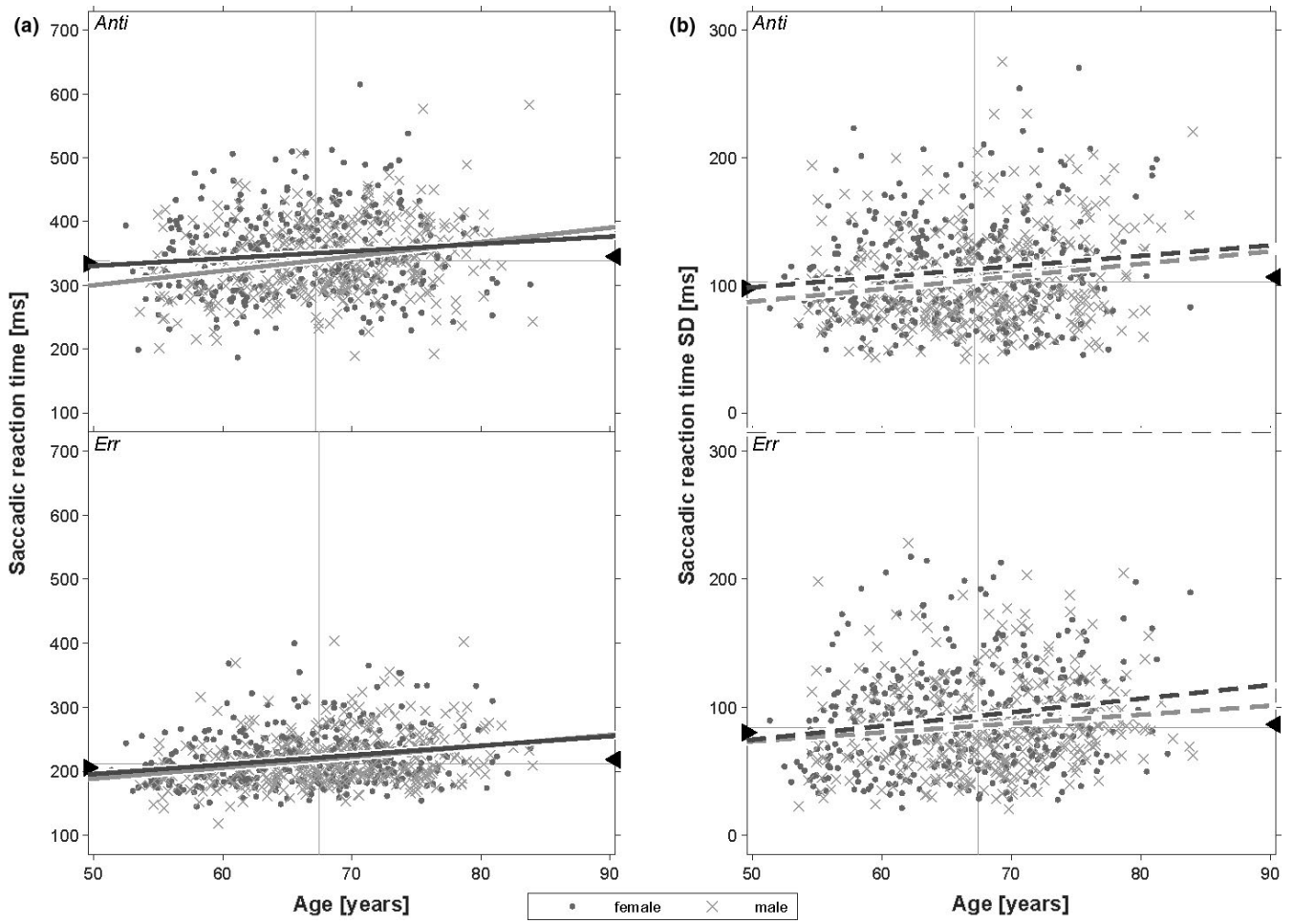

FIGURE 6 Dependency of (a) SRT and (b) intra-individual standard deviation of the SRT on age, gender, and saccade type. Vertical lines give median age, and horizontal lines give median gain and standard deviation of gain, respectively. See legend of Figure 4 for further explanation. Results of linear mixed-effect models are given in Tables 6 and 7

TABLE 6 Linear mixed-effect model on SRT

SRT ~ Age*Gender*SaccType + (Age | ID)			
Model: LME (ML), Fixed effect *df* 1,400			
Model Stats: R^2 .761, Intercept 273 (**$p < .001$**)			
Fixed effects			
Name	Estimate	tStat	*p*-value
Age	1.1	2.8	**.01**
Gender	−85.9	−2.2	**.03**
SaccType	−151.4	−4.7	**.0001**
Age:Gender	1.1	1.9	.06
Age:SaccType	0.3	0.7	.5
Gender:SaccType	67.3	1.4	.15
Age:Gender:SaccType	−0.9	−1.3	.2

TABLE 7 Linear mixed-effect model on SRT variability

SRT_*SD* ~ Age*Gender*SaccType + (Age | ID)			
Model: LME (ML), Fixed effect *df* 1,400			
Model Stats: R^2 .453, Intercept 57.3 (**$p = .004$**)			
Fixed effects			
Name	Estimate	tStat	*p*-value
Age	0.8	2.7	**.01**
Gender	−19.3	−0.7	.5
SaccType	−35.9	−1.7	.1
Age:Gender	0.2	0.4	.71
Age:SaccType	0.2	0.7	.46
Gender:SaccType	36.7	1.2	.24
Age:Gender:SaccType	−0.5	−1.1	.25

et al., 1996; Butler et al., 1999; Fujiwara et al., 2010; Harsay, Buitenweg, Wijnen, Guerreiro, & Ridderinkhof, 2010; Irving, Steinbach, Lillakas, Babu, & Hutchings, 2006; Klein et al., 2005; Munoz et al., 1998; Olincy et al., 1997; Peltsch et al., 2011; Raemaekers et al., 2006; Shafiq-Antonacci et al., 1999). We found a similar increase of SRTs for direction errors and anti-saccades and consequently did not observe an age-related change in the anti-saccade costs. This

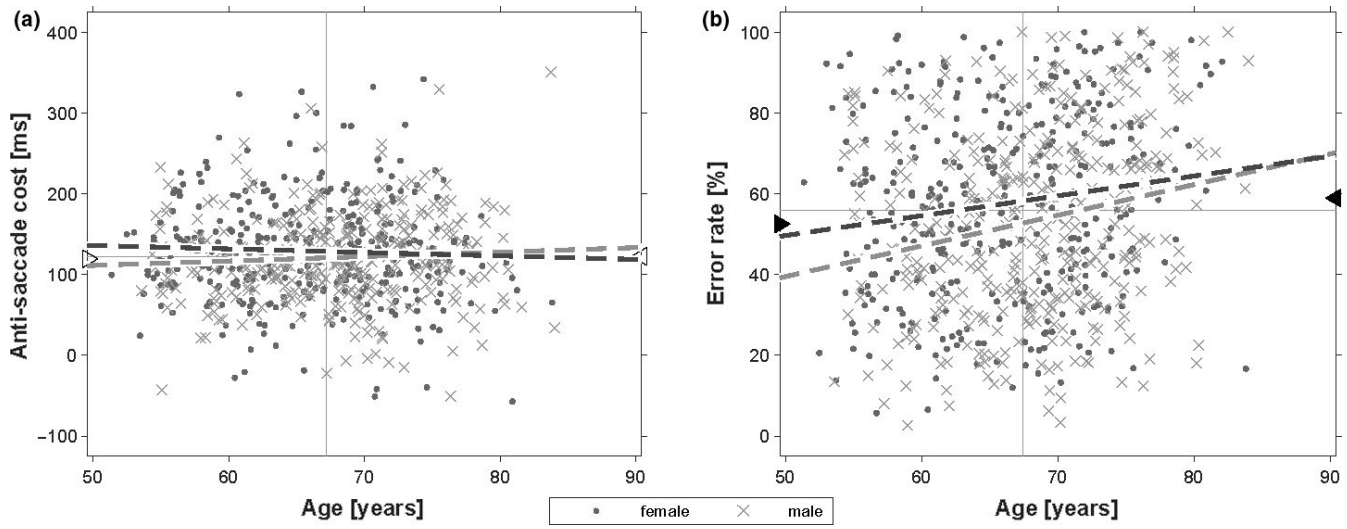

FIGURE 7 Dependency of the anti-saccade costs (a) and error rate (b) on age and gender. Vertical lines give median age; horizontal lines give median anti-saccade costs and error rate, respectively. Dashed black (female) and gray lines (male) represent the result of the linear model dependency of age and gender. Open triangles give the age median split of the anti-saccade, filled triangles the age median split of error rate (b). Results of the linear models for the anti-saccade costs are given in the Table S8, for the error rate the information is given in Table 8

TABLE 8 Linear model on error rate

Error Rate ~ Age * Gender			
Model: LM			
Model Stats: R^2 .0412, Intercept 25.6 ($p = .028$)			
	Estimate	tStat	*p*-value
Age	0.5	2.8	**.01**
Gender	−23.6	−1.4	.16
Age:Gender	0.3	1.1	.28

is in line with reports on SRTs of pro- and anti-saccades (Butler et al., 1999; Klein et al., 2005; Munoz et al., 1998). In contrast, other studies showed increasing costs with age, suggesting that the execution of anti-saccades is more affected by age than the execution of pro-saccades (Crawford et al., 2005; Fujiwara et al., 2010; Olincy et al., 1997; Peltsch et al., 2011). This could be taken as an indication of special deterioration of frontal function by age. The cognitive load of the subject in the anti-saccade task is higher compared to pro-saccade task. Without explicitly asking the subjects about the difficulty of both tasks, SRTs can be interpreted as a proxy for the actual cognitive load. It has been shown earlier that more complex task instructions result in longer SRTs (Mosimann, Felblinger, Colloby, & Muri, 2004; Taylor & Hutton, 2009). Direction errors during anti-saccade blocks have longer SRT as saccades collected in pro-saccade blocks (unpublished observation) (Noorani & Carpenter, 2014). On one hand, in studies in which pro- and anti-saccades are measured in two different block of trials, an age-related increase in the anti-saccade costs (Crawford et al., 2005; Fujiwara et al., 2010; Olincy et al., 1997; Peltsch et al., 2011) might be caused by the difference in the cognitive load of the two paradigms. On the other hand, if only a single paradigm is used as in our study, the cognitive load of direction errors and anti-saccade is identical. Because of this equality, there is no differential effect of age on the latency of both saccade types resulting in our observation that anti-saccade costs are not confounded by age.

The general increase in SRTs with age might be accompanied by a shift in activity from posterior to frontal cortical areas for pro- and anti-saccades after young adulthood (Raemaekers et al., 2006). Cortical processing of visual information starts in the primary visual cortex (V1, Brodmann area 17). It has been shown that intra-cortical micro-stimulation (Tehovnik, Slocum, & Schiller, 2003) or optogenetic stimulation (Jazayeri, Lindbloom-Brown, & Horwitz, 2012) in this area can elicit saccades in non-human primates. Studies exploring age-related anatomical and neurophysiological changes in V1 found decreased selection selectivity and increased spontaneous activity in senescent monkeys (Fu, Yu, Ma, Wang, & Zhou, 2013; Schmolesky, Wang, Pu, & Leventhal, 2000). These observations can be explained by a reduced intra-cortical inhibition, which may lead to a decreased signal-to-noise ratio quite early in visual processing. This could be the root of increased SRTs in elderly participants. Moreover, reaction times should increase similarly in all visual tasks with age. In addition to these findings from single-unit recordings from non-human primates, evidence from neuro-imaging studies in humans suggests that the elderly exhibit decreased parietal activation during the anti-saccade task compared to young individuals (Alichniewicz et al., 2013), which might parallel the above mentioned age-related shift from posterior to anterior areas (Raemaekers

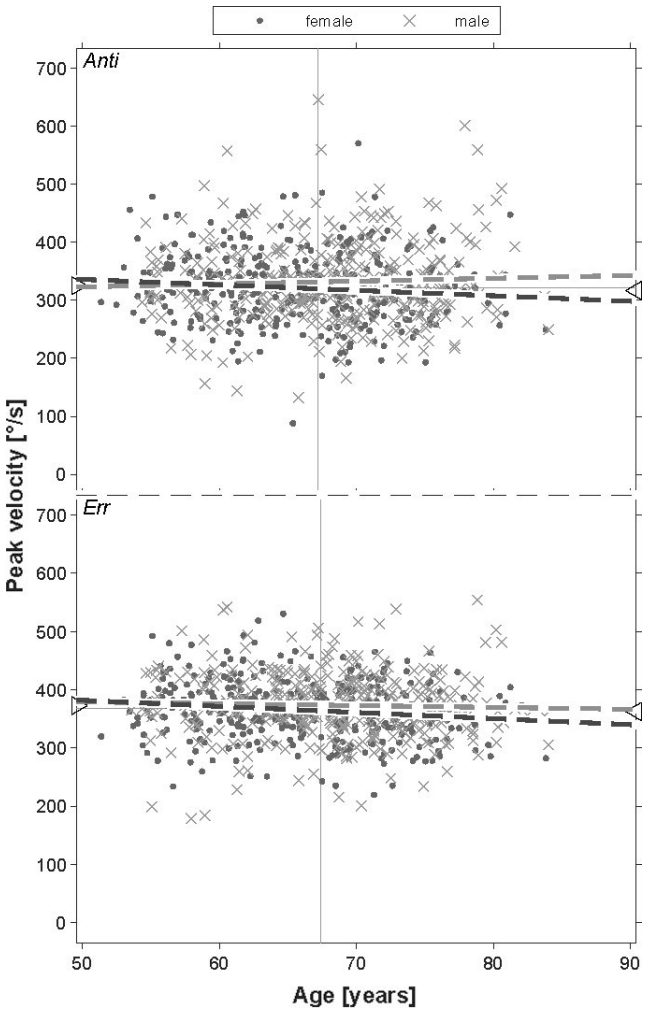

FIGURE 8 Dependency of saccade peak velocity on age and gender. Vertical line gives median age; horizontal lines give median peak velocity of anti-saccades and direction errors, respectively. See legend of Figure 4 for further explanation. Results of linear mixed-effect models are given in Table 9

et al., 2006). So in summary, it remains questionable whether the increase in SRTs may be the consequence of age-related changes in a specific cortical area, especially the frontal lobe. Rather, it may reflect the general slowing of processing in the entire elderly central nervous system (Salthouse, 2000).

Finally, it should be noted that the existence of an age-related slowing might be disputed at all. Recently, it was proposed with respect to verbal fluidity that this slowing might not represent cognitive decline, but rather reflects the consequence of lifelong learning, that is, increasing of vocabulary size (Ramscar, Hendrix, Shaoul, Milin, & Baayen, 2014). As attractive as this idea might be, it is difficult to account lifelong learning for the age-related decline of saccadic eye movement performance. There is definitively no lifelong accumulation of possible target locations for saccadic eye movements. However, lifelong learning might result in being careful when selecting the target of the next saccade.

TABLE 9 Linear mixed-effects model on saccade peak velocity

PeakVelocity ~ Age*Gender*SaccType + (Age | ID)			
Model: LME (ML), Fixed effect *df* 1,400			
Model Stats: R^2 .77, Intercept 377 ($p < .00001$)			
Fixed effects			
Name	Estimate	tStat	*p*-value
Age	−0.9	−2	.05
Gender	−84.8	−1.8	.07
SaccType	51.1	1.9	.05
Age:Gender	1.4	2.1	**.04**
Age:SaccType	−0.1	−0.3	.79
Gender:SaccType	45.7	1.2	.23
Age:Gender:SaccType	−0.7	−1.2	.22

4.2 | Error rates increase with age

Increased error rates in the elderly as found here have also been reported by others (Bonnet et al., 2013; Butler et al., 1999; Fujiwara et al., 2010; Olincy et al., 1997; Peltsch et al., 2011; Raemaekers et al., 2006; Shafiq-Antonacci et al., 1999). However, other reports fail to show this age-related increase in error rate (Crawford et al., 2005; Harsay et al., 2010; Munoz et al., 1998; Raemaekers et al., 2006). It is a peculiarity of the anti-saccade paradigm that the error rate is a direct measure of the executive function of the frontal lobe, that is, selection of the appropriate action in a given situation as shown by recordings of single units in awake and behaving monkeys (Johnston & Everling, 2006; Johnston et al., 2014; Munoz & Everling, 2004) as well as patient studies (Muri & Nyffeler, 2008). Therefore, the increased error rates might indicate a possible decline of frontal function in the elderly (Madden et al., 2010), in other circumstances expressed as decline in inhibitory control (Dempster, 1992; West, 1996). However, age-related changes in the frontal areas FEF and SEF might not be the only source for the age-related increase of error rates. As already discussed, parietal activation is reduced in elderly participants (Alichniewicz et al., 2013). The parietal eye fields are also thought to be important for the selection of the appropriate saccade (Pierrot-Deseilligny, Muri, Nyffeler, & Milea, 2005). So, it remains to future studies to determine whether the age-related increase in error rate is due to age-related changes in frontal or parietal areas, respectively.

4.3 | Saccade accuracy is preserved while its variance increases with age

While SRTs and error rates increase with age, the accuracy of saccades, as measured by saccadic gain, did not change with

TABLE 10 descriptive statistics (total numbers: ≤67 female $n = 203$; ≤67 male $n = 162$; >67 female $n = 166$; >67 male $n = 200$)

Variable	Age	Sex	Mean	*SEM*	Median	iqr	min	max
Age	≤67	Female	60.9	0.27	61.22	6.11	51.37	67.29
Age	≤67	Male	62.16	0.3	63.09	6.24	53.58	67.42
Age	>67	Female	72.22	0.26	71.66	4.64	67.43	83.82
Age	>67	Male	73	0.26	72.46	5.86	67.43	84.01
ErrorRate	≤67	Female	55.57	1.53	55.32	31.73	5.68	99.17
ErrorRate	≤67	Male	49.21	1.74	46.29	32.88	2.63	100
ErrorRate	>67	Female	59.52	1.8	59.24	36.43	0	100
ErrorRate	>67	Male	56.55	1.68	58.19	37.86	3.41	100
Validity	≤67	Female	51.8	1.17	52.5	25.62	12.5	90
Validity	≤67	Male	53.18	1.44	56.25	26.88	8.75	89.38
Validity	>67	Female	47.96	1.35	47.5	27.5	10.62	90
Validity	>67	Male	49.57	1.23	50.62	25.94	11.25	93.12
AntiEffect	≤67	Female	130.92	4.45	126.52	73.52	−27.76	326.31
AntiEffect	≤67	Male	121.01	4.28	116.55	66.03	−42.81	305.56
AntiEffect	>67	Female	126.93	5.47	123.88	73.77	−57.08	341.71
AntiEffect	>67	Male	121.19	4.47	121.83	78.85	−50.61	350.55
SRTAnti	≤67	Female	345.19	4.42	339.44	90.53	186.76	510.04
SRTAnti	≤67	Male	330.23	4.5	323.88	76.03	201.22	506.88
SRTAnti	>67	Female	352.75	5.53	342.83	92.03	226.19	615.18
SRTAnti	>67	Male	350.26	4.49	348.21	81.88	189.13	583.16
SRTErr	≤67	Female	214.26	2.84	208.26	45.5	144.89	399.87
SRTErr	≤67	Male	209.22	2.95	201.92	43.57	118.59	369.26
SRTErr	>67	Female	225.82	3.5	217.02	50.23	154.27	365.19
SRTErr	>67	Male	229.07	3.22	220.36	63.82	161.79	403.76
SRTSDAnti	≤67	Female	108.62	2.48	102.57	46.44	46.72	223.24
SRTSDAnti	≤67	Male	99.87	2.78	90.1	45.01	42.13	204.21
SRTSDAnti	>67	Female	115.84	3.51	110.56	50.42	45.42	270.6
SRTSDAnti	>67	Male	110.27	3.02	105.48	53	42.4	275.28
SRTSDErr	≤67	Female	88.69	2.81	84.38	51.2	21.28	217.52
SRTSDErr	≤67	Male	82.06	2.95	74.6	49.16	22.74	228.29
SRTSDErr	>67	Female	96.9	3.31	94.27	59.88	27.92	212.95
SRTSDErr	>67	Male	90.37	2.69	84.71	44.42	20.56	204.65
PeakVelocityAnti	≤67	Female	328.6	4.21	324.73	67.58	87.91	481.26
PeakVelocityAnti	≤67	Male	330.79	5.67	328.54	71.94	132.16	646.04
PeakVelocityAnti	>67	Female	316.64	5.29	309.66	75.45	169.73	570.89
PeakVelocityAnti	>67	Male	335.98	5.54	326.58	94.6	140.17	601.68
PeakVelocityErr	≤67	Female	374.55	3.61	373.51	54.89	233.88	529.76
PeakVelocityErr	≤67	Male	376.69	4.82	373.33	67.03	179.05	542.54
PeakVelocityErr	>67	Female	358.59	3.9	359.9	59.76	219.37	463.61
PeakVelocityErr	>67	Male	372.88	4.18	366.44	66.87	200.51	554.22
GainAnti	≤67	Female	0.87	0.01	0.85	0.23	0.57	1.37
GainAnti	≤67	Male	0.84	0.01	0.84	0.2	0.55	1.23
GainAnti	>67	Female	0.85	0.01	0.84	0.23	0.52	1.39
GainAnti	>67	Male	0.85	0.01	0.85	0.22	0.52	1.33

(Continues)

TABLE 10 (Continued)

Variable	Age	Sex	Mean	*SEM*	Median	iqr	min	max
GainErr	≤67	Female	0.88	0.01	0.88	0.19	0.48	1.23
GainErr	≤67	Male	0.86	0.01	0.86	0.21	0.48	1.24
GainErr	>67	Female	0.88	0.01	0.89	0.21	0.5	1.24
GainErr	>67	Male	0.88	0.01	0.87	0.21	0.52	1.32
GainSDAnti	≤67	Female	0.31	≤0.01	0.31	0.06	0.17	0.41
GainSDAnti	≤67	Male	0.31	≤0.01	0.31	0.05	0.15	0.46
GainSDAnti	>67	Female	0.32	≤0.01	0.32	0.06	0.16	0.43
GainSDAnti	>67	Male	0.31	≤0.01	0.31	0.05	0.16	0.48
GainSDErr	≤67	Female	0.24	≤0.01	0.24	0.07	0.1	0.38
GainSDErr	≤67	Male	0.25	≤0.01	0.25	0.08	0.1	0.38
GainSDErr	>67	Female	0.25	≤0.01	0.26	0.08	0.12	0.4
GainSDErr	>67	Male	0.26	≤0.01	0.26	0.07	0.13	0.4

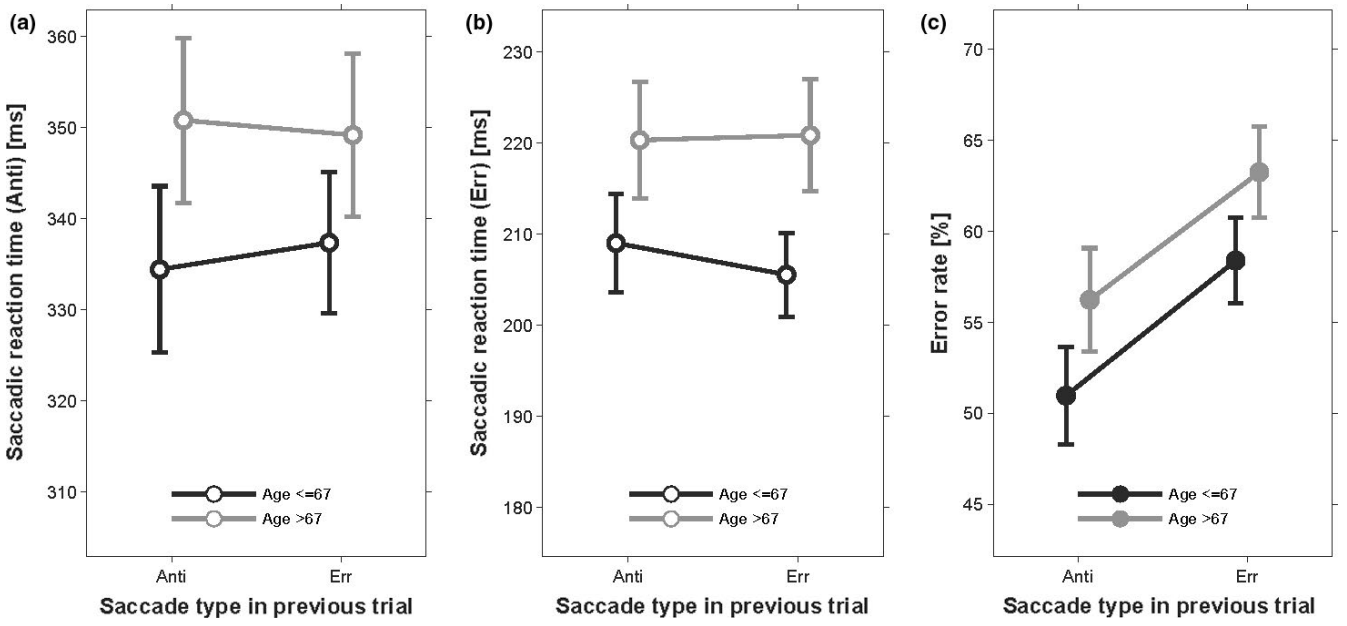

FIGURE 9 Saccade type history, (a) shows SRTs of anti-saccades, (b) gives the SRTs of direction errors, and (c) the error rate. Open circles represent no significant effect of factor previous saccade type, and filled circles inform about significant effect of factor previous saccade type. Solid lines indicate significant effects of factor age

age. This corresponds to previous findings (Bono et al., 1996; Butler et al., 1999; Gottlob et al., 2007; Harsay et al., 2010; Irving et al., 2006; Klein, Rauh, & Biscaldi, 2010; Olincy et al., 1997; Pratt, Dodd, & Welsh, 2006; Shafiq-Antonacci et al., 1999) and shows that the core function of the saccadic system, that is, precisely moving the eyes to the location of the next fixation target, is lifelong preserved. There is a mechanism to maintain high accuracy of saccades: adaptation of amplitude (McLaughlin, 1967). This ability does not decrease with age (Huang, Gegenfurtner, Schutz, & Billino, 2017).

Although the accuracy of the system remains intact, it seems that its precision decreases, as the intra-individual saccadic endpoint variability, as measured by the standard deviation of the gain, increased with age. It is difficult to disentangle whether the increase in variability is related to age-related changes in sensory processing or in motor preparation. In favor of changes in the sensory processing are the above-mentioned changes in the selectivity in the primary visual cortex (Fu et al., 2013; Schmolesky et al., 2000). However, age-related changes in motor preparation cannot be excluded. Age-related increase in spatial and temporal

variability is a common hallmark of the oculomotor and skeletal motor control (Seidler et al., 2010).

4.4 | Dynamic saccade parameters are determined by the brainstem

It is important to note that the selection of saccade direction (i. e. the execution of anti-saccade or direction error) and the SRTs are direct outcomes of the interplay of the cortical eye fields, basal ganglia, cerebellum, and the SC before saccade onset. In contrast, kinematic saccade properties like the peak velocity are precisely determined during the execution of the saccade by brainstem saccade generators located in the paramedial pontine reticular formation (PPRF) and rostral interstitial medial longitudinal fasciculus (riMLF), respectively (Scudder, Kaneko, & Fuchs, 2002; Sparks, 2002). With respect to the influence of age on saccadic peak velocities, results in the literature are not consistent. On one hand, there are reports that age does not affect saccadic peak velocity emphasizing that saccade generator function is resistant to aging (Abel et al., 1983; Bonnet et al., 2013; Munoz et al., 1998; Pratt et al., 2006; Shafiq-Antonacci et al., 1999). On the other hand, some studies have shown reduced peak velocities in the elderly (Bono et al., 1996; Irving et al., 2006; Mirsky et al., 2011; Velazquez-Perez et al., 2009; Wilson, Glue, Ball, & Nutt, 1993). Our data show higher peak velocities during direction errors compared to anti-saccades as shown by others (Edelman et al., 2006; Mack & Ilg, 2014; Smit et al., 1987; Van Gelder, Lebedev, & Tsui, 1997). However, our data do not show an influence of age or gender on saccadic peak velocity. This supports the notion that the function of the burst neurons in brainstem saccade generator (Sparks, 2002) is indeed resistant to aging. To explain this resistance, it is important to note that the output of the brainstem saccade generator is modulated by the cerebellum (Thier, Dicke, Haas, & Barash, 2000). In addition to balance the effect of age, the possibilities to adapt the amplitude of saccades as well as to counteract fatigue are important functions of the cerebellum (Prsa & Thier, 2011).

4.5 | Effect of gender

Our study is, to our knowledge, the first that analyzed gender effects on oculomotor behavior in a large sample of healthy aging participants. We found strong gender difference of SRT in our data: Male subjects were approximately 85 ms shorter than female subjects, independent of saccade type. A study (Bargary et al., 2017) with a similar data size (1,058 participants) reports also shorter SRT for males compared to females, although the difference is smaller (anti-saccade SRT of males 297 ms compared to 310 ms of females). However, the age of the subjects in the study of Bargary and colleagues was 16–40 years, so it extends perfectly our own finding related to elderly participants.

For younger subjects (24–33 years), Becker and Fuchs reported faster saccadic peak velocities for females (Becker & Fuchs, 1969). Li and colleagues (Li et al., 2012) reported higher error rates in anti-saccade performance in females compared to males, but no differences in SRTs. Bonnet and colleagues (Bonnet et al., 2013) failed to find any influences of gender. Despite the discrepancies between our data and the literature, it is important to note that gender composition of the cohort of an oculomotor study should be disclosed to allow for a detailed comparison of published data.

4.6 | Saccade type history

If subjects had to learn an arbitrary mapping of color and eye movement response, task switches between pro- and anti-saccades produce costs in SRTs and errors, but only in the first trial after task switches (see experiment 2 of Hodgson et al. (2004)). When the subjects had to perform either only pro- or anti-saccades in uniform blocks, the SRT was in general longer as in blocks with switches in the instructions (see experiment 1 of Hodgson et al. (2004)). Hodgson and colleagues explained this finding that their subjects played less attention in the uniform (eventually boring) blocks compared to the more demanding blocks with task switches. If the SOA between response type instruction (pro-saccade or anti-saccade, respectively) and target presentation was 200 ms, an increase in SRT and error rate of the first trial after a change in task was observed (Hunt & Klein, 2002). Single-unit recordings from the SC reflect the changes in SRT and error rate associated with task switches (Chan, Koval, Johnston, & Everling, 2017).

As we only measured a single block with the instruction to perform anti-saccades, we do not have data addressing possible effects of task switches. However, our participants did not always produce anti-saccades. In some cases, participants produced direction errors according to the individual error rate. Therefore, we were able to analyze our data depending on the previously executed saccade type. One could therefore assume that the previous direction error affected the execution of anti-saccades. The ongoing conflict monitoring might result in changes in strategy, for example, post error slowing, that is, shift to more cautious responses characterized by a long latency after a direction error (Botvinick, Braver, Barch, Carter, & Cohen, 2001; Hodgson et al., 2004; Hutton, 2008; Rabbitt, 1966). However, our findings do not support this assumption. Error rates were higher if a direction error was produced in the previous trial. With respect to the error rates, we replicate an earlier finding (Tatler & Hutton, 2007), which showed that error rates were increased in trials following an error. With respect to anti-SRTs, we did not find an influence

of the previous saccade type. The SRT of direction errors is shorter following a direction error compared to anti-saccades. Overall, SRT and error rate increase with age, which is not altered by saccade type history.

5 | CONCLUSIONS

With the statistical power of a huge sample of participants and linear mixed-effect models, we show that SRT of anti-saccades and direction errors increase similarly with age. Male participants have shorter SRT than female participants. The error rate increases with age, whereas anti-saccade cost, accuracy, and peak velocity of anti-saccades and direction errors are not affected by age. These changes represent healthy aging beyond 50 years characterized by uniform slowing of processing speed.

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CONFLICT OF INTEREST

The authors have no conflict of interest.

AUTHOR CONTRIBUTIONS

All authors contributed substantially to the design of the study; DM wrote the Matlab code for data acquisition and analysis; UI, SH, and AP contributed specific aspects to the Matlab code; KS, GE, US, and DB scheduled the participants and designed the TREND study; LS, SL, and LG collected the data, DM and UI wrote the manuscript, and all authors revised the manuscript.

DATA AVAILABILITY STATEMENT

Matlab scripts as well as experimental data are available upon personal request.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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