
IMPACT OF HEALTHY AGING ON SPATIAL COGNITION
SPATIAL NAVIGATION AND GAZE DYNAMICS IN ECOLOGICAL CONDITIONS

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ABSTRACT

Healthy aging is associated with changes in the way people navigate in space. Spatial disorientation and wayfinding deficits have a tremendous impact on older adults' autonomy and well-being, including decreased mobility and increased avoidance of unfamiliar environments, which leads to social isolation and lower cognitive stimulation in this population.

How older adults make use of geometric relative to landmark cues has received little attention as compared to the large body of studies postulating a shift from allocentric to egocentric spatial strategies with aging. Additionally, there is a growing interest for the active visual processes involved in spatial navigation, which are mediated by eye movements in foveated species. Eye movements discretize the continuous flow of visual information which we are exposed to when navigating the real world. The analysis of eye movements can thus inform us about, when, what, and how we extract relevant spatial information to serve navigation purposes.

The objectives of this doctoral work are: *i*) to characterize the impact of aging on spatial cue processing (landmark vs. geometry) and to understand how differential cue processing may affect the use of spatial strategies (egocentric vs. allocentric) in aging; *ii*) to understand how spatial information, and more specifically geometric cues, are extracted and encoded through spatio-temporal gaze patterns. Even though the project primarily focuses on aging, it complementarily explores spatial cognition in children, in the attempt to provide a continuum of visuo-spatial changes across lifespan.

The methodological approach adopted throughout the project relies on testing spatial cognition in ecological environments, where the full set of idiothetic sensory inputs (e.g., vestibular, proprioceptive) can be experienced and combined with allothetic cues (e.g., visual, auditory). This approach is meant to increase the probability of transferring our experimental findings to natural real-life conditions, by better accounting for the multi-modal and multi-process nature of spatial behavior. Another methodological asset of this work lies in the manifold clinical and functional assessment of a large study population, prior to the running of the actual experiments. Since healthy aging is characterized by a high inter-individual variability, this approach takes into account the heterogeneity of age-related effects, by controlling for multiple sensory-cognitive dimensions and their impact on spatial navigation.

Overall, our results suggest an age-related spatial reorganization, in which mental representations are preferentially anchored on geometric cues, rather than landmarks, with advancing age. To the best of our knowledge, very few human navigation studies addressed so far the impact of aging on the interplay between landmark and geometric spatial information. Moreover, these studies were based on computer-screen tasks and their results drew an unclear picture. Our findings shed light on how aging modifies the preferential encoding of task-relevant information when young and older adults naturally navigate in real environments. We show that older adults reorient and navigate preferentially according to the geometric properties of the environment.

On the other hand, young adults preferentially use landmarks. Strikingly, gaze dynamics provide spatio-temporal markers that are predictive of the spatial coding preference. Brought closer to previously demonstrated geometric preference in children, these results show that spatial cue preference undergoes a lifespan development in an inverted-U shape.

These results challenge the current view that focuses on egocentric versus allocentric strategies in aging, and they question whether it is a matter of availability of spatial cues rather than strategy *per se*. We verified this prediction by directly testing to what extent older adults and children can be as efficient as young adults in using allocentric strategies if geometry is made available among the environmental cues. The results confirm that providing geometric information eliminates age-dependent differences in egocentric vs. allocentric strategies, suggesting that changes in spatial cue processing may sub-serve differences in navigation strategies across lifespan.

This work highlights the need for enriching the allocentric/egocentric framework, classically used to interpret the impact of healthy aging on spatial cognition, by integrating the spatial cue processing dimension. This enriched framework may be useful to develop innovative solutions to prevent/counteract the autonomy loss induced by visuo-spatial cognitive aging. This larger scope is in line with public policy priorities supporting gerontechnology and sustainable well-being programs.

ABBREVIATIONS

	Morris Water Maze – MWM
	Stimulus-response – S-R
	Path integration – PI
	Microsaccades – MS
	Square-wave jerk – SWJ
	Vestibulo-ocular reflex – VOR
	Optokinetic reflex – OKR
	Optic flow – OF
	Pro-saccade – PS
	Anti-saccade – AS
Functional magnetic resonance imagery – fMRI	
	Retrosplenial cortex – RSC
	Parahippocampal place area – PPA
	Occipital place area – OPA
Mini Mental State examination – MMSE	
General Health Questionnaire – GHQ	
Corsi block-tapping test – CORSI	
Figural Memory Test – FGT	
Mental rotation test – 3D	
Perspective taking / Spatial orientation test – PERSP	
	Trail Making Test – TMT
	Go/no go – INHIB
Falling Efficacy Scale International test – FES	
Head-mounted display – HMD	
	Virtual reality – VR
	Alzheimer’s disease – AD

TABLE OF CONTENTS

	Page
List of Tables	ix
List of Figures	xi
1 Overview	1
1.1 Rationale of the project	1
1.2 Roadmap of this thesis	4
I THEORETICAL FRAMEWORK	5
2 Spatial cognition	7
2.1 Spatial cognition: what is it?	8
2.1.1 Background	8
2.1.2 The dichotomy between landmark & geometric cues	8
2.1.3 The dichotomy between allocentric & egocentric strategies	10
2.1.4 Neural bases of spatial cognition	12
2.2 Human navigation across lifespan	15
2.2.1 Landmark & geometric cues	15
2.2.2 Allocentric & egocentric strategies	15
2.2.3 Other functional changes that affect spatial cognition in aging	16
2.3 Objectives	19
3 Eye movements	21
3.1 Oculomotor control: what is it?	22
3.1.1 Background	22
3.1.2 Different types of eye movements	22
3.2 The aging eye movement control	25
3.2.1 Ocular fixation	25
3.2.2 Saccadic movements	25
3.3 Objectives	26

TABLE OF CONTENTS

4	Gaze dynamics during spatial navigation	29
4.1	Gaze-mediated spatial cognition: what do we know?	30
4.1.1	Background	30
4.1.2	Identification of task-relevant spatial cues from gaze patterns	30
4.1.3	Characterization of individual differences based on gaze patterns	31
4.2	Objectives	32
II	EXPERIMENTAL CONTRIBUTIONS	35
5	Methodological contributions	37
5.1	Ecological approach to study spatial cognition in humans	38
5.2	Multidimensional screening of the study population	40
5.3	Cognitive assessment of the SilverSight cohort	42
5.3.1	Rationale	42
5.3.2	Methods	43
5.3.3	Results	45
5.3.4	Discussion	48
6	Contributions to spatial cognition	49
6.1	Spatial cues: landmark & geometry coding	50
6.1.1	Article 1: <i>Age-related preference for geometric spatial cues during real-world navigation</i>	50
6.2	Spatial strategies: egocentric & allocentric navigation	96
6.2.1	Rationale	96
6.2.2	Methods	96
6.2.3	Results	99
6.2.4	Discussion	100
7	Contributions to eye movement control	103
7.1	Fixation area	104
7.1.1	Article 2: <i>Impact of healthy aging on ocular fixation stability</i>	104
7.2	Microsaccades detection	122
7.2.1	Article 3: <i>Unsupervised detection of microsaccades in a high-noise regime</i>	122
7.3	Fixational saccades	139
7.3.1	Rationale	139
7.3.2	Methods	139
7.3.3	Results	141
7.3.4	Discussion	146
7.3.5	Supplementary information	150

7.4	Regular saccades	157
7.4.1	Rationale	157
7.4.2	Methods	157
7.4.3	Results	159
7.4.4	Discussion	159
III GENERAL DISCUSSION		163
8	Discussion	165
8.1	Discussion on aging & spatial cognition	165
8.1.1	Achievements	165
8.1.2	Implications	165
8.1.3	Raised questions & future studies	167
8.2	Discussion on aging & eye movement control	171
8.2.1	Achievements	171
8.2.2	Implications	171
8.2.3	Raised questions & future studies	172
8.3	Discussion on eye movements & spatial navigation	173
8.3.1	Achievements	173
8.3.2	Implications	175
8.3.3	Raised questions & future studies	176
9	Conclusion	177
A	List of Contributions	181

LIST OF TABLES

TABLE	Page
5.1 Cognitive and psychological tests	42
7.1 Statistical effect of the experimental conditions on fixational saccade frequency	151
7.2 Statistical effect of the experimental conditions on fixational saccade amplitude . . .	153
7.3 Statistical effect of the experimental conditions on fixational saccade peak velocity . .	155

LIST OF FIGURES

FIGURE	Page
5.1 The Streetlab research platform	39
5.2 Immersive virtual reality setup	40
5.3 Multidimensional screening of the SilverSight cohort	41
5.4 Perspective taking / Spatial orientation test	44
5.5 Cognitive performance of the participants	46
5.6 Statistical comparison of cognitive performance according to age	47
6.1 Experimental conditions of the Y-maze	98
6.2 Probability of using an allocentric strategy according to age	100
7.1 Main sequence of fixational saccades	140
7.2 Amplitude and peak velocity of fixational saccades	142
7.3 Fixational saccade direction	143
7.4 Aging effect on fixational saccade frequency	143
7.5 Properties of pairs of consecutive fixational saccades	144
7.6 Influence of optic flow on fixational saccade frequency	145
7.7 Influence of optic flow on fixational saccade direction	146
7.8 Directional bias in the radial optic flow conditions	147
7.9 Properties of fixational saccade pairs as a function of the amplitude of the first event	150
7.10 Influence of optic flow on fixational saccade amplitude	152
7.11 Influence of optic flow on fixational saccade peak velocity	154
7.12 Inward/outward fixational saccades for condition 5	156
7.13 Saccadic task	158
7.14 Properties of regular saccades during the pro-saccade task	160
7.15 Proportion of error during the anti-saccade task	161
7.16 Partial correlations between oculomotor and visual variables	161

1.1 Rationale of the project

Healthy aging progressively affects sensory, cognitive, and motor faculties. The impact of aging on visuo-spatial functions constitutes the core subject of this doctoral thesis. The focus is on age-related consequences on the action-perception loop, which are investigated within a spatial cognition framework. Spatial cognition is at the crossroad of the multi-scale, complex processes involved in the action-perception loop. In order to navigate in space, we explore the world through active vision, integrate visual percepts with other sensory modalities, and select, process and memorize the most relevant information to support decision making and trajectory planning.

The methodological backbone of this work stems from the hypothesis that traditional ways to assess spatial cognition in humans (e.g., computer screen-based tasks) are not ecological enough to fully account for the complexity of this high-level function, especially in older adults. A key asset of this project lies in the use of real-condition paradigms to study visuo-spatial cognitive aging. Furthermore, through the analysis of visual exploration patterns, we explore how aging shapes the focus of attention dynamics during navigation. Eye movements discretize the continuous flow of visual information to which we are exposed during spatial behavior. The analysis of eye movements can thus be informative about, when, what, and how we discretize spatial information to serve navigation purposes. By focusing on eye and body kinematics mediating active sensing of the environment, we study age-induced changes in how mental spatial maps are anchored on spatial cues, and how these changes alter wayfinding behavior. Therefore, this doctoral project targets, to the best of our knowledge for the first time, the intersection of three research fields:

healthy aging, spatial cognition, and gaze dynamics serving visual spatial coding.

Natural aging leads to gradual changes in the imaging structures of the eye, sensory transduction, neural transmission, and perceptual functions (Owsley, 2011). Structural changes in the eye include increases in lens and media opacities, corneal thinning, and constriction of the pupil, a phenomenon called miosis (Loewenfeld, 1979). These ocular changes combine to augment intraocular light dispersion and aberrations, which deteriorate the quantity and the quality of light that reaches the retina. These optical consequences, in turn, reduce high spatial frequency resolution (especially at near distances), and increase glare. Adding to these structural alterations are changes in higher-order neural processing (both at retina and cortical level), early pre-attentive processing, and attention-based processing. These alterations lead to perceptual losses such as visual acuity, contrast sensitivity, and motion perception (Owsley, 2011). Age-related cognitive changes are overlaid on visual perception, as it was demonstrated using spatial cognition in both animals and humans (Lester et al., 2017).

Healthy aging affects all levels of spatial cognition, and in particular the ability to encode and use visual information to perform complex navigation tasks (Mahmood et al., 2009). Age-related deficits in handling complex visual scenes are associated with autonomy loss in driving (Conlon and Herkes, 2008) and walking (Cavanaugh, 2002). Spatio-temporal gaze patterns were examined in pure locomotion studies with older adults (Chapman and Hollands, 2007). However, there is a gap in the understanding of how aging modifies the dynamics of visual exploration underpinning the acquisition of spatial maps, which is addressed in this thesis. Another key goal of this work is to study how age-related changes in the ability to process visual information are reflected in the use of geometric vs. landmark spatial cues. Geometric cues (the shape of an entrance hall, or the arrangement of buildings at a road junction) provide information about the spatial organization of the surrounding space. In non-symmetric environments, which urban inhabitants encounter most of the time, geometry provides sufficient and stable information for the unambiguous localization of a target position. A large body of studies showed that adult primates and other nonhuman animals use geometric cues for navigation (Cheng and Newcombe, 2005). Experiments with humans suggested that while young children orient themselves by primarily relying on room geometry and ignoring landmarks (such as a colored wall), young adults can successfully use both of cue types (Hermer and Spelke, 1996).

The work presented here extends these findings by directly testing the hypothesis of a change in the preferential encoding of geometry vs. landmark cues across lifespan. In a series of experiments in ecological conditions, we compare spatial learning and navigation in children, young and older adults, with a focus on the use of geometry, relative to landmarks, to reorient and solve spatial tasks. Our approach complements existing works that suggest that the use of allocentric (hippocampal-dependent) spatial maps decreases with aging, in favor of egocentric strategies (Lester et al., 2017). By directly assessing the impact of cue reliance on the use of egocentric and allocentric strategies across lifespan, the rationale of this work is to focus on

age-related differences in spatial information processing, which shapes downstream map learning and navigation strategies.

Ecosystem of this doctoral project. This doctoral thesis was realized at the laboratory of Aging in Vision and Action, and it benefited from the synergistic ecosystem provided by the Vision Institute, in Paris. The Vision Institute is a center for integrated research on vision and eye diseases. It is set up in the heart of the Quinze-Vingts National Ophthalmology Hospital, Paris, which allows scientists to work hand-in-hand with clinicians. The Quinze-Vingts Hospital harbors the Clinical Investigation Centre, which provides a large spectrum of high-tech facilities (e.g., optical coherent tomography, OCT; adaptive optics high-resolution retinal imaging) to explore physiological and pathological aspects of vision as well as audio-vestibular functions. As mentioned above, a methodological asset of this doctoral work is the investigation of age-related consequences on spatial cognition in ecological-like conditions, which is a challenging task. We were able to address this goal thanks to the Streetlab research facilities available at the Vision Institute. Streetlab is a living lab that aims at improving the autonomy, mobility, and life quality of visual impaired people and older adults. It offers a set of innovative platforms enabling real and virtual experimental conditions. Among these, we primarily employed the "Artificial street", which physically reproduces a portion of a shopping street (Chapter 5).

Socio-economic impact. Probing the impact of aging on spatial cognition can shed light on behavioral and mobility-related markers of autonomy loss in older adults. A corollary (mid-term) objective of this doctoral work was the development of innovative solutions to counteract age-related deficits in visuo-spatial perception and cognition. This technological transfer activity was facilitated by the fact that the project was framed in the SilverSight Research Chair, an academic-industrial partnership between the Vision and Institute and Essilor International, the world's leading ophthalmic optics company. The investigation of visuo-cognitive aging targets a crucial socio-economic issue insofar as it is linked to the quality of life associated with demographic evolution. Global population changes will make the number of people aged 65 or older to nearly triple between 2010 and 2050 and become about 1.5 billion, i.e. 16% of the world's population (NIH National Institute of Aging). In Europe, which harbors most of the world's oldest countries in terms of population age, nearly 25% of people in 2030 will be aged 65 years or older (source: Vienna Institute of Demography). At a world level, people over 65 yo account for 50% of the loss of productivity due to poor vision, which is calculated at \$275 billion a year (source: ESSILOR Vision Impact Institute). Aged people are subject to a loss of productivity and autonomy due to visual disturbances and vision-cognitive deficits. The loss of autonomy is directly related to the capability of aged people to move around in complex dynamical environments. For instance, driving in crowded conditions clearly requires rapid visual information processing, attention-mediated functions, and anticipatory executive capabilities that are deteriorated through healthy visual aging. Thereby, the transfer of basic knowledge on age-related effects on visual and spatial navigation functions into innovative assistive technologies can anticipate and account for changes

in visual needs and performance of large populations of stakeholders.

Ethical considerations. This doctoral thesis involved both clinical screening and experimental testing of a human study population. All clinical examinations were performed under medical supervision at Clinical Investigation Center of the Quinze-Vingts Hospital. All experiments were non invasive and they were conducted at Vision Institute in authorized laboratories for biomedical research (approved by the "Agence Régionale de Santé Ile de France", ARS). All clinical and experimental procedures were ethically approved by the "Comité de Protection des Personnes Ile de France V" (CPP) and by the "Agence Nationale de Sécurité du Médicament et des Produits de Santé" (ANSM). They were compliant with European ethical regulations (including Helsinki Declaration and the Charter of Fundamental Rights). Data management procedures were approved by the "Commission Nationale de l'Informatique et des Libertés" (CNIL) and they were compliant with the newly enforced GDPR European regulation. All subjects were informed about the purpose of the study and the clinical and experimental protocols, they signed a consent form on a voluntary basis, received compensation per each clinical/experimental session, and they were able to retract any time.

1.2 Roadmap of this thesis

Part I of this manuscript provides the reader with the theoretical framework of this doctoral work. The three chapters of this part (i.e., Chapters 2, 3, 4) review the state-of-the-art by crossing the research fields that are at the core of this thesis, i.e., healthy aging, spatial cognition and eye movements. At the end of each chapter, a section presents the objectives that stemmed from the reviewed body of work and that have been experimentally addressed by this project.

Part II presents the main experimental contributions of this thesis. The first chapter (i.e., Chapter 5) describes the methodological approach set forth to address all experimental questions (e.g., the use of ecological setups and the multidimensional screening of the study population). Then, Chapter 6 presents the main outcomes of this work, which concern the effect of aging on spatial cognition and navigation. Finally, Chapter 7 describes several secondary contributions regarding the effect of aging on eye movement control. Five original articles and one patent originated directly from this project (see Appendix A for a complete list of contributions, i.e., journal papers, patents, oral and poster presentations). Part II presents three of these articles in the format in which they were submitted to or published by the concerned journals. Thus, every article is presented with its own references and supplementary information. Two other articles, still in preparation, are presented in the standard format used throughout this thesis.

Part III first provides a general discussion (i.e., Chapter 8) of all main contributions, in the light of the theoretical considerations reviewed in Part I. Finally, it provides the general conclusions (i.e., Chapter 9) drawn from this doctoral work.

Part I

THEORETICAL FRAMEWORK

SPATIAL COGNITION

This chapter is dedicated to the presentation of classical concepts used throughout the spatial navigation domain, in order to familiarize the reader with questions such as: What type of spatial cues (landmarks and geometry) can we use when feeling disoriented? or, What type of spatial strategies (egocentric and allocentric) can we use to go from a point A to a point B? Then, this chapter reviews the state-of-the-art knowledge on the impact of aging on spatial cognition and navigation capabilities. We will see that the question of the relative influence of landmark versus geometric information has received little attention, comparatively to a large body of evidence postulating a decreased capacity to use allocentric strategies in aging.

The main goals that stem from this state-of-the-art and are addressed in this doctoral work are: *i)* to characterize the impact of aging on spatial cue processing (landmark vs. geometry), and *ii)* to understand how differential cue processing may affect the use of spatial strategies. Importantly, the approach set forth in this work posits that the age-related impact on spatial navigation should be assessed in ecological experimental conditions.

2.1 Spatial cognition: what is it?

2.1.1 Background

Spatial cognition may be defined as a "*navigator's ability to acquire spatial knowledge (...), organize it properly, and employ it to adapt its motor response to the specific context*" (Arleo and Rondi-Reig, 2007). Spatial cognition requires the integration of multimodal cues into a representation of surrounding space that allows an agent to know its own position and to select the proper navigation strategy to achieve its intended goal. It thus implies the use of a myriad of perceptual, cognitive and motor processes, varying in complexity.

Spatial information is acquired by our senses and it can be classified according to two distinct classes: idiothetic and allothetic. Idiothetic inputs are based on sensory mechanisms that detect body movements or "self-motion" signals like vestibular, proprioceptive, motor efference copy or optic flow information. They serve to dynamically update our estimation of travelled linear and angular distances and to keep track of one's position, a process known as path integration (Mittelstaedt and Mittelstaedt, 1980). Allothetic stimuli, on the other hand, inform the organism about the external environment through different modalities (visual, olfactory or auditory). Allothetic cues include objects, potentially serving as *landmarks*, and *geometric* properties of the environment, as the shape of a room or a street intersection. Human navigation, in contrast to that of other animals, is thought to primarily depend on vision, and for this reason it was very often studied in vision-dependent tasks (Head and Isom, 2010; Rodgers et al., 2012; Gunther et al., 2004; Ekstrom, 2015; Ekstrom et al., 2014).

Spatial information about location can be represented according to two distinct types of reference frames. In an *egocentric* frame of reference, locations are represented relative to the subject's body, whereas in an *allocentric* frame of reference the point of origin is centered on an element of the external world (Burgess, 2008).

2.1.2 The dichotomy between landmark & geometric cues

Defining landmarks & geometric cues. A landmark is a discrete element of the environment which is associated with a position, a behavioral response or a relation with other cues (Presson and Montello, 1988; Tommasi et al., 2012). A particular object in the environment can serve as a landmark (e.g., the Eiffel Tower or a notable tree), but landmarks can also be embedded in a surface (e.g., a shop in a street). To be used in a navigation context, it is important for landmarks to be persistent (i.e., immutable, stable), salient (i.e., large and clearly identifiable), informative (i.e., unique) and distal with respect to the observer (Stankiewicz and Kalia, 2007; Biegler and Morris, 1996).

On the other hand, geometric cues are provided by continuous surfaces (e.g., walls) arranged in a certain spatial relationship (e.g., the shape of a junction or a room; Tommasi et al., 2012).

Surfaces generally occupy a larger portion of the visual field, when compared to discrete landmarks (Sheynikhovich et al., 2009) and they critically frame the navigable space by restricting locomotion to the boundaries on the environment. Surfaces are more ubiquitous and enclosed in man-made environments and they can be manipulated in laboratory studies so as to be polarized (e.g., a rectangular room) and unpolarized (e.g., a circular arena). Geometric information can also be present in a spatial arrangement of landmarks (e.g., several objects arranged in a certain spatial relationship contain a geometric information) and this information can be used for navigation in some cases (Lew, 2011). In this work, we focus on geometric cues provided by a surface arrangement.

Experimental paradigms for dissociating geometric vs. landmark cues. The reorientation paradigm, initially proposed by Cheng (1986), has been used to study the contribution of the different types of cue to orientation and navigation. In this paradigm, an animal has to retrieve food previously hidden in one of four corners of a rectangular room, after being disoriented. Disorientation in this case disrupts the idiothetic information and forces the animal to use allothetic, environment-based information to find the correct corner. To do so, the animal could rely on the geometric polarization of the room (its rectangular, anisotropic shape) or on landmark information (e.g., a painted wall). The reliance on geometric cues (i.e., looking for a corner with a short wall to the left and a long wall to the right) is associated with searching in the correct corner or its rotationally symmetric corner (an error termed "rotational error") at an equivalent frequency, while relying on landmark information is associated with a higher frequency of searching in the correct corner. The reliance on landmark, as opposed to using geometry, is assessed based on a difference in the frequency of correct vs. symmetrical search (Cheng, 1986). When tested using this paradigm, rodents (Cheng, 1986) as well as children under 6 years of age (Hermer and Spelke, 1994, 1996; Hermer-Vazquez et al., 2001) showed a preference for geometric information, disregarding landmark cues while searching for the reward. This point will be further detailed in Sec. 2.2.1.

In a variant of the reorientation paradigm, a conflict is introduced between landmarks and geometry in order to disambiguate search behaviors (Newcombe and Ratliff, 2008)). After learning the position of the reward, the conflict was introduced by putting the landmark at a different position in the environment. Under such circumstances, a preference for one cue is clearly indicated by the searching behavior. In such conflict paradigm, young adults were shown to prefer to reorient with landmarks in large rooms (Newcombe and Ratliff, 2008).

Theoretical considerations. The primacy of geometric cues in disoriented rodents and human children was taken as an evidence for postulating the existence of an encapsulated "geometric module" (Cheng, 1986; Gallistel, 1990), i.e., an abstract brain process, the use of which is obligatory (i.e., it is always employed by the navigator) and which is impervious to other types of cue (i.e., landmark cues). In Gallistel's conception, rodents are matching (by putatively aligning principal axes) the global shape of the perceived environment to the one stored in memory

(Gallistel, 1990), whereas others have argued that a matching of local geometric properties (such as angle and wall length) would be sufficient (Pearce et al., 2004).

According to the proposal of some researchers, the above formulation of the *modular view* is too strict (see review by Cheng and Newcombe, 2005), stirring the ongoing theoretical debate concerning the issue of whether or not geometry and landmarks are treated as equals during reorientation. In other terms, the question is whether geometry and landmark cues obey the same learning rules and share the same neuronal substrates, or geometry processing is prioritized in some way as a consequence of, for instance, some evolutionary adaptation. To answer this question, it has been examined whether classical conditioning phenomena predicted by the *associative learning theory* (Rescorla and Wagner, 1972), such as blocking (in which learning of one cue prevents the learning of a second one if presented sequentially) and overshadowing (in which learning of two cues is decreased when they are presented simultaneously, compared to when they are presented separately) were observed between landmarks and geometric cues. Whereas some evidence confirmed the associative nature of both landmark and geometric cues in certain experimental conditions (Horne and Pearce, 2009; Buckley et al., 2016), in other conditions learning a location according to geometry was shown to be impervious to blocking by landmarks, thus indicating a particular role of geometry (Hayward et al., 2003; Doeller and Burgess, 2008; Cheng, 1986; Pearce et al., 2001).

As an alternative to the modular view, other explanations were proposed since 1986 to account for the apparently prioritized geometry processing. In particular, it is possible that the balance between cue could be influenced by specific cue properties such as *i*) cue reliability, *ii*) cue size, and *iii*) prior experience with the cue (Cheng et al., 2013; Cheng and Newcombe, 2005; Tommasi et al., 2012). The *adaptive-combination model* (Newcombe and Ratliff, 2007) states that reorientation is flexible and that cue use is dependent on a weighting mechanism in which the weight associated with each cue is modulated by the variance associated with each cue, the variance being dependent on factors such as reliability, validity and salience of the cue. According to the authors, the apparent primacy of geometric cues is related to the fact that in many situations, geometric information is encoded easily, with less uncertainty and less variability than landmarks.

2.1.3 The dichotomy between allocentric & egocentric strategies

Defining egocentric & allocentric strategies. Navigation strategies can be classified according to whether the goal location is directly visible or not and further according to the way spatial locations are represented (Arleo and Rondi-Reig, 2007). When the target destination is visible from one vantage point or directly cued, the *guidance strategy*, also termed target or beacon approaching, is the easiest and less cognitively demanding strategy that implies orienting and approaching the target (Arleo and Rondi-Reig, 2007). An *egocentric strategy*, sometimes called response learning, is used whenever the goal is not directly visible and implies learning of a

stimulus-response (S-R) association such as turn right (response) at the bakery (stimulus). Egocentric strategies form a basis for so called route learning, in which spatio-temporal relationships of events (sequences of S-R associations) are associated with a goal. The term "egocentric" means that the origin of the reference frame, with respect to which locations are defined, is tied to the body position/orientation and is thus moving together with the subject. The goal position in this case is represented by an egocentric vector relative to the subject's body (Wolbers and Wiener, 2014). Finally, an *allocentric strategy*, also called map-based strategy or place learning, implies localizing a goal according to the spatial relationships between elements of the environment. The origin of the reference frame is, in this case, tied to a specific location in the external world (e.g., a corner of a room or a salient landmark) which is independent of the subject's position and orientation. The way we use strategies is determined by the structure of the environment, its complexity and stability (Trullier et al., 1997; Hartley et al., 2003). For example, navigating using an egocentric route strategy is useful and less resource consuming when exposed to an environment that is familiar and stable. However, if either landmarks are unstable, or a route is unexpectedly blocked, or taking a new shortcut is desired, then the use of a more flexible allocentric representation becomes mandatory (Hartley et al., 2003).

Experimental paradigms for testing navigation strategies. Various experimental paradigms, initially proposed to study spatial navigation in rodents, have been used to understand the use of spatial strategies by human navigators. The version of the Morris Water Maze (MWM, Morris, 1981, 1984; Kallai et al., 2005) adapted to human studies is an open-field arena surrounded by distal landmarks. The navigator has to learn the position of a goal which is visible at the beginning of the learning phase. In order to test the use of an allocentric representation to retrieve the goal location, the goal is rendered invisible and the navigator is placed at a random position/orientation in the arena (thus rendering egocentric vectors to the target inefficient), from which he or she has to navigate to the hidden goal location. The use of an allocentric strategy is then indirectly estimated from behavioral variables such as the escape latency (time to goal), the travelled distance or the proportion of time spent searching in the actual goal quadrant.

A more precise paradigm for dissociating egocentric and allocentric strategies makes use of structured (as opposed to open-field) environments. Often such environments consist of a number of intersecting alleys, or arms (e.g., 3 arms as in the Y-maze, 4 arms as in the Plus-maze; Packard and McGaugh, 1996; Rodgers et al., 2012), surrounded by distal cues. The navigator learns to approach a goal hidden in one of the arms (goal arm), always starting from a specific arm of the maze (start arm). Suppose, for example, that during learning the navigator always starts in the south arm of a Plus-maze, and the goal arm is the west arm (i.e., the subject has to turn left at the intersection). When the goal arm is successfully learned, the use of spatial strategies is tested by placing the subject in a novel start arm (e.g., north arm in our example), unbeknownst to the subject. Under such circumstances, if the subject is using an egocentric strategy (i.e., "the goal is located to the left arm relative to my body"), he or she will implement a habitual response of

turning left at the intersection, disregarding distal landmarks. In contrast, if the subject is using an allocentric strategy (i.e., "the goal location is defined relative to distal landmarks"), he or she will realize that the start arm is different and therefore the right turn should be performed.

Although these and other experimental paradigms may give some indication towards strategic preference in navigating subjects in specific experimental conditions, it should be kept in mind that real-world navigation generally involves more than only one cognitive process (Hamilton et al., 2004). It might therefore be better conceptualized as a spectrum going from purely egocentric to purely allocentric strategies, with many of the tasks used in the literature lying somewhere in between these two extremes (Ekstrom et al., 2014).

2.1.4 Neural bases of spatial cognition

Spatial cells. The hippocampal formation is thought to be at the center of the neural navigation network as it contains so called spatial, or spatially sensitive, cells that are thought to provide the neural substrate of an allocentric "cognitive map", i.e., a global representation of the allocentric relationships between places (Tolman, 1948) that support spatial memory and navigation (O'Keefe and Nadel, 1978). Four different types of spatial cells have been identified since the seminal work of O'Keefe & Dostrovsky (1971), in which *place cells* in the rodent's hippocampus were discovered. The cells were shown to fire when the rat occupies a particular location in a given environment (O'Keefe and Dostrovsky, 1971). *Head direction cells* fire depending on the head orientation of the animal, independently of its location and are found in many cortical and subcortical regions, including the subiculum and the entorhinal cortex (Taube et al., 1990; Taube, 2007). A population of head direction cells sensitive to different orientations is thought to serve as a neural compass providing the brain's navigation system with an allocentric direction signal. *Grid cells* in the entorhinal cortex have multiple firing locations in an environment forming a repeating hexagonal grid-like pattern (Hafting et al., 2005). A population of such cells is thought to provide a stable self-motion-based metrics to the cognitive map (McNaughton et al., 2006). Finally, *border cells* fire when the rodent is at particular distance and direction relative to a boundary. Border cells are found in the subiculum and in the entorhinal cortex and are thought to encode environmental borders, an important navigational cue (Solstad et al., 2008; Lever et al., 2009).

Sensory determinants of spatial cell firing. Both idiothetic (self-motion) and allothetic cues strongly influence the firing of spatial cells (Taube et al., 1990; McNaughton et al., 2006). Activity of grid and head direction cells is affected by external landmarks to a high degree (Knierim and Hamilton, 2011; Clark et al., 2012), especially when landmarks are salient, large, numerous, stable and distal (Clark et al., 2012; Biegler and Morris, 1996). Environmental geometry can also exert a strong control over spatial cells tuning. For instance, varying the size and shape of the experimental room was shown to affect the shape of the firing fields of hippocampal place cells accordingly, such that they remain active at a fixed distance and direction from the room

walls (O'Keefe and Burgess, 1996). The firing patterns of grid cells (Weiss et al., 2017) and head direction cells (Clark et al., 2012; Dudchenko and Zinyuk, 2005) also rotate and shift so as to align with the room geometry (either rectangular, triangular rooms and T-junction mazes) in disoriented animals. Interestingly, grid patterns were only influenced in geometrically polarized arenas but not in isotropic circular ones (Krupic et al., 2015). Although landmarks and geometric information can compete in controlling spatial cells tuning (Clark et al., 2012), environmental geometry is thought to be of primary importance when animals are disoriented (Julian et al., 2018; Epstein et al., 2017), mirroring behavioral results in rodents and human children (Cheng et al., 2013). Keinath et al. (2017) have used Cheng's reorientation paradigm in mice to show that hippocampal place fields aligned with the rectangular shape of the room, discarding landmark information. While not used for reorientation, landmarks in their experiment were shown to serve as contextual cues (i.e., signaling *which* room they were in, but not the orientation they had in that room). The authors associated this primacy of geometric cues during reorientation with the fact that geometry generally appears to be more stable than landmarks. Interestingly, hippocampal place fields were shown to shift their orientation by 180° on certain trials due to the symmetry of the rectangular environment. On such trial, mice were more likely to produce a rotational error (i.e., search for food in the symmetric corner), making it possible to predict the behavioral response based on the neural pattern on a trial-by-trial basis (Keinath et al., 2017).

View and spatial cells in primates. Spatial representations in primates are much more related to visual coding mechanisms, in comparison to rodents. One possible explanation could lie in the different visual systems in rodents and primates: primates, unlike rats, benefit from a foveated, higher resolution visual system (Ekstrom, 2015) that discretize the visual inputs by the mean of eye movements which have impact on downstream hippocampal activity (Meister and Buffalo, 2016; Wirth et al., 2017). The existence of visual analogues of spatially-tuned cells have been described in primates (Nau et al., 2018b). Similar to place cells, which fire whenever the animal occupies a particular location, the primate hippocampus contains allocentric *spatial view cells* that fire whenever an environmental location is viewed, independent from the body position or the eye position in the orbit (Rolls, 1999). When actively exploring 2D images, *visual grid cells* in the entorhinal cortex of primates were shown to fire in a hexagonal pattern dependent on the position of gaze on the display (Killian et al., 2012). Similarly, a fMRI signal in the entorhinal cortex of humans exhibited a sixfold symmetry as a function of gaze direction that furthermore aligned to the border of the visual display (Doeller et al., 2010). The entorhinal cortex of monkeys was also shown to contain neurons that specifically fire when the gaze is close to a border of the visual stimuli (Killian et al., 2012) or for a particular saccade direction (Killian et al., 2015). These cells were termed *visual border cells* and *saccade direction cells*, akin to the border and head direction cells described in rodents, respectively (Nau et al., 2018a). Although these recent works raised several questions (e.g., whether these cells also code for visual exploration in 3D Nau et al., 2018a), it nevertheless strengthens the need to study visual and gaze-mediated exploratory

mechanisms on navigation (Meister and Buffalo, 2016; Wirth et al., 2017).

The human navigation network. Human analogues of place (Ekstrom et al., 2003) and grid (Jacobs et al., 2013) cells have been demonstrated in studies that used intracranial recordings in the hippocampal formation of epileptic patients. Moreover, fMRI experiments as well as lesion studies have coherently shown an involvement of hippocampal areas when participants performed virtual navigation tasks involving allocentric processes (Hartley et al., 2003; Iaria et al., 2003; Astur et al., 2002). On the other hand, guidance and response strategies are generally thought to be less dependent on the hippocampal processing (Packard and McGaugh, 1992; Doeller et al., 2010). In young adults, response strategies have been associated with increased gray matter and functional activity in the striatum (Galati et al., 2010; Iaria et al., 2003), whereas route strategies involve many structures including the hippocampus (Rondi-Reig, 2006).

In addition, frontal lobe regions have been implicated in the human navigation network (Spiers and Maguire, 2006), as well as the retrosplenial cortex (RSC), the parahippocampal place area (PPA) and the occipital place area (OPA), which are active during virtual navigation, but also respond to passive viewing of scenes (like buildings, landscapes or rooms). For this reason, these areas are thought to be implicated in visual processing of navigation-related stimuli (Epstein and Kanwisher, 1998; Julian et al., 2018). For instance, OPA has been causally involved in boundary perception: transcranial magnetic stimulation on the OPA, which creates a virtual lesion of the site, impairs learning locations relative to boundaries but not to local landmarks (Julian et al., 2016b). PPA, on the other hand, is sensitive to the presence of both boundaries (Park et al., 2011) and landmarks in a scene, especially when those are large and stable (Cant and Goodale, 2007; Julian et al., 2016a).

The role of the hippocampus in processing landmarks and/or geometry is still a matter of debate in the human literature. Indeed, learning of a goal location according to boundary (a geometric cue) has been hypothesized to be incidental and based on the hippocampus, whereas learning the location relative to landmarks follows S-R learning rules and relies on striatal reinforcement-based computation (Doeller et al., 2008; Doeller and Burgess, 2008). Note, however, that the geometry in this fMRI paradigm was isotropic (i.e., circular) and could not be used as an orienting cue. Orientation was given by distal landmarks (projected at infinity). It is not clear thus whether the higher involvement of the hippocampus under such conditions reflects the processing of distal landmarks for orientation or the proximal geometry for goal positioning. Using the reorientation paradigm, Sutton and colleagues found that processing of a landmark (i.e., a colored wall in the room) was associated with a stronger signal in the medio-temporal areas including the hippocampus, whereas processing of geometric cues involved frontal areas to a greater extent (Sutton et al., 2010).

2.2 Human navigation across lifespan

2.2.1 Landmark & geometric cues

As mentioned earlier (Sec. 2.1.2), young children were shown to preferentially use geometric cues when reorienting: they are not able to use a polarizing landmark (colored wall) to disambiguate the goal position in an environment with rectangular shape (Hermer and Spelke, 1994, 1996). However, approximately at the age of 6 children start using landmark cues (Hermer-Vazquez et al., 2001), and this developmental transition has been initially attributed to the mastering of spatial language (Hermer-Vazquez et al., 2001) or to the fact that children are more exposed to geometric enclosures than open-field distal landmarks early in life (Newcombe and Ratliff, 2007). This view was questioned by intriguing evidence showing that when the room was large enough (8 x 12 feet, as opposed to 4 x 6 feet in Hermer-Vazquez et al., 2001), children were capable of using the colored wall (Learmonth et al., 2001, 2008) and this ability gradually evolved from 4 to 6 years of age (Cheng and Newcombe, 2005). The effect of room size has been related to the fact that large rooms encourage active exploration (by reducing environmental restrictions on possible movements) and provide relatively more distal cues, more likely to be used in a navigation situation (Newcombe et al., 2005; Learmonth et al., 2008).

When young adults were exposed to the reorientation paradigm, they were shown to accurately combine the two types of cue when they provided unambiguous information about the goal location, and to prefer landmarks in case of cue conflict. This was true in large, and thus more ecologically valid, rooms (Newcombe and Ratliff, 2008). Experimental evidence in older adults remains unclear. Earlier studies proposed that older adults were impaired in using the geometric layout of an environment, based on the comparison of hand-drawn diagrams of the experimental space (a MWM circular arena inside a larger room with an anisotropic shape; Moffat and Resnick, 2002) or based on their ability to navigate to a goal location (in a circular, isotropic arena surrounded by distal landmarks; Schuck et al., 2015). More recent evidence, on the other hand, suggested that older adults, compared to young subjects, experienced more difficulties in using landmarks (Picucci et al., 2009) and that they did not express any differences between landmark and geometry-related learning (Caffò et al., 2017).

2.2.2 Allocentric & egocentric strategies

Developmental and aging data suggest an inverted U-profile of allocentric processing, probably reflecting the maturation (in development) and deterioration (in aging) of the brain areas involved in spatial navigation (Ruggiero et al., 2016). Indeed, the ability to use allocentric representations is thought to develop gradually from 5 to 10 years of age and to become integrated with spontaneously used egocentric ones around the age of 6, as suggested by studies of navigation in complex mazes (Bullens et al., 2010). The developmental shift from egocentric to allocentric

representations could be related to the mastering of executive functioning and to the maturation of hippocampal regions and frontal lobes (Ruggiero et al., 2016).

At the other end of the curve, some evidence suggests that aging is associated with reduced ability to use egocentric route-based strategies (Head and Isom, 2010; Ruggiero et al., 2016). However, the most striking and reliably observed age-related difference is a decreased spontaneous use of allocentric strategies by older subjects (Wiener et al., 2012, 2013). Barnes' study was the first to notice this shift toward response strategy preference in older rats (Barnes et al., 1980), further confirmed in human studies (Bohbot et al., 2012; Davis and Weisbeck, 2015; Driscoll et al., 2005). For instance, a reduced use of allocentric strategies was evident in participants' self-report (Bohbot et al., 2012), but also through direct observation of older participants' performance in tasks requiring the use of allocentric spatial representations. Other studies consistently showed a significant increase in distance travelled by older subjects when solving tasks such as the MWM (Moffat and Resnick, 2002) or in a more complex maze (Head and Isom, 2010). A stronger evidence comes from Rodgers and colleagues (Rodgers et al., 2012), who assessed strategy preference of young and aged subjects in the Y-maze, using a strategy dissociation paradigm adopted from rodent experiments. During training, the subjects learned to approach a goal location in one of the arms from a fixed start arm. When starting from a novel arm during testing, the strategy preference was classified as egocentric when the subject made the same turn as during the learning phase, and as allocentric when he or she moved to the correct goal location. Results show that older adults more often used an egocentric strategy than an allocentric one (84% and 18%, respectively), whereas younger subjects did not (46% and 54%, respectively). Furthermore, the older subjects were impaired at locating the platform in a virtual MWM, proposed after the Y-maze, whereas young adults classified as allocentric learners were quicker to locate the hidden platform in this second experiment.

This age-related shift is traditionally attributed to hippocampal as well as frontal function decline (Harris and Wolbers, 2012; Wiener et al., 2012; Moffat, 2009; Lithfous et al., 2013), which are the earliest structures to show atrophy with advancing age (Raz et al., 2004). This hypothesis is further supported by neuroimaging studies, which show that hippocampal activation is reduced or absent when older people perform navigation tasks (Antonova et al., 2009; Moffat et al., 2006). Moreover, the hippocampal volume is positively correlated with navigational skills in the MWM in young but not in older subjects, indicating that older people may rely on extra-hippocampal strategy to solve the task (Moffat et al., 2007a).

2.2.3 Other functional changes that affect spatial cognition in aging

Multisensory integration. Healthy aging is associated with deficits in extracting sensory information that is useful to navigation. For instance, optic flow perception decreases in older adults, as they require a higher threshold for detecting coherent movement in optic flow, which in turn is associated with a poor performance on both paper-pencil tests of spatial orientation

(Mapstone et al., 2003) and real world navigation tasks (Kavcic et al., 2006).

As stated before, path integration is of interest for studying multimodal integration of sensory information for navigation purposes. Experimental paradigms used in humans evaluated path integration by asking subjects to reproduce a travelled distance, an experienced rotation, or a combination of those. In the triangle completion task, the participant is asked to complete the third arm of a triangle after having travelled the first two arms (Adamo et al., 2012; Harris and Wolbers, 2012; Mahmood et al., 2009). Additional attempts were made to restrict sensory information (visual, vestibular, proprioceptive) in order to assess the contribution of each modality to path integration. In young adults, path integration is still effective when restricted to visual information only (by use of joystick-controlled virtual environment; Mahmood et al., 2009), exclusively to vestibular and proprioceptive information (by testing blindfolded subjects; Wiener et al., 2011) or just to vestibular information (by pushing the subject in a wheelchair while blindfolded; Adamo et al., 2012). As for older people, studies consistently showed that age-related differences are dependent on the quantity of information available. When both vestibular and proprioceptive sensory cues were available, older people were as efficient as young ones (Adamo et al., 2012), whereas restricting sensory cues to only one modality exacerbated older subjects' difficulty in the triangle completion task, especially for larger distances and rotations (Adamo et al., 2012; Harris and Wolbers, 2012; Mahmood et al., 2009). For instance, in a study from Mahmood et al. (2009), path integration was tested when visual cues were the only available sensory information in distance reproduction and the triangle completion tasks. While older people were as efficient in reproducing a short distance, they showed robust deficits in reproducing longer distances, especially when they were combined with rotation. Moreover, making visual information more rich in the virtual environment by adding landmarks or walls did not help older people to improve their PI performance (Harris and Wolbers, 2012; Mahmood et al., 2009).

Cognitive functions. Successful navigation requires cognitive processes varying in complexity. Specifically, sensory information critical for successful navigation must be selected and remembered for subsequent use. In addition to the maintenance of isolated features in memory, navigation requires encoding of spatial, temporal and contextual information (Wiener et al., 2012). Additionally, successful navigation relies on executive processes, i.e. the capacity of the navigator to monitor its own behavior and adapt its search strategy to the situation (Moffat et al., 2007b).

The ability to follow a particular route is based on the knowledge about *which* landmarks have been encountered along the route. Additionally, contextual information must also be encoded: spatial ("where was the landmark encountered?"), directional ("which way did I turn when I saw the landmark?") and temporal ("what was the sequence of landmarks encountered?") aspects of the landmarks must be learned for a successful route strategy (Head and Isom, 2010; Wiener et al., 2012). Experimental studies of these abilities in aging show a relative preservation of free recall for landmarks (Head and Isom, 2010; Wilkniss et al., 1997). In contrast, retrieval of the contextual

information about landmarks seems to be more problematic: memory for spatial (Jansen et al., 2010) as well as temporal (Head and Isom, 2010; Wilkniss et al., 1997) organization of landmarks is decreased in older subjects. Moreover, they fail to focus on the relevant directional information associated with landmarks (Head and Isom, 2010) and they tend to base their performance on salient landmarks instead of critical landmarks (i.e., those associated with important route events, such as turns; Lipman, 1991). These results are sometimes interpreted as a manifestation of an associative memory deficit in aging (Naveh-Benjamin, 2000), in which binding of directional information with landmarks is impaired (Head and Isom, 2010).

Some evidence suggests that the observed aged-related deficit in tasks relying on allocentric processes can be modulated by cognitive dysfunctions that are critical for spatial information acquisition, being thus inconsistent with a strictly hippocampus-based interpretation of age-related navigation difficulty. Indeed, Moffat and Resnick (2002) noted that older people's deficit is evident even on the very first trial of the MWM, i.e., before any spatial memory about the goal location is involved. Where search should normally be random, older people travelled longer distance and they tended to physically revisit areas already explored. This behavior could be an evidence of an inappropriate *search strategy* or an inability to monitor their own behavior during search (Moffat and Resnick, 2002). Extending this observation, Moffat et al. (2007a) found that tests measuring executive functions (e.g., working memory) and the volume of the prefrontal cortex correlated with spatial navigation performance. However, impairments in executive functions was not associated with the performance on the first trial. Authors' interpretation suggests that other cognitive functions could be at stake during the first exploration of the maze, and experimental characterization of these functions is an open question.

Motor functions. The link between motor-related functions, attention and navigation has been discussed by Lövdén et al. (2005). According to their view, locomotor gait is a highly attention-demanding activity in older adults, unlike in young people. Therefore, in multi-task situations, cognitive processes and sensorimotor functions compete for limited attentional resources and the preference is given by older adults to the locomotor activity, to the detriment of cognitive functions (Li and Lindenberger, 2002). This was tested in the navigation context by an experimental paradigm involving wayfinding in a complex maze. Results show that older people were slower to learn the task during natural free-walk conditions. However, when given a walking support (holding on to a handrail while navigating), age-related differences in learning were attenuated, leading to the conclusion that sensorimotor demands related to walking could have a negative influence on navigation performance. In addition, basic binding of features is impaired when attentional resources are overloaded, in both young and older adults (Brown and Brockmole, 2010).

2.3 Objectives

The **first objective of this work is to understand what spatial cues are used by older adults during navigation**. Indeed, the question of relative influence of landmark versus geometric information in aging has received little attention, and the scarce available experimental evidence seems inconsistent. As demonstrated in the above review, the geometry of an environment is an important cue in both tuning the neural representation of space and guiding orientation and navigation behavior. Despite some counter-examples in the literature, geometric cues seem nevertheless to hold a special place in many species, including children humans, when bearings are lost. It is our hypothesis, therefore, that studying how older adults make use of these ubiquitous cues will help us characterize and maybe explain the age-related influence on spatial navigation.

Several important aspects have to be taken into account in order to address this question experimentally. First, cue reliance has to be tested in an ecological environment. This implies testing older adults in an environment that is large enough to be ecologically valid (Newcombe and Ratliff, 2008). Second, joystick-operated motion in virtual reality setup limits the use of proprioceptive information and prevents using vestibular cues for navigation. This constitutes a problem since it has been consistently shown that age-related differences depend on the availability of multi-sensory information, with greater navigation difficulties observed with larger sensory restrictions (as shown, e.g., by path integration performance Adamo et al., 2012; Harris and Wolbers, 2012; Mahmood et al., 2009). Moreover, screen-based setups limit the extent of the visual field and they can therefore potentially restrict the use of geometric cues for reorientation (Sturz et al., 2013; Kelly and Spetch, 2004). Third, we think that hand-drawing or self-report are less informative tools than direct behavioral tests for the assessment of navigation abilities, as they require the use of additional cognitive processes that can themselves be age-dependent. These might include, e.g., mental rotation to compute in bird-eye view of the environment in a drawing or a form of metacognition necessary for self-report, metacognition being also impacted by aging (Hertzog, 2002). For instance, it has been shown that if participants were able to report landmarks, e.g., a color of the wall in the reorientation paradigm (Hermer and Spelke, 1996) or a picture on the wall in a MWM (Davis and Weisbeck, 2015), very few participants noticed the geometric shape or geometric-related information like the floor or corners, suggesting that the geometric information is not as consciously accessible to the subject as are landmarks (Davis and Weisbeck, 2015; Hermer and Spelke, 1996) and can not be tested by self-report. For these reasons, we will therefore seek to test reorientation and navigation performances by studying how participants naturally interact (i.e., with no limitations in the idiothetic cues) with an ecological environment resembling, by its size and by its richness, the real world. Finally, we will focus on the assessment of visual, cognitive and motor correlates of navigation performance in older adults, and their potential in explaining inter-individual differences (Wolbers and Hegarty, 2010).

The **second objective of this work is to understand the impact of cue reliance on**

the use of egocentric and allocentric strategies. If indeed there are differences in the way older adults use landmarks and geometry, the classical view for an egocentric preference having a primary effect on navigation in aging is questioned. In particular, in standard tests dissociating egocentric and allocentric strategies, experimental paradigms often used an isotropic geometric layout, that provide ambiguous information about goal location. The ability of the navigator to perform an allocentric behavior is thus exclusively dependent on its capacity to use distal landmarks. Such an age-related impairment in landmark processing can therefore be the primary cause of navigation deficits previously attributed to degradation of allocentric processing. More generally, addressing this question is important to understand the functional link between spatial cue processing and spatial navigation strategies to offer a more integrated view on human navigation behavior.

EYE MOVEMENTS

This chapter describes the different types of eye movements produced by the human oculomotor system, with a focus on fixational and saccadic movements. While keeping in mind that we study eye movements within a spatial navigation framework, we nevertheless point out some gaps in the literature of aging eye movement control. Indeed, available evidence shows a lack of clear results regarding the aging effect on fixation-related eye movements, probably due to methodological issues in the assessment of such small-sized eye movements in older adults.

Based on this state-of-the-art, the objectives drawn for this doctoral work are: *i)* to better characterize, in a large sample of subjects, the impact of healthy aging on oculomotor control, including fixation stability, saccades, microsaccades and square-wave jerks; *ii)* to better understand how oculomotor control is influenced by optic flow conditions, as occurring during locomotion and spatial navigation.

3.1 Oculomotor control: what is it?

3.1.1 Background

The main function of a foveated oculomotor system is to keep an image clear on the retina and keep an object of interest close to the foveal region of the retina (the area of highest photoreceptor density and highest visual acuity) for subsequent visual processing. Different types of oculomotor events can be distinguished. *Saccades* correspond to a rapid, ballistic motion of the eye, that brings the line of sight from one location to another, whereas *ocular fixation* occurs in-between saccades and it corresponds to the moment where the eyes are stationary on a spatially localized stimulus (Leigh and Zee, 2015). It is assumed that the processing of visual information occurs during ocular fixation, whereas we are blind during saccades, a phenomenon called saccadic suppression (Leigh and Zee, 2015). However, even when fixating, our eyes are never completely still. Small-sized ocular movements occur incessantly such as fixational eye movements (e.g., slow drift, *microsaccades*, tremor) or saccadic intrusions (e.g., *square-wave jerks*) (Leigh and Zee, 2015).

Fixating in the real world is furthermore complicated by the fact that external objects and the self are moving (Angelaki and Hess, 2005). Our oculomotor system has evolved to compensate for a constantly moving world. Indeed, during locomotion, our head is moving and this motion creates image slips on the retina. The resulting pattern of retinal motion, called *optic flow*, depends on the speed and direction of travel and the direction of gaze (Lappe et al., 1998). During locomotion, retinal slips are reduced by two oculomotor reflexes. The vestibulo-ocular reflex (VOR) uses labyrinth signals in order to compensate a head movement by an eye movement, optimally of same amplitude but opposite direction. The optokinetic reflex (OKR) is a visually-mediated reflex that uses the optic flow to patterns stabilize retinal slips. The OKR is composed of two phases: a slow phase, in the direction of the flow, and a saccadic phase in direction opposite to the flow. The optic flow is of importance in a variety of daily-life, navigation-related activities, such as postural control, perception of heading direction and obstacle avoidance (Warren et al., 1988; Warren, 2013; Angelaki and Hess, 2005).

3.1.2 Different types of eye movements

Fixation. Fixation stability corresponds to the capacity to maintain an object on the fovea and encompasses both microsaccades and smooth drift without distinction of these two types of eye movements (Otero-Millan et al., 2014). Ideally, a focused image should *i*) rest on the fovea and *ii*) be held relatively steady in order to achieve clear vision. Although the locus of fixation is not exactly localized on the area of highest foveal cone density but slightly displaced from it (Putnam et al., 2005), an overall fixation should be kept in the central 2° of the visual field, as visual acuity declines quickly from the fovea to more eccentric areas of the retina. For instance, the visual acuity decreases by about 50% at 2° from the center of the fovea (Jacobs, 1979; Leigh

and Zee, 2015). Accordingly, ocular fixation instability has been associated with difficulty in daily-life, high-acuity tasks such as reading (Falkenberg et al., 2007). The notion of steadiness of the image on the retina is better described as a balancing act, as too little motion on the retina can entail image fading (Martinez-Conde et al., 2006) whereas too much motion (i.e., if retinal-image slip velocities exceed 4 deg/s) entails blurring and oscillopsia, an illusionary movement of the visual world (Abadi, 2008). The capacity to maintain a steady fixation is linked to several cortical (e.g., frontal eye field, posterior parietal cortex) and sub-cortical (e.g., superior colliculi) areas of the brain which contain neurons that are active during periods of fixation and attenuate their activity during saccades (Munoz and Wurtz, 1992; Leigh and Zee, 2015). Fixation stability (and eye movements in general) is altered by a number of ophthalmological (Tarita-Nistor et al., 2011; González et al., 2006; Macedo et al., 2011) and neurological pathologies such as Alzheimer's (Kapoula et al., 2014) or Huntington's diseases (Collewijn et al., 1988).

Saccadic eye movements. Saccades are rapid, ballistic and conjugate movements of the eyes. The neuronal circuitry underpinning saccades is complex but relatively well known. The superior colliculi receive inputs from the visual, parietal and frontal (i.e., frontal eye field, supplementary eye field, and dorsolateral prefrontal cortex) cortexes and project to the reticular formation that connects to the motoneurons of the extra-ocular muscles (Munoz and Everling, 2004). Different types of saccadic movements can be distinguished, mainly according to their size and function. Large saccades (that we will call "regular saccades" throughout this work) are movements of the eyes which can be triggered voluntarily or involuntarily and observed by the naked eye. Their undisputed function is to bring a particular detail to a more central retinal location, for further visual processing. Regular saccades have a latency (i.e., a reaction time) of approximately 200 ms, they do not last longer than 100 ms and they have a peak velocity that can reach up to 800°/s, according to their amplitude.

Microsaccades are small-sized saccades that are produced involuntarily when attempting to fixate on an object. They occur in healthy individuals with a typical rate of 1-2 Hz (Alexander et al., 2018). The amplitude of genuine microsaccades, especially the upper limit, is still a matter of debate in the literature. Indeed, some have argued that microsaccades are any saccades produced "involuntarily while the subject is attempting to fixate" (Martinez-Conde et al., 2006), whereas others have used an upper threshold of 0.5° (Poletti and Rucci, 2016) or 1° (Martinez-Conde et al., 2009). There is no consensus regarding this question, to date. Different roles for microsaccades have been postulated and constitute, again, a long-lasting debate in the literature of eye movements. The proposed roles include *i*) prevention of eccentric image fading (Ditchburn et al., 1959; Martinez-Conde et al., 2006), *ii*) relocation of gaze (Ko et al., 2010; Poletti, 2010; Cornsweet, 1956), and *iii*) no useful purpose to vision at all (Kowler and Steinman, 1980; Collewijn and Kowler, 2008). The maintenance of visibility by counteracting eccentric image fading, a phenomenon called Troxel fading, is thought to be due to neural adaptation when the image is too stable. Under such circumstances, the core function of microsaccades would be to

"refresh" the image by bringing it in and out of peripheral receptive fields to restore visibility (Martinez-Conde et al., 2006). However, the fact that any retinal image slip experienced during more natural viewing conditions (i.e., due to slow drift, blink, head or stimulus movement) can restore visibility, has lead many authors to doubt this function (Collewijn and Kowler, 2008; Poletti, 2010). Other teams have argued that microsaccades, just like large-sized saccades, are useful to relocate the line of sight to potentiate the perception of fine spatial details (Ko et al., 2010; Rucci and Victor, 2015) or to correct fixation error. The hypothesis according to which microsaccades correct for fixation error induced by drift (Cornsweet, 1956) or blinks (Costela et al., 2014) is however tainted by other evidence showing that drift itself can also correct for fixation errors (Steinman et al., 1973). It is now recognized that both drift and microsaccades introduce and correct for fixation errors (Engbert and Kliegl, 2004; Rolfs, 2009).

Saccadic intrusions are small involuntary saccades, although larger than microsaccades on average, that interrupt steady fixations (Leigh and Zee, 2015). Those movements are observed in healthy subjects but they are more frequent and larger in size in neurological disease such as progressive supranuclear palsy (Otero-Millan et al., 2011b) or Alzheimer's disease (Leigh and Zee, 2015). Different types of saccadic intrusions can be distinguished, based on their morphology. The most common type of saccadic intrusions, square-wave jerk, corresponds to a horizontal saccade, away from fixation, that is followed by a corrective saccade of the same amplitude and opposite direction, with an inter-saccadic interval of 200 to 400 ms (Abadi et al., 2003; Abadi and Gowen, 2004). The typical amplitude of a square-wave jerk is 0.6° (range: $0.1 - 4^\circ$) with a mean rate of 18 events per minute (range: 1.0 – 54 Hz Abadi and Gowen, 2004).

Many research findings support the hypothesis that all saccadic movements (microsaccades, saccadic intrusions, saccades) lie on the same continuum (Otero-Millan and Troncoso, 2008; Otero-Millan et al., 2011a,b; Hafed et al., 2009; Otero-Millan et al., 2013), sharing a common neural generator (Otero-Millan and Troncoso, 2008; Hafed et al., 2009), common motor properties (Bahill et al., 1975) and being influenced, almost in the same manner, by endogeneous and exogeneous attention (Hafed and Clark, 2002; Gowen et al., 2007) or fatigue (Di Stasi et al., 2013, 2014; Abadi and Scallan, 2000). For instance, all saccadic eye movements, irrespective of their size lie on the main sequence: they share a common motor property that refers to the relationship between the peak velocity, amplitude and duration of the saccade (Bahill et al., 1975). The relationship between these variables are generally used to detect abnormal saccades or nonsaccadic eye movements. Although microsaccades and square-wave jerks have been initially described as two separate events (and in two separated populations, healthy and pathological individuals, respectively), some evidence argues that they could be the same oculomotor event, but with different names (Gowen et al., 2007). The link between the two is thought to be amplitude-related as large microsaccades are more prone to be followed by a corrective microsaccade in opposite direction, thus forming a square-wave jerk (Otero-Millan et al., 2011a, 2013; Hafed and Clark, 2002).

3.2 The aging eye movement control

3.2.1 Ocular fixation

Very few studies have examined age-related consequences on ocular fixation stability. Furthermore, these studies provide inconsistent results. Some studies found no age-related difference in ocular fixation (Kosnik et al., 1986, 1987; Crossland et al., 2008), whereas others reported larger fixation areas in older adults as compared to young subjects (Cutini et al., 2014; Agathos et al., 2015; Morales et al., 2016).

Part of these discrepancies can be linked to the small sample size used in several studies (Kosnik et al., 1986, 1987; Crossland et al., 2008), which can provide misleading results. Other extrinsic factors, known to influence fixation stability, such as the properties of the fixation target used, the degree of immobilization of the head, measuring instrument and methodology of quantification used (Castet and Crossland, 2012; Dunbar et al., 2010; Snodderly and Kurtz, 1985; Steinman et al., 1982; Thaler et al., 2013; Crossland and Rubin, 2002), can also explain those inconsistencies. This point will be further developed in Sec. 7.1.

3.2.2 Saccadic movements

The effects of aging on regular saccade generation and inhibition have been well characterized. Overall, it has been consensually found that automatic processes (saccade generation) are less impacted by age than voluntary ones (saccade inhibition; Peltsch et al., 2011; Fischer et al., 1997). Two well-known tasks are generally used in this domain: the pro-saccade and the anti-saccade task. The pro-saccade task evaluates the properties of saccades triggered exogeneously in reaction to a visual target appearing in the visual field. It is considered to evaluate more automatic processes of the saccadic system. On the other hand, the anti-saccade task requires the subject to inhibit the saccade and it assesses a more voluntary and cognitive aspect of the saccadic system (Munoz and Everling, 2004). Saccade inhibition (as assessed by the anti-saccade task) is more related to frontal integrity, whereas reflexive saccade generation (visually-guided as in the pro-saccade task) is more related to the parietal and occipital cortexes (Munoz and Everling, 2004; Pierrot-Deseilligny et al., 1991). In anti-saccade tasks, older adults are impaired in inhibiting an unwanted saccade (Peltsch et al., 2011; Abel and Douglas, 2007). The properties of pro-saccades are also impacted by age, although to a less extent, as older adults produce saccades with a reduced temporal and spatial precision (reduced saccadic latency and accuracy; Peltsch et al., 2011; Irving et al., 2006). The effect of aging on saccade peak velocity is however still debated with some studies suggesting no differences (Huaman and Sharpe, 1993; Munoz et al., 1998; Shafiq-Antonacci et al., 1999) or a decrease in peak velocity, this effect being maybe larger for saccades exceeding 20° (Moschner and Baloh, 1994; Abel et al., 1983).

There is also much less consistency as to whether or not age influences the properties of microsaccades and saccadic intrusions. Indeed, to our knowledge, only two studies have evaluated

microsaccades in aging. Port et al. (2015) found a small increase in microsaccade frequency in older adults, during a visual search task. However, this study included only a sample size of $n=7$ subjects aged between 60 and 75 years old. In a larger cohort of subjects ($n=66$, among which $n=22$ subjects were aged between 56 and 77 years old), Gao et al. (2018) found no influence of aging on either microsaccade frequency, amplitude or peak velocity (with a slight increase of peak velocity in older adults that did not survive the correction for multiple comparisons, though). These two studies did not assess the occurrence of square-wave jerks. Four different studies have provided contradictory evidence as well, regarding the occurrence of saccadic intrusions in aging. Some studies found a significant age effect on saccadic intrusion frequency (McGivern and Gibson, 2006; Herishanu and Sharpe, 1981), whereas others did not (Shallo-Hoffmann et al., 1990; Abadi and Gowen, 2004). The age effect on saccadic intrusion amplitude is also inconsistent, with some evidence arguing in favour of an impact of aging (Abadi and Gowen, 2004), whereas others do not (Shallo-Hoffmann et al., 1990; McGivern and Gibson, 2006).

3.3 Objectives

The **third objective of this work is to characterize the aging effect on eye movement control** (i.e., fixation stability, microsaccades and square-wave jerks) as it has been surprisingly poorly and inconsistently studied. We will also study the age effect on regular saccade generation: if most aspects of saccade generation and inhibition have been fully characterized, the influence of aging on peak velocity is still inconclusive. Given that *i*) oculomotor control is a key component for many daily activities (Kowler, 2011) and that *ii*) eye movements are often used to comprehend higher-order cognitive or age-related pathological processes (Noiret et al., 2016; Martinez-Conde, 2006), we think that this characterization, although factual, will feed many domains of the aging research.

One complication needs to be underlined, however. The detection of small saccadic movements in older adults is complicated by the presence of miosis (a constriction of the pupil; Loewenfeld, 1979) and ptosis (a drop of the upper eyelid; Salvi et al., 2006; Damasceno et al., 2015) in older adults, that can increase the level of noise in the eye movement signal recorded by video-based eye tracking systems. Because most of the microsaccade detection methods are based on velocity thresholds, the presence of a high noise regime critically interferes with microsaccade detection by increasing the frequency of false positives. Video-based eye trackers, however, are by far the most used in human studies (Irving et al., 2006; Port et al., 2015; Holmqvist et al., 2011) as they do not require subjects to wear lenses, which is an important practical constraint in aging research. So, one incidental objective of the project has been to solve the problem of detecting small saccades from noisy video-based eye tracking recordings.

The **fourth objective of this work is to characterize oculomotor control in optic flow conditions**. Passive viewing of a unidirectional flow field is known to elicit an optokinetic

reflex (OKR) with eye movements in the slow phase following the direction of the local stimulus motion (originating from the foveal and parafoveal regions; Lappe et al., 1998), whereas the fast phase saccades replace the eye, after the slow phase, in the direction opposite to the flow (Lappe and Hoffmann, 2000). This pattern of eye movements is much less stereotyped when experiencing an unstructured radial optic flow mimicking a forward movement of the observer, where saccades are evenly distributed (Lappe et al., 1999). Furthermore, when a visual anchor is available in a scene (e.g., when a person fixates on a target while walking), the OKR is almost suppressed, despite residual eye movements (Williams et al., 2006; Wyatt et al., 1995). Under such circumstances, a "micro-OKR" can nevertheless be observed, with microsaccade direction biased in the opposite direction to the visual motion, and slow drift in the direction of the motion (Laubrock et al., 2008; Piras et al., 2016). Again, this directional bias has been shown for lateral motion of the visual scene (for 2D Laubrock et al., 2008 and 3D patterns Piras et al., 2016). It remains to be tested, however, whether microsaccades are biased in direction opposite to the flow (i.e., inward) under a radial flow condition where the direction of travel and direction of gaze coincide.

GAZE DYNAMICS DURING SPATIAL NAVIGATION

This chapter reviews the existing studies that recorded eye movements in human navigation tasks. The goal is to uncover those factors that determine spatio-temporal gaze patterns during spatial behavior. Specifically, the following questions have to be addressed: Which cues are looked at by a subject during navigational decision-making? Where are these behaviourally-relevant cues located in the 3D space? Is it possible to identify differences in the pattern of eye movements that are associated with inter-individual differences in spatial behavior? The aim of this review is to set the stage for our project, which aims at investigating the role of eye movements in spatial navigation in the context of aging. To the best of our knowledge, previous research accounts on this topic (i.e., lying at the intersection between spatial cognition, eye movements, and aging) are missing. Furthermore, available evidence focuses on landmark extraction, whereas how geometric information is extracted by eye movements for navigation purposes has received, to our knowledge, no attention.

Stemming from this state-of-the-art, the goals this doctoral work are: *i)* to elucidate how the active process of extracting spatial information, and more specifically geometric cues, is mediated by spatio-temporal gaze dynamics in ecological environments; *ii)* to characterize how aging shapes eye movement statistics during active visual sensing, resulting in age-related inter-individual navigation differences.

4.1 Gaze-mediated spatial cognition: what do we know?

4.1.1 Background

Although experimentally dissociable, the gaze position and the focus of attention are tightly linked in human vision (Carrasco, 2011). A shift in gaze location is always preceded by a shift of attention (Kowler et al., 1995; Peterson et al., 2004) and both rely on distinct but highly overlapping frontoparietal networks (Corbetta, 1998). This has led researchers to use eye movements as an overt proxy to study the dynamics of attention in different situations. While attention can be attracted by low-level visual features (such as, e.g., the visual salience of an image; Itti and Koch, 2000) in a bottom-up fashion, the main factor that influences gaze distribution under natural conditions is the behavioral demand of the ongoing task (Hayhoe and Ballard, 2005; Jovancevic-Misic and Hayhoe, 2009; Rothkopf et al., 2007). This top-down influence has been first described by Yarbus while tracking the eyes of subjects during image scanning (Yarbus, 1967) and later extended to more natural ecological behaviors with the advent of mobile eye-tracking and immersive virtual reality (Diaz et al., 2013a; Hayhoe and Ballard, 2005). Indeed, natural vision-based behaviors are associated with a temporal and spatial coupling of gaze with the task periods (Tatler et al., 2011; Hayhoe and Ballard, 2005). Fixations are directed to task-relevant objects, but not to distractors, with objects of interest being fixated "just-in-time", i.e., shortly (0.5 to 1 sec) before being involved in the ongoing action (Hayhoe et al., 2003). This tight coupling is furthermore consistent across individuals, according to the data showing a low inter-individual variability in gaze patterns during ecological navigation (Koehler et al., 2014).

Besides their role in steering locomotor trajectory (Patla and Vickers, 2003; Bernardin et al., 2012), the role of eye movements in spatial navigation is manifold: they are important for discretizing the visual flow of information in order to identify task-relevant spatial cues, for spatial localization of these cues, for self-orientation when the bearings are lost and, potentially, for the anchoring of the cognitive map. We have identified two lines of behavioral evidence indicating that task-relevant spatial cues (Sec. 4.1.2) and individual differences (Sec. 4.1.3) can be identified based on the subject's dynamic gaze pattern.

4.1.2 Identification of task-relevant spatial cues from gaze patterns

To date, the clearest evidence showing that gaze spatio-temporal patterns can identify which information is selected for further memory storage has been provided by Hamid et al. (2010). In their experiment, participants navigated in a complex maze composed of intersecting corridors in the presence of landmarks distributed uniformly inside the maze. Analysis of eye movements showed that participants spent more time looking at landmarks located at the intersections than those on the sides of corridors. Once the environment was accurately learned, subjects' spatial knowledge was tested by showing pictures with different views of the virtual environment. The

task was to identify corresponding locations on the map of the maze. There was a clear drop in performance when the landmarks that were most often fixated on during the learning phase were removed from the pictures. On the other hand, removing the least fixated landmarks had no effect on the performance. Coherently, participants following a route were shown to spend more time gazing at task-informative landmarks (i.e., uniquely associated with directional information) than at distractors (i.e., objects that were not informative to solve task Jin et al., 2004).

In addition to be determined by the properties of landmarks, the way we explore the environment also depends on the type of spatial task to be solved. In experiments testing route learning, de Condappa and Wiener (2014) showed that visual attention at decision points was biased towards the "route-congruent landmark", i.e., the landmark that coincides with the direction of turns relative to the route. Livingstone-Lee et al. (2011) analyzed gaze patterns associated with a beacon strategy (i.e., learning to navigate to a proximal landmark) and a place strategy (i.e., leaning to navigate to a position defined with respect to several distal landmarks). They found that attention was directed to the type of landmarks that was critical for a particular strategy, i.e., proximal and distal landmarks for a beacon and place strategy, respectively. Interestingly, they also observed that the orienting gaze component was present only at the very beginning of each trial (i.e., the first second).

4.1.3 Characterization of individual differences based on gaze patterns

We are not all equal when it comes to navigation: some individuals are better than others and multiple factors contribute to the inter-individual navigation differences (Wolbers and Hegarty, 2010). Hamilton et al. (2009) tried to identify gaze pattern components associated with successful and poor navigation. They analyzed gaze patterns of human subjects in a virtual MWM task with the objective to find oculomotor behavioral differences in good, relative to bad, navigators. Good navigators, i.e., those who execute a direct trajectory to the hidden platform, had a specific temporal organization of their gaze patterns: they spent the first part of the trial looking at distal landmarks and the remaining trial time looking at the pool and the arena wall. In contrast, bad navigators (as indicated by their lower navigation performance) spent very little time looking at distal landmarks. The interpretation of these results proposed by the authors is that distal landmarks in the MWM are used to determine a general direction to the goal in the initial phase of the trial, whereas distance to pool walls determines subsequent search behavior.

Regarding gender, it has been postulated that female subjects are more dependent on landmarks when navigating, whereas males can use different cues (including landmarks, the room geometry or Euclidian distances; Sandstrom et al., 1998; Saucier et al., 2002). For instance, removing the landmarks in spatial tasks had a critical effect on navigation in females only (Sandstrom et al., 1998; Andersen et al., 2012). Two studies tested whether these differences could be seen in the pattern of eye movements. The studies used different tasks (a MWM and a more complex maze composed of 8 arms) where distal landmarks could be used allocentrically to

solve the task. Note, however, that in both tasks, the geometry was isotropic and thus no effort was made to distinguish landmark or geometry-related gaze patterns. These studies provided somewhat contradictory results. In the MWM, male subjects were more efficient than females to navigate to the platform position (which may be an indicator better allocentric processes in males). However, females and males spent the same amount of time gazing at the "allocentric space", which the authors define as encompassing distal landmarks and the room unpolarized walls (Mueller et al., 2008). In the more complex maze, males and females selected allocentric and egocentric strategy in the same proportion, but the pattern of eye fixations was more clustered on landmarks in females (Andersen et al., 2012). Interestingly, females were slower to solve the task given that they spent more time exploring landmarks, likely indicating that the preference for landmarks was associated with different gaze patterns, which in turns affected navigation efficiency.

Regarding the age factor, surprisingly, we did not find any study that recorded gaze patterns of young and older participants during a navigation task.

4.2 Objectives

The experimental evidence cited above points out a potentially important role of eye movements in navigation. Yet, a low number of available human studies focused on active vision and gaze-mediated spatial exploration as crucial components of successful navigation. Methodological issues are likely to be a major impediment for conducting similar experiments in more ecological settings, since mobile eye-tracking relies on time-consuming analysis of eye movements and a precise experimental control over environmental variables in the real world is hard, if not impossible. A second drawback of these studies is that they all focused on landmark information only. Where present, boundaries of the experimental space were isotropic and they could not be used for self-orientation and navigation. In particular, to the best of our knowledge, no study has addressed the question of whether a specific oculomotor strategy is associated with geometric processing for navigation purposes.

In the light of these considerations, the **fifth objective of this work is to understand how spatial information, and more specifically geometric cues, are extracted through the adopted spatio-temporal gaze dynamics in ecological environments.** We hypothesize that perceiving depth and relative size of geometric surfaces is an important component of navigation, instrumental to the extraction of environmental layout information using active vision. Perceiving depth and size in a visual scene has been associated with several retinal and extra-retinal cues (e.g., perspective convergence, texture gradient, binocular disparity, accommodation, convergence; Goldstein, 2009). Additionally, estimating distances between objects was shown to be computed in reference to the ground surface (Bian and Braunstein, 2005; Bian et al., 2006). Therefore, one of the questions that we will address is to what extent the ground surface is of

particular importance during navigation tasks involving geometric processing.

The **sixth objective of this work is to characterize individual age-related navigation differences by analyzing eye movement statistics**. Other, less cognitively demanding natural behaviors, such as locomotion (Chandra et al., 2011; Chapman and Hollands, 2007; Di Fabio et al., 2005; Uiga et al., 2015; Yamada et al., 2012; Young and Hollands, 2010) and visual search (Becic et al., 2007; Beurskens and Bock, 2012; Scialfa et al., 1994) have previously been associated with suboptimal gaze strategies in aged subjects. We will thus test whether navigation differences in older adults (e.g., lower navigation efficiency in older adults, Rodgers et al., 2012; Head and Isom, 2010) are associated with or can be explained by maladaptive gaze dynamics.

Part II

EXPERIMENTAL CONTRIBUTIONS

METHODOLOGICAL CONTRIBUTIONS

This chapter presents the methodological approach set forth throughout the project. First, the chapter focuses on the experimental platform that allowed us to assess human spatial cognition in ecological conditions, i.e., the Streetlab "Artificial Street" platform. The first phase of this doctoral work contributed to *i*) setting of the realistic modular panels used to ensure visual immersion in the Artificial Street; *ii*) testing the synchronous recordings of biometric variables (i.e., body kinematics and eye movements); *iii*) complementing the Artificial Street scenarios with an immersive virtual reality headset to be used within the StreetLab.

The second part of this chapter describes the SilverSight cohort, i.e. the study population used to enroll all participants of the cross-sectional experiments carried out in the project. An important contribution of this work consisted in enriching the (already) large spectrum of measures performed to screen all participants of the cohort (e.g., visual, audio-vestibular, sensorimotor screening). In particular, the two following evaluations were conducted during this project across the entire study population: *i*) a neuropsychological and cognitive screening; *ii*) an oculomotor evaluation (which is presented in details in Chapter 7 as it gave rise to three original contributions). The rationale beneath such a multivariate screening of all participants is to control, as much as possible, for multiple co-factors at stake during spatial cognition, possibly entailing an unbiased interpretation of spatial behavioral data (e.g., with respect to inter-individual variability).

5.1 Ecological approach to study spatial cognition in humans

As highlighted in the Theoretical Framework part, the traditional ways to assess spatial cognition in humans by joystick/computer screen-based navigation tasks are not ecological enough to account for the complexity of spatial behavior, especially in older adults. Joystick-operated motion in such setups prevents the subject from using proprioceptive and vestibular cues for reorienting and navigating. This constitutes a problem since it has been shown that age-related differences depend on the availability of multi-sensory information, with greater navigation difficulties observed with larger sensory restrictions (Mahmood et al., 2009; Adamo et al., 2012; Harris and Wolbers, 2012). Moreover, a screen-based setup limits the extent of the visual field, potentially restricting the use of geometric cues for reorientation (Sturz et al., 2013) and perturbing active visual exploration as compared to natural conditions.

In order to run ecological-like spatial navigation experiments, we used the Streetlab™ platform, which allows real maze navigation to be tested under fully controlled conditions. This research platform is a reconstitution of a 9.2 x 4.7 m portion of a shopping street (Figs. 5.1A,B). Visual immersion is provided by realistic decorative elements, which are modular and could be reconfigured to meet the needs of our diverse experimental protocols. In order to improve visual immersion, we extended the existing set of decorative panels by building a new ensemble of homemade elements. The Streetlab also enables a 3D surround sound immersion through a set of speakers evenly distributed around the environment. Lighting is produced by a set of LED panels to provide a uniform illumination. Light is controllable in intensity and color temperature. The control of different environmental parameters (e.g., light intensity, color temperature, street sounds intensity) is done from the control room (Fig. 5.1C) and it allows standardized and reproducible experiments to be run. During spatial navigation protocols, the subject's behavior is monitored through a set of biometric sensors. Full body kinematics is recorded by an optical motion capture system (VICON®, Oxford Metrix) by means of 16 infrared T-Series (T160) cameras at a 120 Hz frame rate (Fig. 5.1D,E). The participant is equipped with a black neoprene suit with high IR reflective passive markers positioned on each body segment. Eye movements are recorded monocularly at 60 Hz by a Mocalab eye-tracker. Data from all sensors are synchronized and recorded in real time, allowing any kinematic recording to be replayed offline. A custom-made electronic/software synchronization device ensures the precise temporal alignment between the Vicon cameras and the eye-tracker. Data gathered during this project were pre-processed by means of a custom-made software which computes and visualizes both body movements and the gaze vector in the 3D model of the room we designed.

Complementary to the protocols that physically reproduced real-life scenarios, we also used the Streetlab platform to perform Virtual Reality (VR) experiments. Virtual environments were created using the Unity3D game engine (Unity Technologies) and they were displayed by using a mobile panoramic HTC VIVE headset equipped with a Tobii Pro VR binocular eye tracking system. The HTC VIVE display has a nominal field of view of $\sim 145^\circ$ diagonal through two 1080 x

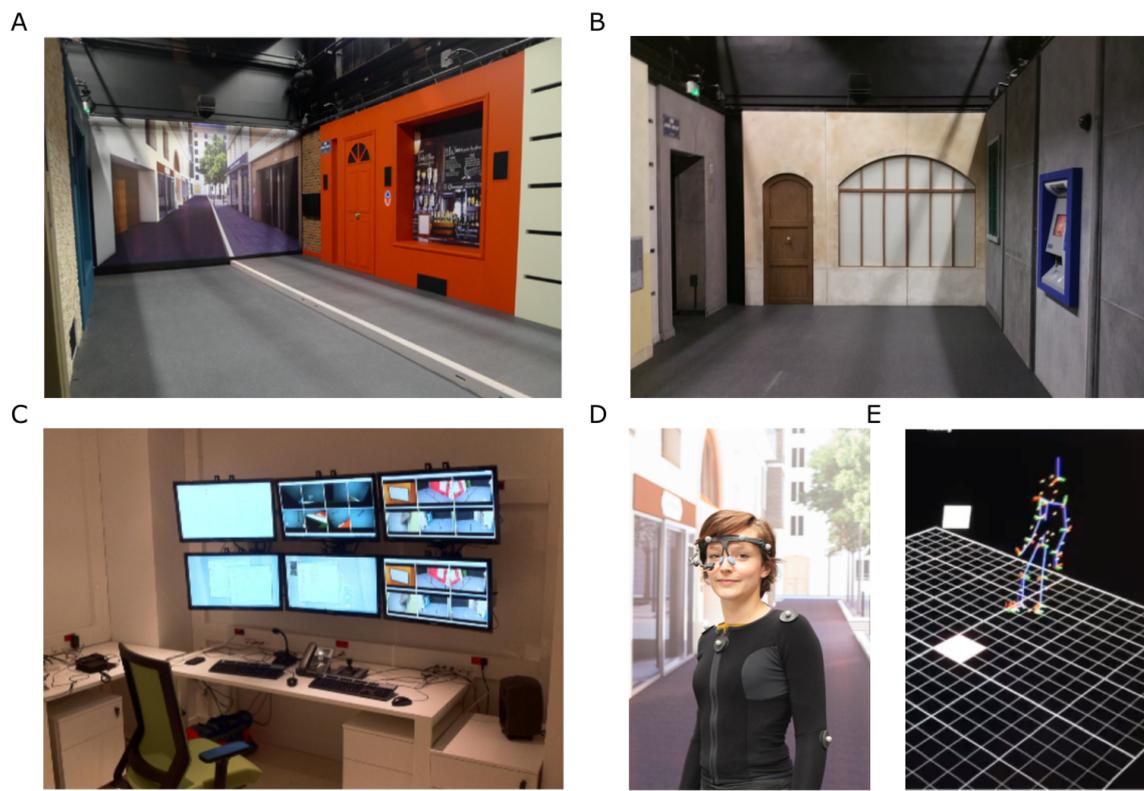


Figure 5.1 – The Streetlab research platform. (A, B) Urban settings obtained with modular panels representing doors, windows, outside walls, ect. (C) The control room for running and monitoring the whole experiment. (D) Black neoprene suit with IR reflective markers for the recording of the subject's body movements. The eye-tracking device (Mocaplab) used for recording eye movements. (E) The kinematics of the body is then reconstructed and it can be replayed and analyzed offline.

1200 pixels displays, updated at 90 Hz. The pixel density of the display was about 12 pixels/degree. The integrated Tobii eye-tracker records binocular eye movements at a rate of 120 Hz.

Besides enabling subjects to navigate in immersive environments, VR navigation paradigms provide a full control of the environmental dynamic features (e.g., appearance, size, shape etc.). During the experiments, participants were equipped with a VR capable backpack computer (VR One, MSI), which is wireless and allows the subject to move freely and explore the virtual environment while experiencing the full sets of idiothetic information (e.g., optic flow, vestibular signals, proprioception). The head position is tracked at 30 Hz by two laser emitters placed 9 m away from each other covering an experimental capture area of approximately 16 m². No symptoms of cyber dizziness were ever observed during the series of VR experiments across all participants (i.e., children, young adults, and older adults).



Figure 5.2 – Immersive virtual reality setup with position and orientation tracking combined with a Tobii eye-tracking device.

5.2 Multidimensional screening of the study population

Healthy aging is characterized by a high inter-individual variability (Lindenberger, 2014). Age-related neuronal loss in the prefrontal cortex and the hippocampus are particularly subject to differences from one individual to another across the lifespan Raz et al. (2005). Given that those areas are particularly involved in spatial cognition (Spiers and Maguire, 2006; Hartley et al., 2003), it implies that we will have to have large samples of participants performing our experiments in order to capture the whole heterogeneity of aging. In total, we performed 358 participant assessments in the different experiments presented in this manuscript.

All participants were enrolled in the SilverSight cohort. This study population was initially created in 2015 by our laboratory Aging in Vision and Action at the Institute of Vision, in collaboration with the Clinical Investigation Center, CIC, at the Quinze-Vingts National Ophthalmological Hospital, Paris. The SilverSight cohort counts at present ~350 participants older than 18 years of age and without any pathology or deficit that could interfere with the visual, cognitive, hearing and vestibular functions. The entire cohort population underwent (and follow-ups are regularly done) an ophthalmological screening (conducted by medical doctors at CIC), a functional visual screening (conducted by orthoptists), an otorhinolaryngological examination (conducted by ENT specialists), and a static/dynamic balance assessment (conducted by podiatrists and posture specialists). Importantly, an oculomotor evaluation and a deep cognitive assessment of all participants of the cohort was added to the above screening measures and it was carried out throughout this doctoral project (Fig. 5.3).

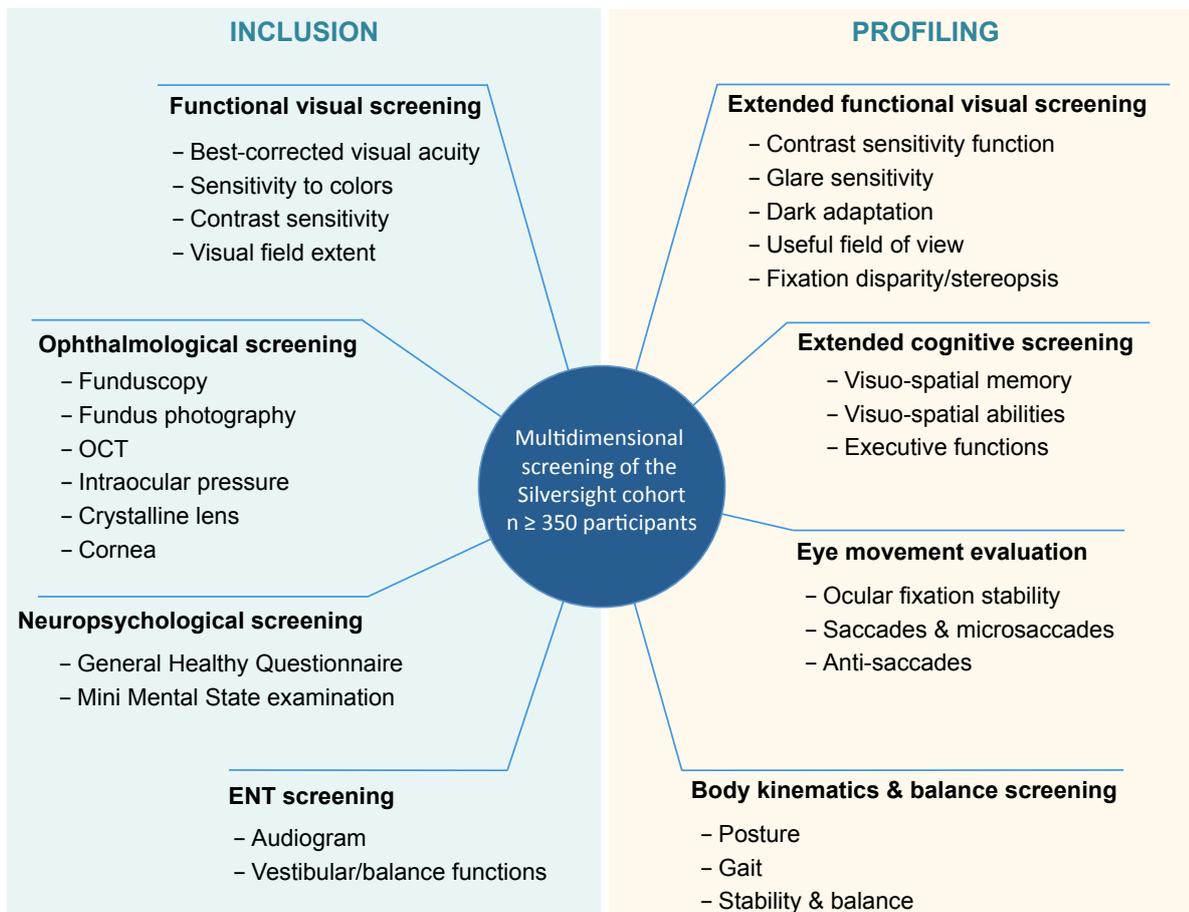


Figure 5.3 – Multidimensional screening of the SilverSight cohort. The evaluations on the left side are for inclusion purposes, i.e., to ensure the fulfillment of the inclusion/exclusion criteria. Once the participant meets the inclusion/exclusion criteria, he/she performs the post-inclusion profiling on the right side of the diagram.

This multidimensional screening has two main functions. First, to exclude potential pathological conditions from the pool of subjects used for the visuo-spatial experiments, and, second, to assess cross-dependencies between different functional losses. In order to be included in the cohort, the participants meet the following criteria: *i*) corrected visual acuity of at least 7/10, or 5/10, in participants with less, or respectively more, than 70 years of age; *ii*) a Mini-Mental State Examination, MMSE, score of 24 or higher; *iii*) a General Health questionnaire, GHQ, score of 4 or lower. Participants are excluded from the cohort if any active ophthalmologic pathology, any active otologic pathology, previous ear surgeries, balance disorder or reported neurological conditions. The fulfillment of these criteria was assessed during the inclusion sessions (Fig. 5.3, left), whereas a series of profiling sessions (Fig. 5.3, right) were conducted afterwards. The cognitive assessment conducted during this project is presented below, whereas the oculomotor evaluation is detailed in Chapter 7 because besides serving as a profiling measure it also produced original contributions.

5.3 Cognitive assessment of the SilverSight cohort

5.3.1 Rationale

The cognitive and psychological assessment of the SilverSight cohort had 3 purposes. First, these evaluations were useful in order to exclude any potential case of neurodegenerative disease and psychological disorders among our participants. Second, these multivariate measurements throughout the entire cohort provided a basis for epidemiological-like statistical analyses (e.g., to assess cross-dependencies between different functional losses). Third, this manifold contextual knowledge allowed the outcomes provided by experiments to be interpreted by controlling for co-factors (i.e., by taking into account individual specific characteristics). We thus selected the tests so as to cover a large range of cognitive functions known to decline with aging, with preference for tests assessing visual and spatial cognition (Table 5.1).

We present here a description and the results of each tests, obtained with the sample of participants that were enrolled in the SilverSight cohort. At this stage, the descriptive data analysis presented here are not meant to answer a particular research hypothesis, but they provide a multi-factorial picture of the cognitive state of our participants.

Functions	Test
Global cognitive performance	
Including attention, calculation, recall, language, and orientation	Minimal Mental State Examination (MMSe)
Visuospatial memory	
Short-term & working memory	Corsi block tapping test (CORSI)
Long-term figural memory	Figural Memory Test (FGT)
Visuospatial abilities	
Mental rotation	3D mental rotation test (3D)
Perspective taking	Perspective taking/Spatial orientation test (PERSP)
Executive functions	
Flexibility and speed of execution	Trail Making Test (TMT)
Inhibition	Go/no go test (INHIB)
Psychological disorder and scales	
Depression & anxiety	General Health Questionnaire (GHQ)
Fear of falling	Falling Efficacy Scale test (FES)

Table 5.1 – Cognitive and psychological tests used to screen participants of the SilverSight cohort.

5.3.2 Methods

Participants. A population of $n=120$ participants (range: 21-82 yrs, $\mu=48$ $\sigma=23$, 63 females and 56 males) underwent the entire cognitive and psychological assessment. Most of these subjects ($n=111$) were aged under 40 or over 65 years, as the strategy was to primarily focus on young and older subjects before middle-aged participants.

Material. The cognitive evaluations were carried out at the laboratory of Aging in Vision and Action at the Institute of Vision, Paris. Half of the computerized tests were internally developed in the form of a Matlab toolbox, whereas the other half were administrated by using the Vienna Test System ©Schuhfried, a commercial software for cognitive screening.

Protocol. The cognitive assessment was divided in two sessions performed on different days: an inclusion and a profiling session. The inclusion session lasted 10 min and involved 2 tests, the Mini Mental State examination (MMSe) and the General Health Questionnaire (GHQ). We used cut-off scores for these two tests to exclude participants with a high probability of presenting neurodegenerative or psychological deficits. The profiling session lasted 75 min and it was performed only for the enrolled participants. The profiling session involved a battery of 7 neuropsychological tests. All inclusion and profiling tests are listed in Table 5.1 and they are described hereafter.

The *Mini Mental State examination (MMSe)* provides a coarse assessment of multiple cognitive functions, including memory, attention and language (Folstein et al., 1975). A cut-off score of 24/30 was used for inclusion purposes.

The *General Health Questionnaire (GHQ)* is a screening tool for psychological disorders (Goldberg and Hillier, 1979). It is a self-report questionnaire that evaluates four symptomatological domains (depression, anxiety, social dysfunction, and hypochondria). A cut-off score of 4/28 was used for inclusion purposes.

The *Corsi block-tapping test (CORSI)* evaluates spatial short-term and working memories (Schuhfried, 2004). The subject is shown a sequence of blocks in specific locations. Then, the subject must immediately repeat the sequence in either forward (short-term) or backward (working memory) order. The test begins with a short sequence of blocks (e.g., sequence length=3). Thereafter, the length of the sequence increases gradually up to 9 blocks. The maximum sequence length that the subject is able to retrieve is called the span.

The *Figural Memory Test (FGT)* is a non-verbal test to assess both short- and long-term visual memory (Schuhfried, 2004). It involves a short-term free recall, a long-term free recall, and a forced-choice recognition of previously learned figures. First, 5 learning and reproduction runs occur involving 9 figures. The subject is asked to reproduce each figure immediately after presentation. Second, after a brief delay (5 min), the subject is required to freely reproduce the learned figures. Finally, after an extended delay (20 min), the test requires a free reproduction of all figures, followed by a forced-choice recognition task.

The *Mental rotation test (3D)* assesses the capability of performing mental rotation of 3D



Example:
 Imagine you are standing at the **flower** and facing the **tree**.
 Point to the **cat**.

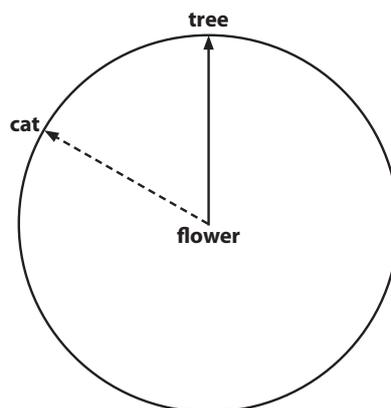


Figure 5.4 – Practice item of the Perspective taking / Spatial orientation test. The subject must draw an arrow from the center to indicate the egocentric direction of a third object (e.g., dashed arrow pointing to the cat).

objects (Schuhfried, 2004). Each item of the test consists of a picture with a number of building blocks of the same shape and size that are placed together to form a structure. The subject must imagine how the resultant object would appear from a different point of view (4 alternative answers are presented to the subject). The entire 3D test includes 30 different items. The number of correctly answered items provides the measure of spatial ability.

The *Perspective taking / Spatial orientation test (PERSP)* was proposed by Hegarty and Waller (2004). The subject is asked to imagine different perspectives or orientations in a given spatial task. A picture with a configuration of 7 objects is presented (Fig. 5.4, top), and the subject is asked to imagine being at the position of one object in the array (e.g., the flower) and facing another object (e.g., the tree). A circle is shown with the first object at the center and the second object at the top (Fig. 5.4, bottom). The subject's heading is shown as an arrow pointing vertically

up. The subject must draw an arrow from the center to indicate the egocentric direction of a third object (e.g., dashed arrow pointing to the cat). The entire test consists of 12 items that sample different perspectives. The score for each item is computed as the absolute directional error (in degrees), i.e., the deviation between the subject's response and the correct egocentric direction of the target object. The total score is the average absolute error across all items. We translated this test into french, as the original version by Hegarty & Waller is in english.

The *Trail Making Test (TMT)* assesses processing speed (TMT A) and mental flexibility (TMT B) (Schuhfried, 2004). The subject has to follow a sequence of letters (A-B-C, TMT A) or alternate between sequences of letters and numbers (1-A-2-B, TMT B). The index of mental flexibility is obtained by calculating the ratio between processing times of part A and B.

The *Go/no go (INHIB)* task evaluates the ability to suppress unwanted reactions (e.g., response inhibition), which is relevant to flexible and appropriate behavior (Schuhfried, 2004). The subject is shown a series of circles and triangles that are presented one by one on the screen for 200 ms with an inter-stimulus interval of 1 second. Triangles occur frequently and the subject must respond to them by pressing a button, which builds up a dominant response tendency. Circles appear rarely and they require no response (i.e., inhibition is required). The sensitivity index (d') is calculated as $d' = Z(\text{hit rate}) - Z(\text{false alarm rate})$.

The *Falling Efficacy Scale International test (FES)* is a self-report questionnaire that assesses the level of concern about falls with respect to a range of active daily behaviors (Tinetti et al., 1990). This range of behaviors includes basic activities as, for instance, preparing a meal, getting in or out of a chair, walking up or down a slope, walking around in the neighborhood, or going out to a social event.

Data analysis. We identified outliers for each variable as any point that was more than three scaled median absolute deviations (MAD) away from the median. We present the distribution of the data with age considered as a continuous factor. However, the statistical analysis was performed with non-parametric Mann-Whitney test for independent samples, with participants under 40 and over 65 years old considered as "Young adults" and "Older adults", respectively. The alpha level for statistical significance was set at $p < 0.05$.

5.3.3 Results

The data of all cognitive tests gathered from all subjects, with age as a continuous factor, can be seen in Fig. 5.5. The scores of older adults were lower on the MMSe ($U = 1670, p < 0.001$; Fig. 5.6, MMSe) and higher on the fear of falling scale ($U = 1008.5, p < 0.001$; Fig. 5.6, FES). However, older adults' scores on the General Health Questionnaire were not different from the scores of young adults ($U = 1446, p = 0.25$; Fig. 5.6, GHQ). We found a significant effect of age on all cognitive functions measured. Specifically, older adults had lower performance on tests measuring short-term retention ($U = 3286, p < 0.0001$; Fig. 5.6, FGT), long-term retention of figures ($U = 3249.5, p < 0.0001$; Fig. 5.6, FGT), recognition of figures ($U = 3256.5, p < 0.0001$;

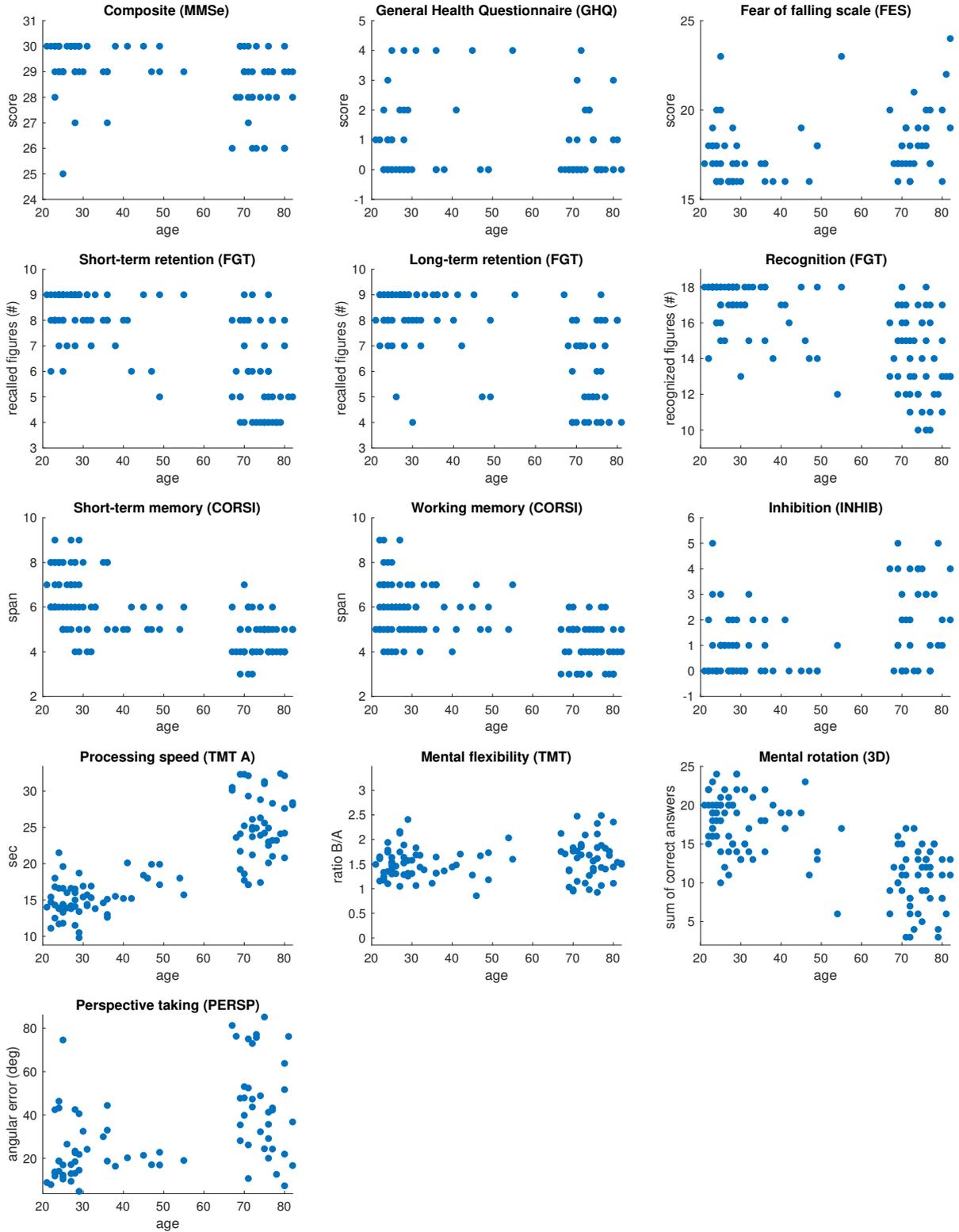


Figure 5.5 – Cognitive performance of the participants, with age as a continuous factor.

5.3. COGNITIVE ASSESSMENT OF THE SILVERSIGHT COHORT

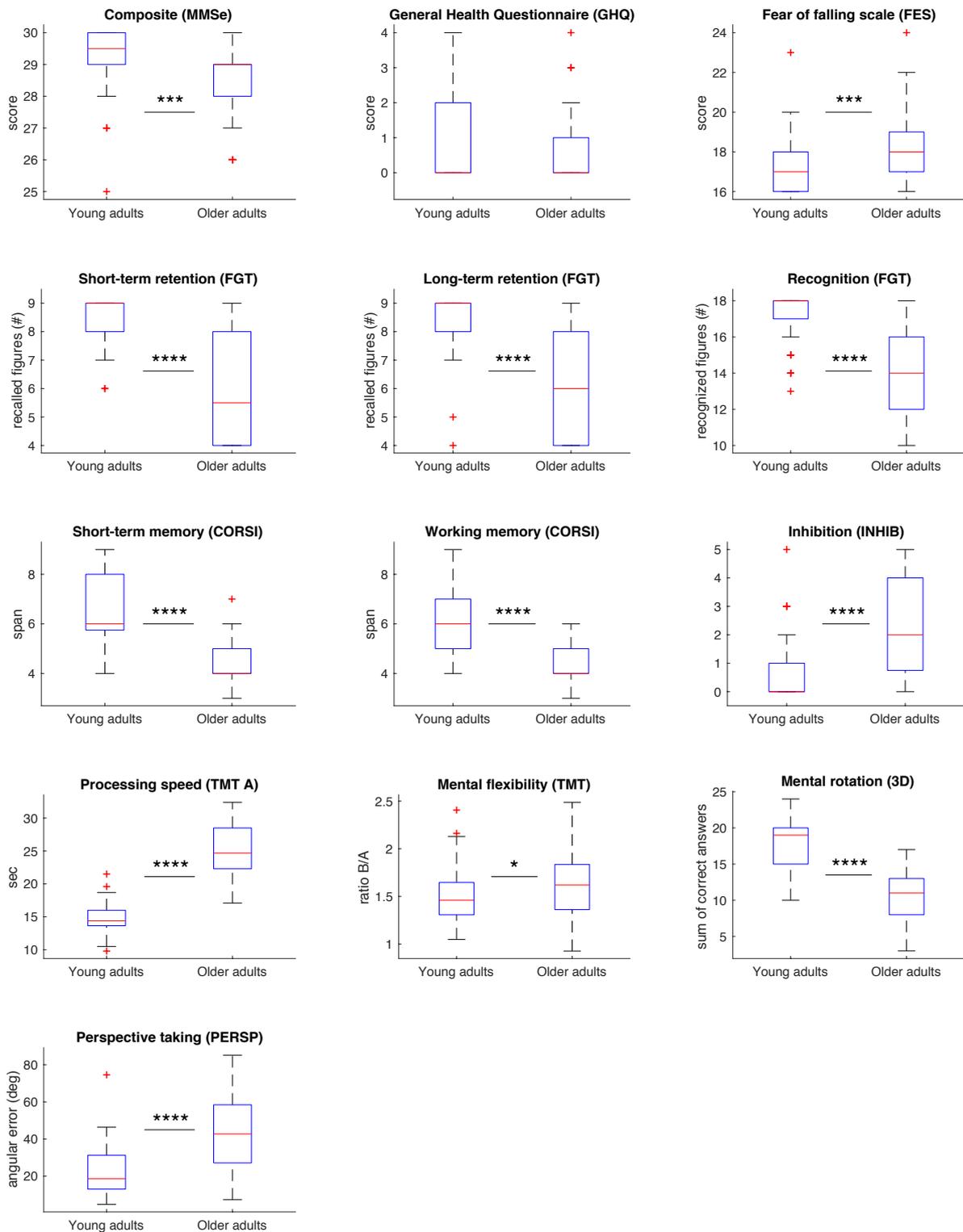


Figure 5.6 – Cognitive performance of the participants, with age as a categorical factor. Each boxplot indicates the median, the 25th and 75th percentiles and the outliers (+). Statistical comparisons correspond to non-parametric two-sample tests with p -values: **** $p < 0.0001$; *** $p < 0.001$; ** $p < 0.01$; * $p < 0.05$.

Fig. 5.6, FGT), short-term memory ($U = 4563.5, p < 0.0001$; Fig. 5.6, CORSI), working memory span ($U = 4489, p < 0.0001$; Fig. 5.6, CORSI), inhibition ($U = 2895, p < 0.001$; Fig. 5.6, INHIB), processing speed ($U = 1201, p < 0.0001$; Fig. 5.6, TMT A), mental flexibility ($U = 2067, p < 0.05$; Fig. 5.6, TMT), mental rotation ($U = 4733.5, p < 0.0001$; Fig. 5.6, 3D) and perspective taking capacity ($U = 927, p < 0.0001$; Fig. 5.6, PERSP).

5.3.4 Discussion

The observed significant age effect on the MMSe score is coherent with a decrease in the global cognitive performance that is expected with healthy aging (Amieva et al., 2005). It is nevertheless higher than the score generally observed in Alzheimer's disease (Amieva et al., 2005). The GHQ score was identical between the two age groups, indicating a low probability of depressive or anxiety symptomatology in our participants, regardless of their age. On the other hand, when compared to young adults, older adults were more concerned about the possibility of falling while performing daily-life activities, as evidenced by their FES score.

Coherent with numerous reports of an age-related decline in memory, attentional and executive functions (Craik and Salthouse, 2011; Craik et al., 1992; Old and Naveh-Benjamin, 2008; Zacks et al., 2000), we found that short- and long-term (FGT) memory as well as working memory (CORSI) were lower in older participants. Executive functions, like the inhibition of the prepotent response (INHIB) and mental flexibility (TMT), which are known to involve frontal lobes (Craik and Salthouse, 2011), i.e., brain areas particularly susceptible to age-related atrophy (Raz et al., 2005), were also negatively impacted by aging.

Older adults had lower scores when performing mental rotation of abstract objects (3D), coherent with previous evidence (Dollinger, 1995; Beni et al., 2006). Their perspective taking ability was also lower, as shown by greater angular errors when indicating directions from an imagined perspective (PERSP). This is in line with a previous study by Zancada-Menendez et al. (2016). Interestingly, this test has been shown to be a predictor of large-scale, real-world navigation ability (Allen et al., 1996; Kozhevnikov et al., 2006).

Ultimately, these data will be useful in order to search for cross-dependencies between cognitive, visual, ophthalmological, oculomotor and balance functions in aging. Moreover, they will help in the understanding of inter-individual navigation differences (Wolbers and Hegarty, 2010) by taking into account individual cognitive characteristics as co-factors.

CONTRIBUTIONS TO SPATIAL COGNITION

This chapter presents two major contributions of this doctoral project, which focus on the effect of healthy aging on spatial cognition and navigation. The first article *"Age-related preference for geometric spatial cues during real-world navigation"* (Sec. 6.1) is currently under review, 2nd round, by the journal *Nature Human Behaviour*. The supplementary information follows the article. The second part of the chapter (Sec. 6.2) presents a follow-up experiment that directly evaluated the impact of cue reliance on the use of egocentric and allocentric strategies across lifespan. The article about this second experiment is titled *"Modulation of spatial cue preference across lifespan: geometric cues enable children and older adults to successfully use allocentric navigation strategies"* and it is currently in preparation. Altogether, these results suggest that the impaired allocentric capability previously observed in older adults might actually be conditioned by the sensory cues present in the environment rather than a cognitive strategic deficit *per se*.

6.1 Spatial cues: landmark & geometry coding

6.1.1 Article 1: *Age-related preference for geometric spatial cues during real-world navigation*

The article reported below focuses on the relative influence of landmark versus geometric information during spatial navigation in young and older navigators. In order to determine cue reliance in our participants, we used an adapted version of the reorientation paradigm (Cheng, 1986; Newcombe and Ratliff, 2008) in which landmarks (visual features on the walls) and geometry (the rectangular shape of the environment) were put in conflict after the subjects had learned to navigate to a unmarked goal position.

Reorientation and goal-oriented navigation performance were tested in an ecological setup (i.e., the Streetlab, see Sec. 5.1), which was rich of visual cues (i.e., multiple and naturalistic landmarks). We could entirely control environmental variables such as light (both intensity and temperature) and 3D sound. We recorded full body motion and eye movements while the participants navigated in space, and we focused on the oculomotor strategies underpinning the extraction of geometric and landmarks cues. Finally, we tested whether the age-related navigation differences were associated with or even attributed to maladaptive gaze dynamics in older adults.

Age-related preference for geometric spatial cues during real-world navigation

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Abstract

Healthy aging is associated with changes in the way people navigate in space. These changes have been previously characterized in terms of age-related deficits in the use of allocentric strategies. However, given that navigation strategies are conditioned by the sensory cues present in the environment, an alternative hypothesis is that navigation difficulties in aged people are associated with spatial cue processing rather than with strategic choices. Here, we tested this hypothesis by studying how geometry and landmark cues control spatial orientation and navigation in young and older adults in a real, ecological environment. We showed that older adults reoriented preferentially according to geometric cues, thus neglecting landmark information, whereas young adults preferentially used landmarks. Recordings of both body and gaze dynamics, as subjects reoriented and navigated in the real open-field maze, revealed specific behavioral patterns associated with either landmark or geometry preference. In particular, the geometry-based spatial coding adopted by older adults manifested itself in the spatiotemporal signatures of oculomotor fixations. Moreover, during reorientation, gaze dynamics were predictive of the spatial cue preference mediating subsequent navigation behavior. Also, the longer reorientation time observed in older subjects was due to the need for a repetitive sampling of visual information, which reflected an unbalanced exploration-exploitation tradeoff in their visual scanning policy. Overall, these results suggest an inverted U-profile of spatial cue processing across lifespan, extending previous findings on geometric cue preference in children. Because navigation paradigms have so far extensively used landmarks to assess human spatial behaviour, these results challenge the traditional view of a specific deficit for allocentric strategies in aging.

Aging is associated with a specific decline of spatial navigation abilities, essential for independence, safety and quality of life^{1,2}. The highly dynamic and multisensory nature of spatial navigation makes it one of the cognitive faculties most severely affected by healthy or pathological aging³⁻⁵. Compensatory adaptations to age-related motor⁶⁻⁸, perceptual⁹⁻¹¹ and cognitive^{12,13} deficits affect the way sensory cues are processed and used to guide goal-directed actions. Age-related changes in spatial navigation have usually been described in terms of a bias towards egocentric strategies (i.e., based on the encoding of subject-to-object spatial relations) to the detriment of allocentric strategies (based on object-to-object relations, independently from the position and viewpoint of the subject)^{1,14-16}. However, the choice of a navigation strategy depends on the availability of sensory cues¹⁷⁻²⁰, and hence difficulties in the processing of different types of spatial cues can determine or bias the subsequent strategic choice.

During navigation in an urban environment, for example, we are constantly faced with street-like layouts rich with visual cues. If disoriented, e.g., upon the exit from an underground subway station, we actively search for visual cues to reorient in space and plan the direction to a desired location. Two different types of visual cues can be used for self-orienting and navigation planning²¹⁻²⁴: while *geometric cues* describe the relationships between surrounding large-scale surfaces (e.g., building walls, the street line, leafy border of a nearby park), landmark cues refer to the featural contents of those surfaces (e.g., shop signs, street signs, colour of the leaves). Children and young adults differentially use these spatial cue types²⁵. In particular, children have been shown to preferentially encode geometric over landmark cues, based on the evidence that the shape of an enclosure dominates their sense of orientation, at the expense of featural wall contents (e.g., wall colour)²⁵. Young adults, on the other hand, are able to use and efficiently combine both types of information²⁶, but they rely preferentially on landmarks when the two types of information are in conflict¹⁹.

While the developmental effects on reorientation and visual cue processing have been relatively well characterized²⁷, little is known about the influence of advanced age on these visuo-cognitive functions and the available evidence remains controversial. A screen-based virtual reality (VR) study²⁸ showed that older adults experience difficulties when reorienting with non-geometric cues. Conversely, another VR study²⁹ found that older subjects were impaired in learning locations relative to environmental boundaries, i.e. a geometric cue. In addition, experimental evidence indicates that the use of screen-based VR to study spatial navigation in older subjects can be problematic. Joystick-

operated motion in such a setup prevents the subject to use proprioceptive and vestibular cues for reorientating and navigating. This constitutes a problem since it has been consistently shown that age-related differences depend on the availability of multi-sensory information, with greater navigation difficulties observed with larger sensory restrictions^{11,30,31}. Moreover, a screen-based setup limits the extent of the visual field, potentially restricting the use of geometric cues for reorientation³² and perturbing active visual exploration as compared to natural conditions.

We therefore sought to test reorientation and navigation performances in young and older adults in a real street-like environment, when geometric and landmark information are in conflict. To gain a deeper insight into behavioural decisions and provide a detailed characterization of information encoding strategies mediating these decisions, we recorded body and eye movements of the navigating subjects during both spatial learning and in the conflict situation. In primates, including humans, spatial representation is tightly associated with visual coding mechanisms and it involves visually-responsive areas of the brain to a much greater extent than in rodents³³⁻³⁷. Unlike rodents, primates benefit from a foveated, high-resolution visual system that can provide a great deal of information about environmental cues based solely on visual exploration of the surrounding scene. Therefore, the analysis of oculomotor behaviour can reveal which spatial cues are employed, in the same way as the analysis of rodent exploratory behaviour can tell us what learning strategy it may be using³⁸. In a virtual water maze study it was shown that good navigators preferentially focused on distal landmarks at the very beginning of the trial, a behavioural component that was not present in bad navigators³⁹. Surprisingly, no study has comparatively examined the link between navigation and gaze dynamics in young and older navigators. Determining oculomotor signatures of landmark- versus geometry-related spatial coding was one of the objectives of this study.

Methods

Participants. Twenty young (range: 19-37 yrs, $\mu=26.25$, $\sigma=4.97$, 11 females, 9 males) and 19 older adults (range: 61-79 yrs, $\mu=71.21$, $\sigma=4.35$, 10 females, 9 males) were included in this study. The participants were part of the SilverSight cohort population (~350 enrolled subjects) at the Vision Institute - Quinze-Vingts National Ophthalmology Centre, in Paris. All screening and experimental procedures were in accordance with the tenets of the Declaration of Helsinki and they were ethically approved by “CPP Ile de

France V” (ID_RCB 2015-A01094-45, n. CPP: 16122 MSB). All participants were voluntary and gave informed consent approval for inclusion based on following criteria: (a) corrected visual acuity of at least 7/10, or 5/10, in participants with less, or respectively more, than 70 years of age; (b) a Mini-Mental State Examination score of 24 or higher; (c) no physical inability in terms of locomoting without assistance, and (d) no neurological condition. The clinical and functional assessment of participants involved: ophthalmological screening (e.g., optical coherence tomography, fundus photography), functional visual screening (e.g., visual acuity, visual field extent, contrast sensitivity, attentional field of view), otorhinolaryngological examination (e.g., audiogram, vestibular function), cognitive-neuropsychological assessment (e.g., visuo-spatial memory, mental rotation, executive functions), oculomotor evaluation (e.g., ocular fixation, saccadic control), and a static/dynamic balance assessment. A series of questionnaires were also administered to evaluate the quality of vision with respect to mobility (e.g., fear of fall). The battery of visuo- cognitive tests is detailed in Supp. Table1.

Experimental setup. The experiment was performed in a real environment using the Streetlab platform at the Vision Institute (www.streetlab-vision.com). The environment was consisted of a rectangular enclosure (8,55m x 4,30m) with an aspect ratio of 1.99. Nineteen panels providing real world wall textures (varying width, 3m high) fully covered the walls of the enclosure (See Supp. Movie 1). The panels imitated street-like relief sceneries such as brick walls, doors and windows. The floor of the room was covered by a black linoleum surface. There were no obstacles within the environment. Light and sound conditions of the environment were fully controlled. A homogeneous illumination (195 lux) and street-like multi-source sounds were provided during the whole experiment in order to increase immersion in the environment. Speakers were evenly distributed in the room so as to not be used by subjects to self-localise.

Body kinematics was recorded by an optoelectronic motion capture system (10 infra-red cameras, model T160) at a sampling frequency of 120 Hz (VICON Motion Systems Inc., Oxford, UK). The cameras were positioned above the panels and were placed symmetrically to avoid spatial cueing. During the experiment, participants wore a tight black suit, equipped with 39 infrared reflective markers, following the Vicon Plug-In-Gait model. Movement of the right eye was recorded by a video-based eye-tracker (Mocaplab, Paris) at 60 Hz. The eye-tracker camera was mounted on light goggles that allowed the participant to wear his own glasses during the experiment as well.

Participants habitually wearing far-vision lenses were encouraged to keep their glasses on during the experiment.

A calibration procedure was done in order to compute the 3D gaze vector in the model of the environment. The calibration involved computing the centre of rotation of the eye relative to the four reflective markers positioned on the eye-tracker goggles. Correspondence between the eye position in the eye-tracker camera coordinates and the room coordinates was subsequently calculated using an ellipsoidal calibration grid composed of 25 markers. The grid was 145cm wide and 100 cm high and it was placed at eye level, approximately one meter away from the subject in order to cover the maximal range of eye orientations. Additionally, in order to correct for potential drift occurring over the course of the experiment, a two-point drift correction was performed before each trial.

Experimental protocol. The task required the subjects to navigate as direct as possible to an invisible goal in the open-field environment. The goal was located in the northwest quadrant of the room and is 80x80cm large (Fig. 1, dashed area “G”). At the beginning of the experiment, all subjects were naives about the environment and the goal position. Importantly, subjects were disoriented before each trial. This procedure required the subject to sit on a chair, with eyes closed, while the experimenter slowly rotated and moved the chair around the whole room. We controlled that this procedure was truly effective by asking the subject to point towards the starting location after each disorientation (Supp. Fig. 10). Once disoriented, subjects were positioned at one of four positions (Fig. 1, dashed areas 1-4) facing one of three orientations (arrows in Fig. 1A) in a pseudorandom manner. Upon the beginning of each trial, no experimenter was present in the environment. As soon as subjects entered the goal zone, a rewarding audio signal was released. Subjects were then instructed to close their eyes and the trial was over. After 8 trials of learning, the entire configuration of panels was monolithically rotated in order to put landmarks and geometric information in conflict: landmarks that were near the goal corner during the learning phase were positioned, after rotation, in the adjacent, geometrically different corner (Fig. 1B). Subjects were not informed of the rotation procedure. One probe trial and 4 post-probe trials were performed after rotation of the environment during which the rewarding area remained the same (“G” on Fig. 1B).

Behavioral and oculomotor analysis. We considered two distinct periods within a trial. The first part of the trial, called the *orientation period*, began when subjects opened their eyes and lasted until subjects started to navigate (i.e., when they exited a virtual radius of 40 cm from the starting position). The second part of the trial, called the *navigation period*, lasted until subjects entered the goal area. This differentiation was inspired by the Hamilton study³⁹ in order to identify differential oculomotor behaviour during the first part of the trial (when the subject is supposed to reorient in space) and the subsequent goal searching behaviour.

Cue preference. Participants' cue preference (landmark or geometry) was defined based on the navigation trajectory employed during the first probe trial after the rotation of the landmark configuration. If a subject first entered the goal "G" (Fig. 1B) or its symmetrical area "S", he/she was assigned to the geometry group. If a subject first entered the landmark area "L", he/she was assigned to the landmark group. None of the subjects went to the error area "E". The gender effect was controlled as females have sometimes been shown to navigate by preferentially using the landmarks in the environment⁷¹.

Navigation variables. Trajectories in the room were calculated by tracing over time the centre of mass of the four markers positioned on the eye-tracker goggles. Any implausible motion (i.e., recording frame with a motion larger than 6 meters/seconds) was discarded. Based on trajectories, we estimated the travelled distance (meters) and walking speed (meters/seconds). The optimality of the trajectory was assessed by the heading deviation (mean angular error of a subject's trajectory with respect to the goal location, in degrees) and path tortuosity (ratio between the length of the trajectory and the shortest distance from starting position to goal location). Last, we estimated the escape latency to reach the goal (i.e., including both the orientation and navigation periods, in seconds) as well as the duration of the orientation period (in seconds). In order to better describe trajectories during the probe trial, we calculated the vector field representation (averaged across spatial areas of 20 cm²) and the mean trajectory (calculated across 10 time steps) during navigation. Rotational errors were taken as corresponding to goal searching in the corner "S" diagonally opposite to the correct corner "G", which shares the same geometric properties. They were considered as an evidence for geometric processing of the environment, as defined by Cheng (1986)²². During the probe trial, the heading deviation of the mean trajectory was estimated

relative to the area “S” for subjects who committed a rotational error and relative to the area “G” for the remaining subjects.

Oculomotor analysis. Oculomotor data were obtained by computing the gaze vector and its intersection within the 3D model of the environment (Supp. Movie 1). In particular, we computed ocular fixations, during which visual information was actively acquired. In order to detect fixations, we calculated the gaze dispersion vector in the environment coordinates, which corresponded to the distance between two successive data points. A continuous period of time during which gaze dispersion was below twice the interquartile range from the median of the distribution was considered as a candidate fixation. Among those candidates fixations, fixations with duration shorter than 100 ms were discarded. We estimated the general properties of fixations, such as their frequency (in Hz), duration (in seconds) and inter-fixations distance (in degrees). Moreover, in order to best describe how the participants explored the environment, we classified fixations in two categories. “Explorative” fixations were defined as fixations made in order to scan the environment. Thus, a fixation was considered as explorative when it was directed to a panel that had not been previously fixated during the course of the same trial. “Exploitative” fixations were fixations that targeted, either successively or subsequently, an already fixated panel during the course of the same trial. These data were estimated over a time window of 1 second sliding over 15 and 35 time steps for the orientation and navigation period, respectively. The spatio-temporal characteristics of fixations were described by the fixation time (normalized by the period length) over 5 and 10 time bins during the orientation and navigation period, respectively. When only the spatial description of fixations was needed, we calculated heatmaps where individual fixation contribution was Gaussian-shaped ($\sigma=20$ cm, maximal distance threshold = $3*\sigma$) and all contributions summed spatially over a 3D grid (cell size = 10 cm). The normalization of heatmaps was computed conjointly for the two groups of subjects and separately for the panels and the floor.

Postural analysis. Postural control analyses were carried out on a subset of subjects ($n=28$, 14 young and 14 old adults) in order to examine if any differences in posture could have constrained the gaze behavior of older participants. Head and trunk orientations were calculated during sequences of straight ahead walking and while standing during the orientation period. Each segment was considered as a rigid body with its own Cartesian coordinate system, the origin being the centroid of the four eye-tracker markers for the head, and the centroid of the two shoulders plus the 7th vertebra (C7)

marker for the trunk. Angle values were calculated in each plane based on Euler's rotation theorem, applied to the coordinate system for each segment. To obtain comparable behavior across participants and trials, we segmented the trajectories of each trial according to the trunk rotation in yaw in order to extract sequences of straight ahead walking, during the navigation period. Trunk orientation in yaw was examined within each step duration for the navigation period. We classified the trajectory during each step as straight ahead walking if the difference between the heading direction and trunk orientation in yaw was less than 15° . Mean orientation in pitch of the head as well as the relative head to trunk pitch angle were analyzed to examine whether an age-related lowering of the head in old adults may bias to direct their gaze toward the floor and potentially lead to a preferential use of geometry cues. Head-to-trunk oscillations in yaw were also analyzed, i.e. the amplitude of yaw rotations about a mean value, as well as the head-to-trunk angular speed in yaw. These variables were chosen in order to examine potential differences in head mobility that could explain a differential exploratory gaze behavior. The head relative to trunk orientation was simply the difference in pitch angle between the two segments.

Data statistics and models. Statistical analyses were performed on data averaged over the learning phase (trials 1 to 8), probe trial (9th), and post-probe trials (trials 10-13) separately. Note that 3 subjects did not perform the 4 post-probe trials due to time limitations. Where applicable, data were preferentially analysed by two-way ANOVA (aging and cue preference), paired or two-sample t-test. Normality of the data was verified quantitatively by the Lilliefors normality test as well as by visual inspection of Q-Q plots. All raw data were transformed with a Box-Cox transformation to achieve normality and equalize variance⁷². When normality and homoscedasticity were dubious, we used non-parametric Wilcoxon signed-rank test for paired samples and the Mann-Whitney test in case of independent samples. Alpha level for statistical significance was set at $P < 0.05$. For the postural characteristics analysis, the Matlab Circular Statistics Toolbox was used to obtain mean, median and standard deviation values across and within trial sequences.

Generalized Linear Model. In order to predict subjects' cue preference from measured oculomotor data we trained a classifier based on generalized linear regression model (binary logistic regression) with the fixation altitude as the explanatory variable and the cue preference as the binary response. The response variable was selected according to the results showing that participants in the landmark group preferentially fixated wall

panels approximately at the eye level, whereas those in the geometry group looked more often at the floor. Fixation altitude was measured as the vertical component of the 3D fixation point in the room reference frame for a particular time bin. For each run of the classifier, subjects were randomly assigned to either training or validation set. Fixation altitudes across all trials from the subjects in the training set, together with the corresponding class labels (i.e., landmark or geometry), constituted the training database. The trained classifier was then used to predict, for each subject in the validation set, whether he or she belonged to the landmark or geometry group according to the mean score across all fixations from this subject. The classifier performance was assessed using two different sizes of the validation set, since a larger validation set provides a more reliable performance estimate but at the expense of a fewer training data. For the validation set consisting of 10 subjects, 1000 runs of the classifier were performed, and the proportion of correctly predicted cue preference was calculated as the performance measure. For the validation set consisting of 1 subject (leave-one-out), all possible combinations were tested and the number of correct predictions. The classification procedure described above was performed (i) with all subjects, including fixations across complete trials; (ii) separately in different age groups (young versus older subjects); (iii) across all subjects, but separately for orientation and navigation periods of a trial. For the latter two cases only leave-one-out cross-validation performance is reported.

Results

Data were collected from 39 participants (20 young and 19 older adults) included in this study. Subjects were clinically and functionally screened to ascertain that their visual, audio-vestibular, postural, oculomotor, and cognitive (in particular visuo-spatial memory) characteristics were in between or above the normal limits according to their age. Both whole body motion and gaze dynamics were recorded as the subjects searched and navigated to an unmarked goal in a real street-like environment (Fig. 1a; see Methods and Supp. Movie 1). During the first 8 trials, constituting the *learning phase*, all cues were fixed in the room, and subjects were instructed to navigate as fast as possible to the unmarked goal zone (“G” on Fig. 1b). At the beginning of each trial, subjects were disoriented (with eyes closed) and placed in one of four pseudo-random locations of the environment, each time with a different orientation. Then, subjects had to reorient (upon eyes opening), plan and initiate their goal-oriented behaviour. Reaching of the goal zone was signalled by a rewarding sound. Before the 9th, *probe trial*,

the whole array of wall panels was rotated, unknown to the subjects, so as to put landmark and geometric information in conflict about the goal location (Fig. 1c). If disoriented subjects relied exclusively on wall landmarks during learning (e.g., they remembered the fact that goal was located between the brown door, the green window, and the ATM machine), they were expected to go to the L corner first on the probe trial. In contrast, if subjects relied exclusively on geometric information (e.g., they recalled that the goal was located in the corner with a long wall on the right and a short wall on the left) they were expected to go to the actual goal location (G) or its geometrically equivalent location (S). While the assumption of an exclusive use of one type of cue is unlikely, we hypothesized that a preference towards one or the other type of cue would emerge during the probe trial. During 4 *post-probe trials*, the same wall panel configuration as in the probe trial was used and the experimental procedure was identical to that of the learning phase (see Methods).

We found that a majority of young adults reoriented and navigated to the goal based on the environmental landmarks during the probe trial (Fig. 2a). In contrast, a majority of older subjects reoriented and navigated according to the geometry of the environment, neglecting the rotation of the landmarks (Fig. 2a). The difference in strategy proportion across the two age groups was significant ($\chi^2=5.77$; $p < 0.02$), thus indicating a preference for geometric cues in the older adults. Indeed, they were 5 times as likely to orient themselves according to geometry than young adults (odd ratio: 5.14; 95% confidence interval: 1.30-20.36), without any significant gender effect ($\chi^2=1.43$; $p=0.23$, Supp. Fig. 1). Among the older subjects that relied on geometry, 75% went to the actual goal corner (G), while 25% committed a rotational error, that is, they went to the corner S diagonally symmetric to the goal (Fig. 1c). The existence of rotational errors confirms the reliance on geometric as opposed to featural cues, since the two corners are identical with respect to the surface geometry of the room, but not with respect to landmarks on the walls^{22,25}. Since the preference for geometric or landmark cues was not exclusive in the two age groups, we further characterized cue-dependent behaviours by separating all subjects according to their spatial cue preference (i.e., landmark or geometry) based on their behaviour during the probe trial. There was a clear separation between the two cue-preference groups in terms of trajectories employed during the probe trial (Fig. 2b), quantified by a statistically significant deviation of the mean group trajectory with respect to the goal location or its symmetric location ($F_{(1,35)}=46.66$; $p < 0.0001$, Fig. 2c). No

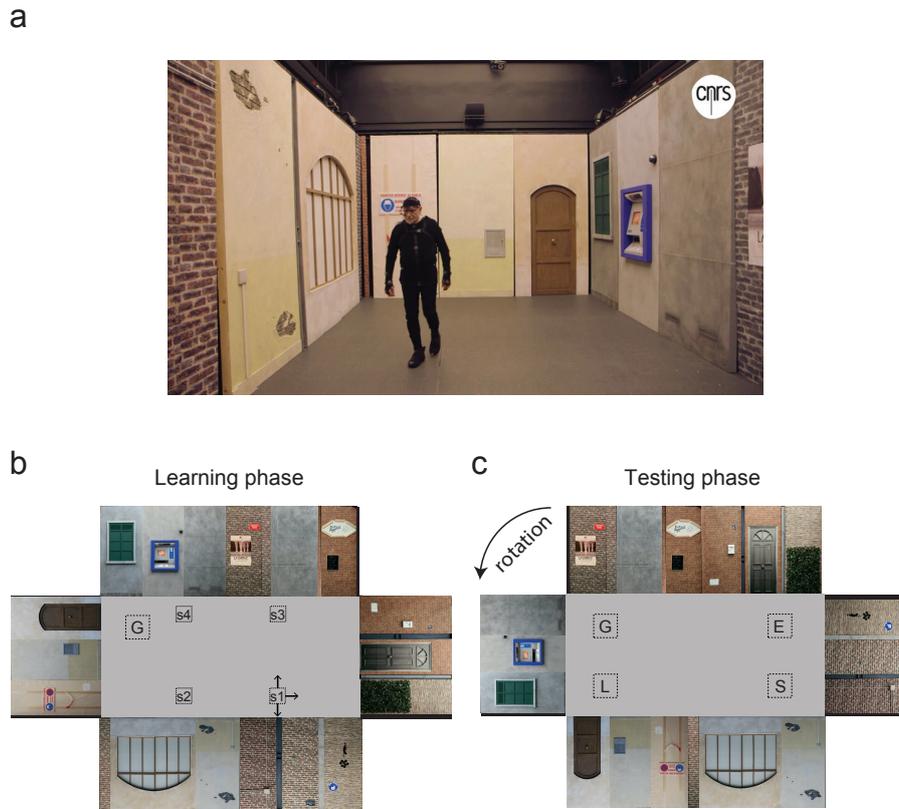


Figure 1. The real, ecological, experimental setup and the spatial task. (a) By using the Streetlab platform (Vision Institute), a street-like open-field maze was set up to have young and older subjects navigating a real, and yet fully controlled, environment (see Methods and Supp. Movie 1). Both whole body and eye motion were recorded (at 120 Hz and 60 Hz, respectively) as subjects navigated in the obstacle-free environment. (b) Configuration of the realistic relief sceneries during *learning phase* (i.e., first 8 trials). Subjects were required to find the unmarked goal location “G”, which triggered a rewarding sound. At the beginning of each trial, subjects were disoriented and placed from one of 4 positions (“s1-4”) and 3 different orientations (indicated by arrows at starting position s1). (c) Configuration of landmarks during the probe, 9th, trial and the following 4 post-probe trials. The whole array of wall panels was rotated to create a conflict between landmark and geometric spatial cues. After rotation, landmarks that were initially near the goal corner “G” were positioned in the adjacent, geometrically different corner “L”. The preference for a spatial cue (landmarks or geometry) was identified during the first probe trial based on subject’s navigation strategy. Entering areas “G” or “S” assigned a subject to the geometry group, whereas entering the area “L” assigned a subject to the landmark group. “E” was the error area.

rotational error was observed among the young subjects that used geometry during the probe trial.

To study whether and how age and cue preference were reflected in standard navigation measures, we analysed travelled distance, path tortuosity, heading deviation and walking speed across learning trials, i.e. before the cue conflict was introduced (see Methods for a detailed description of the variables). To separate a putative information-sampling period from the subsequent generation of motor behavior³⁹, we analysed the behavioural variables separately for the *orientation period*, i.e. the time from eye-opening after disorientation until the initiation of a goal-directed movement, and the *navigation period*, i.e. the rest of the trial time. The analysis of the age factor revealed that both groups reached asymptotic performance by trial 4 on average, but the spatial behaviour of older subjects differed in several respects from that of young subjects (Fig. 3). First, older subjects spent a significantly longer time to reorient compared to younger ones across all learning ($F_{(1, 35)}=47.41$, $p<0.0001$; Fig. 3a). Second, they walked with a significantly slower speed ($F_{(1, 35)}=13.47$, $p<0.001$; Fig. 3b) and they travelled a longer and a more tortuous path to the goal (travelled distance: $F_{(1, 35)}=15.40$, $p<0.001$; path tortuosity: $F_{(1, 35)}=13.95$; $p<0.001$; heading deviation: $F_{(1, 35)}=7.77$, $p<0.01$; Figs. 3c-e). As a result, it took them longer to reach the goal location (escape latency: $F_{(1, 35)}=31.10$, $p<0.0001$; Fig. 3f). There was no effect of the cue-preference factor (orientation period duration: $F_{(1, 35)}=0.15$, $p=0.70$; walking speed: $F_{(1, 35)}=0.05$, $p=0.83$; travelled distance: $F_{(1, 35)}=0.61$, $p=0.44$; path tortuosity: $F_{(1, 35)}=0.93$, $p=0.34$; heading deviation: $F_{(1, 35)}=0.94$, $p=0.33$; escape latency: $F_{(1, 35)}=2.23$, $p=0.14$) and no significant interaction on any of the analysed navigation variables. The fact that the difference in cue preference was not accompanied by differences in the tested navigation measures suggests that learning according to landmarks or geometry may occur at the same rate²³. On the other hand, we found that 8 subjects committed at least one rotational error during learning (mode: 2nd trial, Supp. Fig. 2). These were all older adults and 7 out of these 8 reoriented according to geometry in the probe test. None of the young subjects committed rotational errors during learning. Importantly, these data show that despite the absence of differences in overt navigation behaviour, the preference for geometric cues manifested itself early during spatial learning, even before the cue conflict, at least in the older subjects.

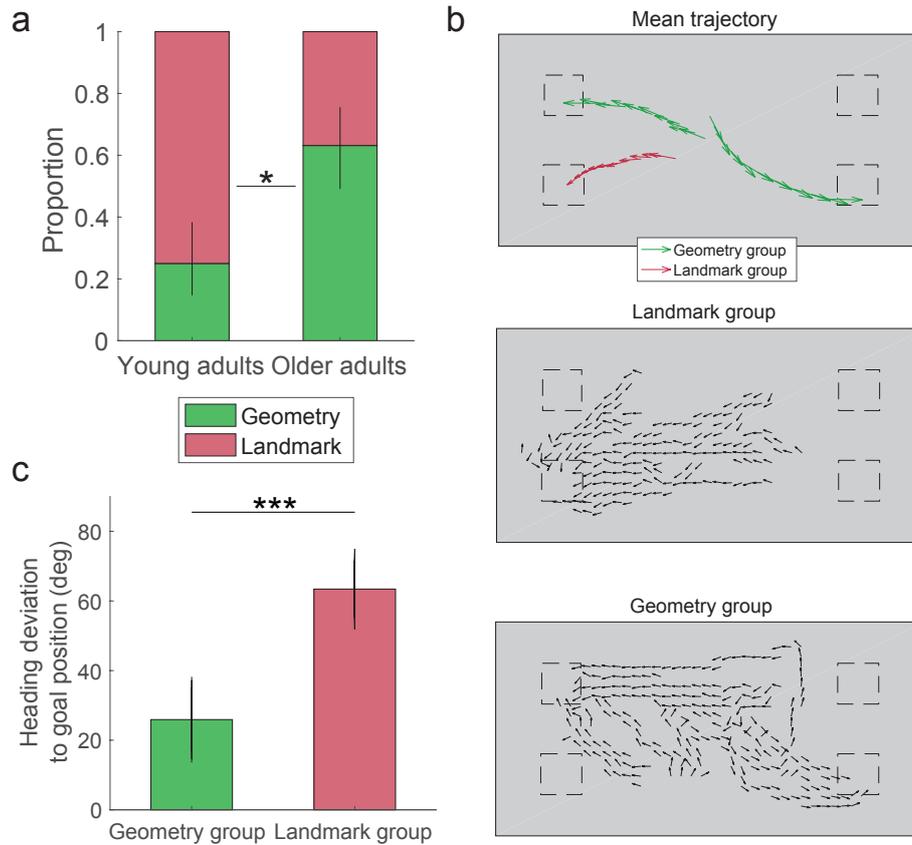


Figure 2. Preference for geometric cues in older adults. (a) Proportion of young and old participants that reoriented and navigated to the goal according to either landmarks or geometry during the probe trial. A majority of young adults used the landmarks, whereas most of older adults anchored their spatial behaviour on the geometry of the environment. Error bars show the 68% confidence interval. (b) Mean trajectory, top, and vector field representations, middle and bottom, associated with the spatial behaviour of the landmark and geometry group. (c) The mean trajectory of the landmark group, as compared to the geometry group, deviated significantly more with respect to the goal position. *** $p < 0.001$; ** $p < 0.01$; * $p < 0.05$.

The analysis of the same navigation variables during the post-probe phase (Supp. Fig. 3) revealed a stable and significant influence of age on the length of the reorientation period ($F_{(1,32)}=9.12$, $p<0.01$), escape latency ($F_{(1,32)}=12.24$, $p<0.01$) and walking speed ($F_{(1,32)}=9.56$, $p<0.01$), similarly to the learning phase. In contrast, the older adults' performance reached the level of young adults in terms of travelled distance ($F_{(1,32)}=1.4$, $p=.24$), path tortuosity ($F_{(1,32)}=2.93$, $p=.09$) and heading ($F_{(1,32)}=1.51$, $p=.22$). The consistently slower walking speed in older adults is associated with well-known age-effects on mobility, both during the learning and probe trials. In contrast, the longer reorientation period, during which the subjects stood at the start location, cannot be explained by the age-induced reduction in walking speed. Moreover, the fact that this period remained consistently longer in older subjects throughout the entire experiment, suggests that it may reflect the general age-related slowing of information collection and/or processing⁴⁰. On the other hand, the equivalence between the two age groups in path-related measures at the end of the experiment suggests that after a sufficient number of trials older adults were as efficient in goal-related path generation as young adults.

Two intermediary conclusions can be made from the behavioural results above. First, advanced age is associated with a stronger preference for geometry processing, which, however, is not associated with any changes in standard navigation performance. Second, advanced age entails a longer reorientation period, observed during both learning and post-probe trials, and which seems unrelated to potential age-related motor deficits. Since visual cues provided most of the spatial information available to the subjects in our task (because subjects were disoriented), the analysis of oculomotor behaviour during reorientation and navigation periods can be informative of goal-related decisions mediating spatial behaviour. It has previously been shown in humans that old age is associated with changes in visual exploration strategies^{41,42}, while recent studies in non-human primates linked oculomotor behaviour with spatial processing in the brain^{38,43}. We analysed the spatio-temporal organization of visual fixational patterns with respect to cue-preference and age. Given the potential link between eye movements and spatial memory³⁸, our analyses aimed at answering the two following questions: Is cue preference (geometry vs. landmark) associated with specific oculomotor fixation patterns? Is the observed age-related difference in goal-directed movement initiation (as

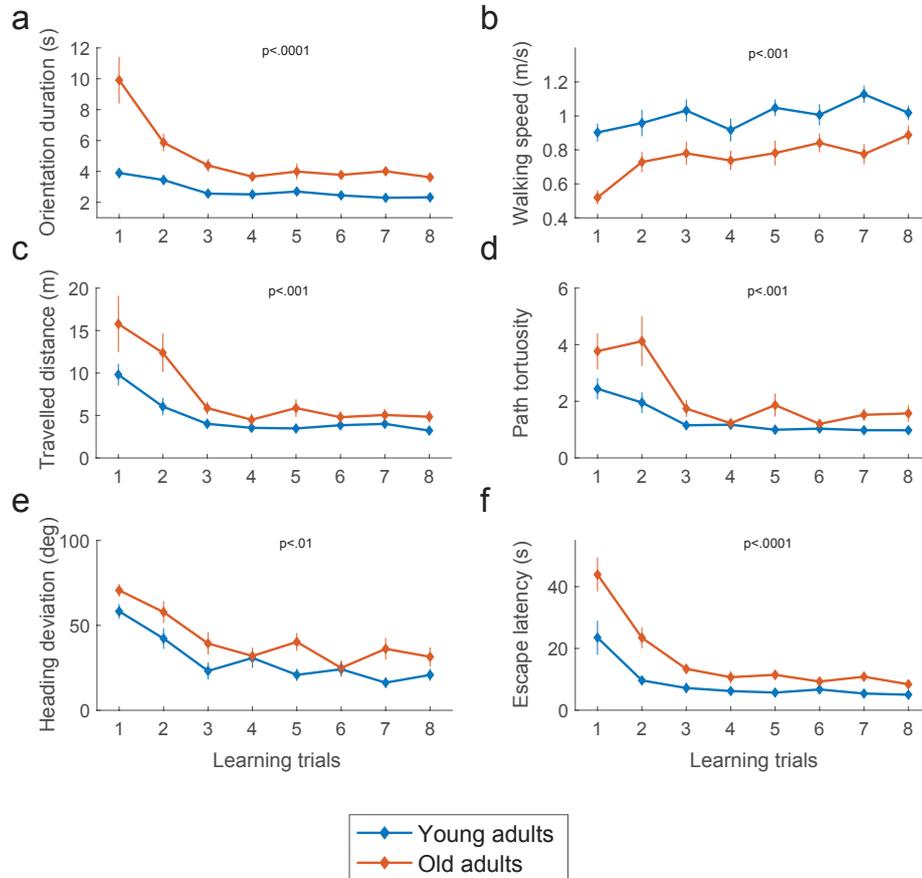


Figure 3. Spatial navigation performance of young versus older adults during learning. Although both groups learned the task and both performance plateaued by training trial 4, age-related effects impacted all navigation parameters, reflecting suboptimal spatial behaviour. (a) The reorientation period was consistently and significantly longer in older adults across the entire learning phase, with a larger difference during the first two trials (error bars show the standard error of the mean). (b) Expectedly, older adults navigated towards the goal at a significantly lower speed, again especially during early learning. (c) The goal-oriented trajectory was less direct in older adults as they travelled significantly longer distances compared to young navigators. (d) Accordingly, older adults' path to the goal was significantly more tortuous. (e) Also, on average, the trajectory of older navigators deviated more from the ideal direct path as compared to young subjects. (f) As a consequence, the latency to reach the goal location was significantly larger in older adults than young subjects.

measured by the duration of the orientation period) accompanied by differences in spatio-temporal fixation characteristics?

Our working hypothesis regarding the first question, was that subjects who reoriented themselves using landmarks, preferentially observed wall panels during learning, whereas geometry-based subjects paid more attention to the floor, which is potentially more informative about the room geometry⁴⁴. We indeed found that the time course of fixational patterns throughout a trial was different between cue-preference groups (Fig. 4a), with the landmark group spending more time observing the wall panels compared to the geometry group (orientation period: $F_{(1,35)}=7.61$; $p<0.01$, navigation period: $F_{(1,35)}=11.06$; $p<0.01$, Fig. 4b). Conversely, the geometry group spent more time observing the floor than did the landmark group (reorientation: $F_{(1,35)}=7.79$; $p<0.01$; navigation: $F_{(1,35)}=10.16$; $p<0.01$, Fig. 4c). The peak in floor fixation time in the second half of the orientation period may indicate that gazing at the floor is a critical behaviour before making a navigational decision according to geometric cues. We found no significant effect of age and no interaction in these data indicating that cue preference is the sole factor influencing oculomotor patterns (Supp. Figs. 4 and 5). We also sought whether or not age-related postural constraints (e.g., natural lowering of the head or potential kyphosis, or mobility limitations in head turning) could bias older adults in their gaze behavior. We did not find any influence of aging on mean head pitch orientation neither during the orientation period (absolute head pitch: $W=208$, $p=0.84$; head/trunk pitch angle: $W=202$, $p=0.34$) nor during straight ahead walking (absolute head pitch: $W=205$, $p=0.95$; head/trunk pitch angle: $W=218$, $p=0.51$). No age effect was found on yaw oscillations of the head relative to the trunk for either trial phase (orientation phase: $W=175$, $p=0.75$; navigation phase: $W=183$, $p=0.37$). There was an effect of age on the angular speed in yaw of the head relative to the trunk during both trial phases (orientation phase: $W=132$, $p=0.02$; straight walking: $W=155$, $p=0.03$). Therefore, the lowered gaze observed among older participants with a preference for geometry was not due to a lowered head orientation in pitch in this group. In addition, while old adults were slower in their side-to-side head turns relative to the trunk, there was no difference in the amplitude of these movements (no difference in yaw oscillations) that would be indicative of a potential age-related mobility constraint in the head-trunk unit.

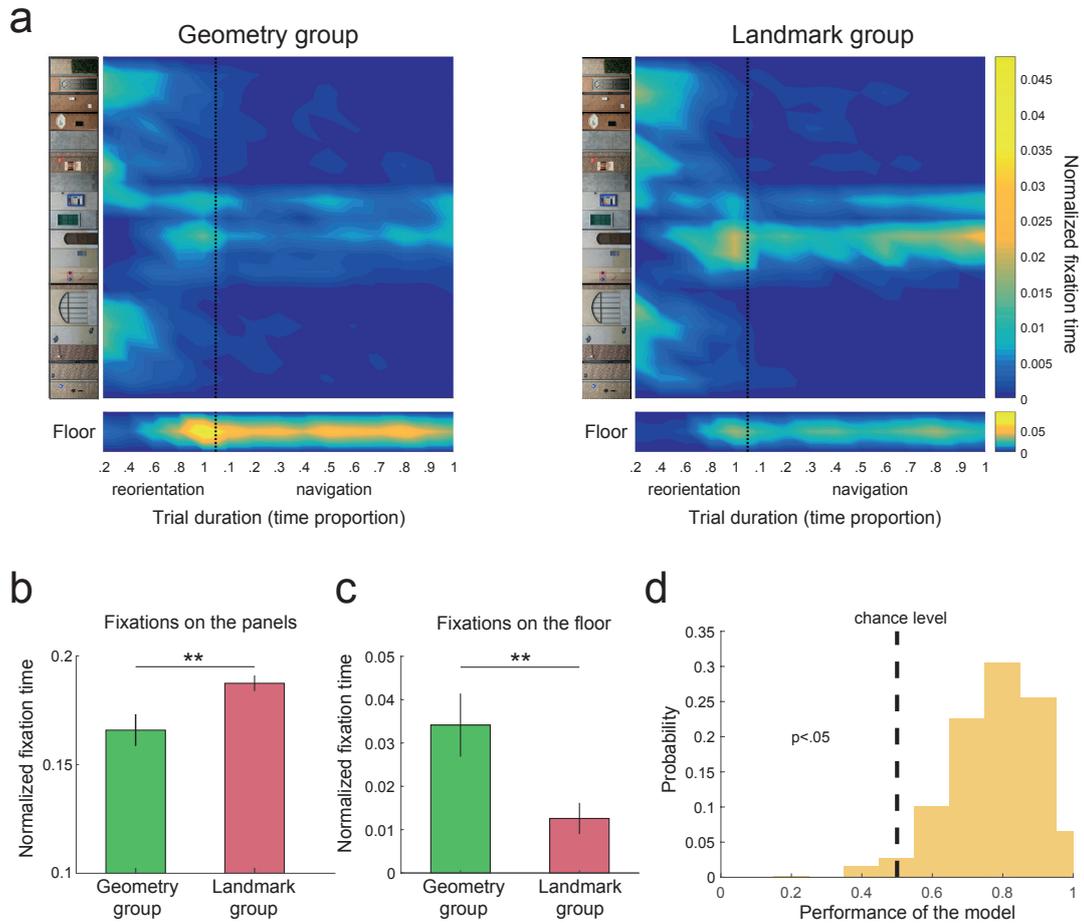


Figure 4. Spatio-temporal signatures of visual fixational patterns predict landmark versus geometry cue preference. (a) Time course of visual fixations over trial duration for the geometry (left) and landmark (right) group. Qualitative representation of the time spent on fixating different spatial locations (panels and the floor of the environment) during both orientation and navigation averaged across learning trials. Dotted line delimits the orientation and navigation periods. (b, c) On average, subjects anchoring their spatial behaviour on landmarks (according to their choice during the probe trial) spent significantly more time fixating at panels, whereas subjects preferring geometry gazed more at the floor, respectively. (d) Performance of a generalized linear model (trained on the basis of fixation spatiotemporal characteristics) in predicting spatial cue preference on a single-subject-single-trial basis. The performance distribution of correct predictions (80%; the indicated p value corresponds to $P(\text{Performance} < 0.5)$) suggests that gaze dynamics is indeed predictive of the spatial cue coding policy used by subjects.

We reasoned that if observing the floor was a critical component for the processing of geometry, then the environment symmetry should be reflected in the oculomotor behaviour. To verify this prediction, we analysed the pattern of floor fixations during the orientation period by counting fixations that fell into 4 floor quadrants (Fig. 5a), such that quadrants **a** and **a'** were geometrically related to the goal area during learning, while quadrants **b** and **b'** were not. We found that fixations in the geometry group were significantly more concentrated in the symmetric quadrants related to the goal, compared to the other two quadrants (Wilcoxon signed rank $W=135$, $p<0.001$; Figs. 5a,b). Moreover, the number of fixations that fell into areas **a** and **a'** were not statistically different ($W=61$, $p=0.29$; Supp. Fig. 6). These data suggest that the symmetry of the environment was indeed reflected in the fixation pattern of the geometry group during the reorientation period. This is in stark contrast with the landmark group, in which we did not observe a difference in ground fixations in the areas geometrically related versus unrelated to the goal ($W=62.5$, $p=0.26$; Figs. 5a,b). In addition, the vast majority of fixations fell within the area **a**, compared to **a'** ($W=78$, $p<0.001$; Supp. Fig. 6), suggesting that landmarks strongly biased fixations in this group. During goal-oriented navigation, subjects in the landmark group gazed preferentially at the wall panels adjacent to the goal location, whereas those in the geometry group concentrated almost exclusively on the floor of the goal quadrant, confirming the importance of floor information for geometric cue preference (Fig. 5c).

Given such a clear distinction between the two cue-preference groups in terms of fixation patterns, we tested whether the navigational decision during the probe trial could be predicted by the analysis of oculomotor behaviour during learning. To answer this question, we trained a binary classifier to predict, on a single-subject-single-trial basis, whether she or he will make a decision according to either geometric or landmark cues, based on the location of fixations executed before the probe trial. To assess the performance of the classifier, fixations from 10 subjects (26%) were included in the validation dataset, while the fixations from the rest of the subjects constituted the training set. The distribution of the classifier performance (i.e., percentage of correctly classified subjects) over different random selections of test sets showed that the cue preference was determined correctly for 80% of subjects on average, while the model performed better than chance level (0.5) in 95.4% of cases (Fig. 4d). When the size of the test set was reduced to 1 subject (leave-one-out cross-validation), the cue preference of 31 out of 39 subjects (79%) was determined correctly. Similar results were obtained when

we analysed navigation and orientation periods separately (orientation: 27 of 39 subjects, 69%; navigation: 28 of 39 subjects, 72%) and in separate age groups (young: 16 of 20, 80%; old: 15 of 19, 79%). These findings demonstrate that the visual scanning policies adopted by subjects are indeed predictive of the spatial cues that will be used to encode their spatial representation and to subsequently resolve cue conflict, preferring either landmarks or geometry.

To further understand whether the age-related difference in goal-directed motion initiation (as measured by the duration of the orientation period) was accompanied by changes in spatio-temporal fixation characteristics, we tested if age and cue-preference related differences were associated with differences in other fixation characteristics. We first sought whether the longer orientation period of older adults could be explained by slower fixation rates or longer fixation durations. The analysis of fixation counts revealed that older adults produced significantly more fixations during the orientation period compared to young adults across learning trials ($F_{(1,35)}=34.01$, $p<0.001$; Fig. 6a). However, we did not find any significant difference in fixation frequency, duration and interfixation distance between the two groups (Supp. Fig. 7). Moreover, fixations in the older group were not produced in order to explore a larger portion of the visual environment, as the number of different panels observed was not significantly different between age groups over trials ($F_{(1,35)}=3.22$, $p=0.08$; Fig. 6b). These results suggest that the longer orientation period in older adults was due to a more repetitive sampling of visual cues, rather than a general slowing of ocular movements. To further verify this conclusion, we classified fixations in 2 groups based on their functional properties: *explorative* fixations were those directed to a wall panel not seen before in the course of the current trial; *exploitative* fixations were directed (either successively or subsequently) to previously fixated panels during the same trial. By averaging the number of explorative and exploitative fixations across the course of trials, we found that older adults produced more exploitative fixations ($F_{(1,35)}=13.32$, $p<0.001$; Fig. 6c) than young adults, while expressing fewer explorative fixations ($F_{(1,35)}=5.29$, $p<0.05$). This difference was more evident during the first half of the orientation period, i.e. well before the initiation and preparation of the goal-directed movement. The analysis of the same data with respect to cue preference showed that the geometry group made less explorative fixations compared to the landmark group (Fig. 6d). No interaction was found between the age and cue-preference factors. These results suggest that the longer reorientation period of older adults was associated with a more repetitive sampling of

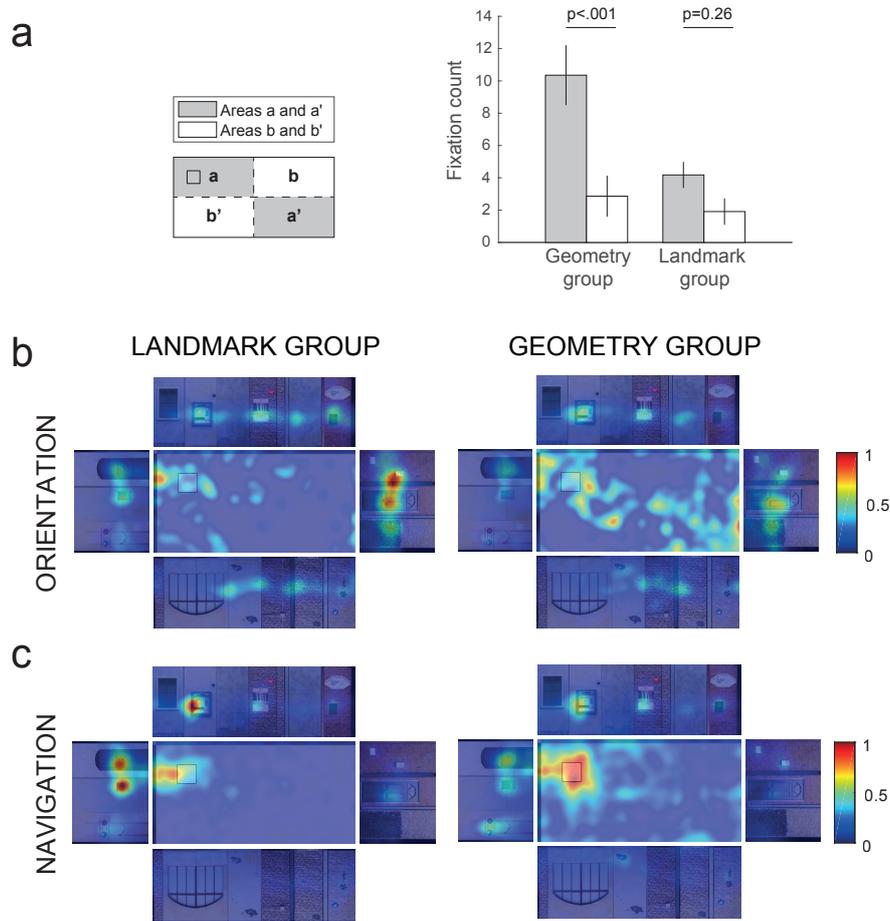


Figure 5. Spatial distribution of visual fixations as a function of cue preference. (a) During the orientation period, ground fixations produced by the geometry group were significantly more concentrated in the quadrants that shared the same rewarded geometric properties (areas **a** and **a'**) as compared to the other adjacent quadrants (areas **b** and **b'**). Ground fixations of the landmark group did not differ across the same pairs of floor quadrants. (b, c) These results are qualitatively illustrated by heatmaps of fixation distribution on the panels and on the floor during the orientation and the navigation periods, respectively. The colormap correspond to normalized fixation count.

visual cues, a suboptimal visual scanning policy potentially reflecting impaired memory or encoding processes³⁸.

Finally, we looked for potential perceptual or cognitive markers of the increased preference for geometry-related spatial coding in older adults. We assessed a variety of visual and cognitive functions through a battery of tests (Supp. Table 1). We first performed a principal component analysis (PCA) on these data and examined whether age or cue-preference factors were associated with differences on principal components scores. We found that the two first principal components accounted for 60% of the total variance. The 1st component discriminated significantly subjects according to their age ($F=77.72$, $p<0.0001$; Fig. 7a), whereas no clear distinction could be seen according to their cue-preference ($F=0.07$, $p=0.79$). There was no effect of either factor on the other components. This analysis was further confirmed by a significant effect of age when considering raw visuo-cognitive data (Supp. Figs. 8 and 9). However, the cue preference correlated significantly with the results of one cognitive test, namely Perspective Taking/Spatial Orientation⁴⁵, with older adults in the geometry group performing significantly poorly in this test than those in the landmark group (Welch $t_{(15.77)}=2.21$, $p<0.05$; Fig. 7b). Thus, a stronger preference for geometric cues in aging was associated with a lower capacity to take different perspectives relative to a constellation of landmarks.

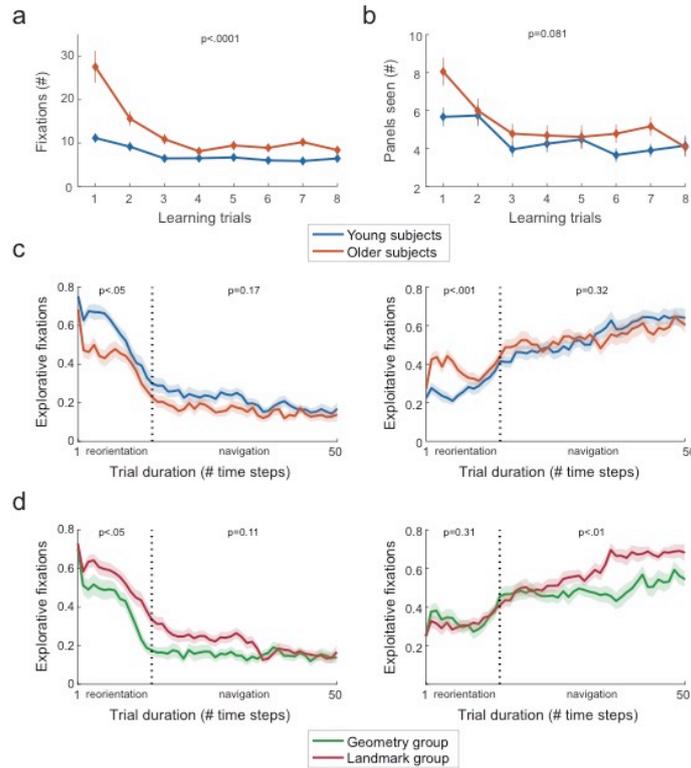


Figure 6. Age and cue-preference related differences in visual fixation characteristics. (a) Older navigators produced, on average across learning trials, a significantly larger number of fixations during the reorientation period, as compared to young participants (error bars represent the standard error of the mean). (b) However, during the same period, older adults did not explore a larger number of panels than young subjects across trials (note that there were 19 panels in total). (c) Proportion of explorative (left) versus exploitative (right) fixations during reorientation and navigation periods averaged across learning trials for both young and older adults (shaded areas indicate the standard error of the mean). The dotted lines separate the reorientation and navigation periods. During reorientation, older adults produced significantly less explorative (and more exploitative) visual fixations than young adults. (d) Analysing the same oculomotor data with respect to cue preference, showed that during reorientation the geometry group produced less explorative visual fixations than the landmark group. Cue preference did not lead to differences in the number of exploitative fixations during reorientation, although landmark subjects tended to do more exploitative fixation when approaching the goal. Note that ground fixations were not taken into account in this analysis.

6.1. SPATIAL CUES: LANDMARK & GEOMETRY CODING

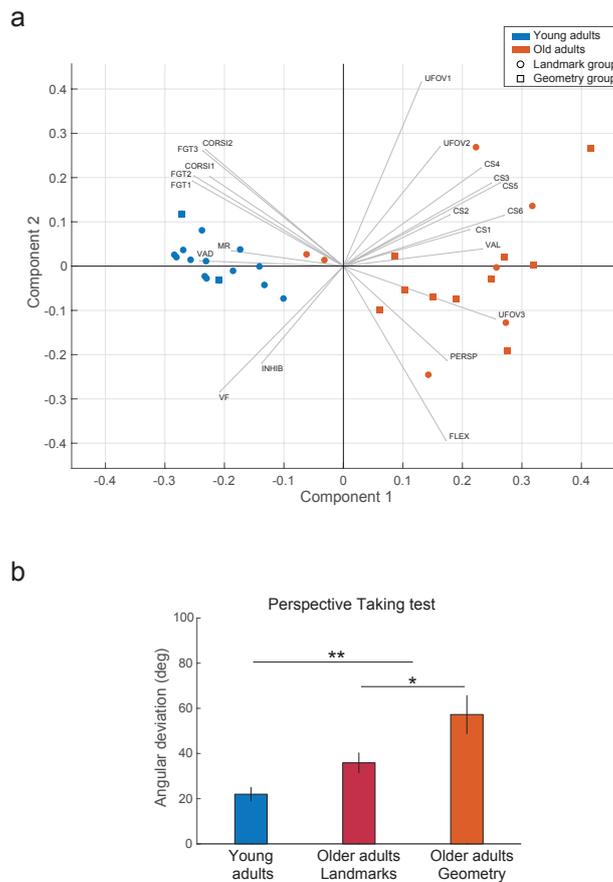


Figure 7. Visual and cognitive correlates of the geometric preference in aging. (a) Principal component analysis (PCA) of visual and cognitive data (abbreviations: MR = mental rotation score (3D), FLEX = mental flexibility index (TMT), FGT1 = visual memory - learning, FGT2 = visual memory – short-term recall, FGT3 = visual memory – long-term recall, CORSI1 = spatial memory – short-term span, CORSI2 = spatial memory – working-memory span, INHIB = inhibition index (go/nogo), PERSP = perspective taking, VAD = visual acuity – diopter, VAL = visual acuity - LogMar, UFOV1 = usefull field of view – processing speed, UFOV2 = usefull field of view – divided attention, UFOV3 = usefull field of view – selective attention, VF = visual field, CS1 = contrast sensitivity – 0.5 cycle per degree, CS2 = contrast sensitivity – 1 cycle per degree, CS3 = contrast sensitivity – 2 cycles per degree, CS4 = contrast sensitivity – 4 cycles per degree, CS5 = contrast sensitivity – 8 cycles per degree, CS6 = contrast sensitivity – 16 cycles per degree). (b) Focus on the performance during the perspective-taking test. Among older adults, those subjects that reoriented and navigated according to geometry had a significantly lower performance than those using landmarks. Errors bars show the standard error of the mean.

Discussion

This study provides novel evidence for a behavioural preference for geometric cues in older adults, as compared to young adults, navigating a real ecological environment. This preference is associated with a decreased capacity to deal with and take perspective from a constellation of landmarks in older subjects. Importantly, our findings indicate that geometry-based spatial coding is mediated by specific oculomotor signatures, independently from age. In particular, gaze dynamics are predictive of the spatial cue preference that determines the anchoring of subjects' spatial representation on either landmarks or geometry. In addition, the need for repetitive visual sampling is the main non-motor correlate of aging in navigation, reflecting a suboptimal exploration-exploitation balance in the visual scanning policy of older navigators, and leading to their longer reorientation period.

We found striking differences in the visual exploration performed by the two cue-preference groups before making a behavioural decision, in that observation of floor cues, especially near symmetric corners, was a marker of geometric processing. The apparent important role of the ground-related information for geometry-based decisions in our study is in agreement with the reported ground-dominance effect when judging distances between objects⁴⁶ and with data demonstrating that a disruption of the structure between the ground and walls prevents geometry from being used as an orienting cue⁴⁷ and it impairs the response of boundary-sensitive areas of the brain⁴⁸.

The fact that the environment geometry was used as an orienting spatial cue is clearly indicated by the presence of rotational errors during learning, the decisions taken during the probe trial, and the oculomotor patterns. Because rotational errors appeared early during learning, the processing of the geometry appears to be quick and it might be incidental²³. Yet, subjects in the geometry group chose the actual goal corner significantly more often than its diagonally opposite one, ruling out an exclusive use of this type of cue. Given that subjects were disoriented at the start of each trial, the most likely explanation for this pattern of results is that both geometric and landmark cues were concurrently used in the two cue-preference groups. In the geometry group, landmarks had a smaller contribution in navigation, but they did contribute to the behavioural decision nevertheless by making the actual goal corner a more reliable choice. Indeed, in the probe trial, the corner G is correct with respect to geometry, at the same time being spatially closer to the location L indicated by the rotated landmarks.

This explanation suggests that the ability to combine both cue types, as observed in young adults^{25,49}, deteriorates with age to a different degree in different subjects. Moreover, if this explanation is correct, it argues against the idea of a geometric module impervious to other types of information^{50,51}.

What are the reasons for the increased reliance on geometric information in older adults, at the expense of landmark cues? First, our results suggest the contribution of a cognitive age-related deficit, since older subjects in the geometric group were impaired specifically in the Perspective Taking test⁵². Functional MRI studies have linked perspective-taking with neural areas involved in spatial navigation⁵³, while deficits in this ability are correlated with impaired route learning and taking novel shortcuts^{54,55}. In Perspective Taking test, subjects are presented with a two-dimensional array of landmarks, and asked to (i) take the perspective of a particular landmark (i.e., orient one's self relative to the array), and (ii) indicate the position of another landmark (i.e., code the position of a third element relative to the array). We could thus suppose that the preferential switch to geometry in older adults is linked to a difficulty to either orient according to and/or associate a direction or a goal position to environmental landmarks. This difficulty, in turn, may push the older subject to use the geometric layout of the environment, since this information may be more easily extracted and learned. Second, perceptual age-related deficits⁵⁶ are also likely candidate reasons. Indeed, impairments in visual processing of high spatial frequencies could lead to difficulties in older navigators to encode fine contents of visual landmarks, biasing the subjects towards reliance on low-frequency global scene context⁵⁸, including its geometry. Although we did not observe any significant correlation of purely visual sensitivity tests (e.g., contrast sensitivity) with cue preference in our data, further specific experiments are required to examine whether diminished visual sensitivity at higher frequencies may contribute to geometric preference.

While other age-related factors are likely to also contribute to the geometry preference observed in the present study, our results argue against an involvement of three potentially related processes. First, the absence of significant differences between groups in the Figural Memory test (Supp. Fig. 9) suggests that the preference for geometry is unlikely to be explained by an impaired ability to memorize features, in agreement with previous studies⁵⁹⁻⁶¹. Second, it could be argued that unspecific difficulties related to the processing of a *large number* of landmarks in our experimental setup might bias older subjects to use geometry. However, it has been shown that older adults are impaired in

reorienting even with a single cue²⁸ (a colored wall), thus making such an explanation unplausible. Third, age-related postural constraints⁶², which may bias old adults to look at the floor⁶³, are unlikely to contribute to the geometry preference, since (i) the ground-dominance effect in visual exploration was statistically significant in young as well as older subjects in the geometry group, and (ii) we did not find any statistical evidence for postural differences in our data.

Previous navigation studies have proposed that aging is associated with a specific difficulty to use allocentric navigation strategies, compared to egocentric ones⁶⁴. Whereas an allocentric strategy implies localizing a goal according to spatial relationships between environmental cues, an egocentric strategy relies on self-centred stimulus-response associations⁶⁵. We note however that the success of an allocentric strategy, as formulated by former paradigms, is critically dependent on the capacity of the subject to process landmarks accurately. Furthermore, geometric cues in these paradigms were always isotropic and uninformative (circular room²⁹, equally-spaced arms^{66,67}), thus preventing them from being used to reorient and navigate towards the goal. If older navigators experience difficulties related to landmark processing, as our results indicate, then age-related navigation problems, previously characterized in terms of strategy preference, may in fact be explained in terms of cue processing. This hypothesis leads to the prediction that making the geometry of an experimental environment unambiguous may improve the use of allocentric strategies in older adults. If correct, this prediction will question the current understanding of age-related navigation deficit in terms of a bias towards egocentric navigation strategies.

A previous study in a virtual Morris water maze proposed that older adults were impaired in using the geometric layout of an environment⁷², based on the comparison of hand-drawn diagrams of the experimental space (a circular arena inside a larger room with an asymmetric shape). Several potential factors may explain the discrepancy between conclusions from this study and ours. First, the poorer bird's-eye-view diagrams produced by older subjects may not have accurately reflected the use of visual cues during navigation (which may be partially be subconscious), or may have been due to memory deficits rather than specific cue use. Second, local visual cues mounted on the circular wall were sufficient for an unambiguous localization of the goal location, and may thus have overshadowed the geometric information provided by the outer wall. Third, the study was conducted using a screen-based virtual reality setup, potentially preventing efficient geometry extraction³², especially from the outer wall of the

environment, which was partially occluded by the circular wall of the experimental arena. Finally, we note that we found no gender effect on cue preference in our study, contrary to two previous virtual-reality studies^{28,73}. These discrepancies may also be due to the use of a more ecological setup in our study.

In summary, by using the combined recording of subject motion and gaze direction during spatial navigation in an ecological experimental setup, our study presents a detailed characterization of landmark- and geometry-related behaviour in young and older navigators. Taken together with previous studies in children and young adults, these findings provide evidence for an inverted U-shaped dependence of landmark cue preference on age. Our data echo aging effects in navigation strategy preference^{67,68} and in the capacity to associate position and direction with landmarks^{59,69}, which are manifestations of global brain changes across the lifespan⁷⁰. This work contributes, therefore, to the characterization of compensatory adaptation of an organism to age-related deficits, an important prerequisite for the development of rehabilitation solutions that can improve safety and quality of life in the aging population.

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Author Contributions. MB, DS, LLB & AA designed the experiment. MB, GT and LLB collected and analyzed the data. MB, DS, and AA wrote the article.

Competing interests. The authors declare no competing interests.

Data availability. The data that support the findings of this study are available from the corresponding author upon reasonable request.

Supplementary information

Age-related preference for geometric spatial cues during real-world navigation

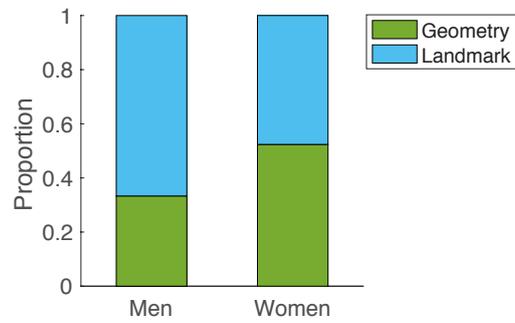
Marcia Bécu^{1,*}, Guillaume Tatur¹, Denis Sheynikhovich¹, Catherine Agathos¹, Luca Leonardo Bologna^{1,2}, Angelo Arleo^{1,*}

¹ Sorbonne Université, INSERM, CNRS, Institut de la Vision, 17 rue Moreau, F-75012 Paris, France

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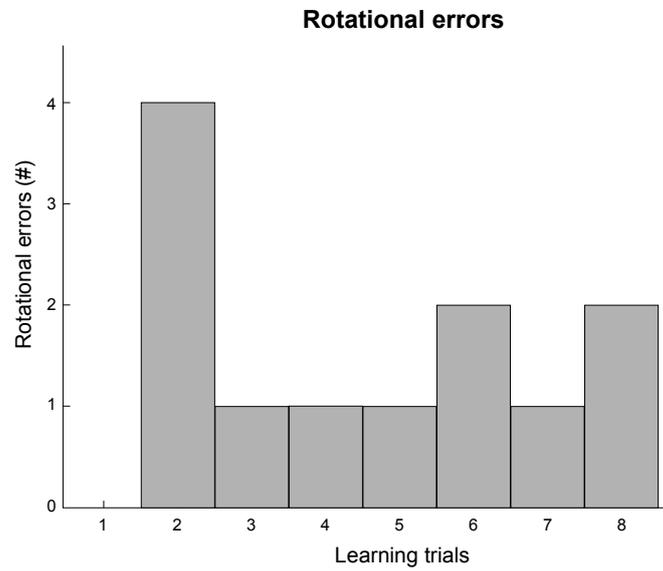
* Correspondence: Marcia Bécu & A Arleo, Institute of Vision, marcia.becu@inserm.fr, arleo.angelo@inserm.fr

Supplementary Figure 1



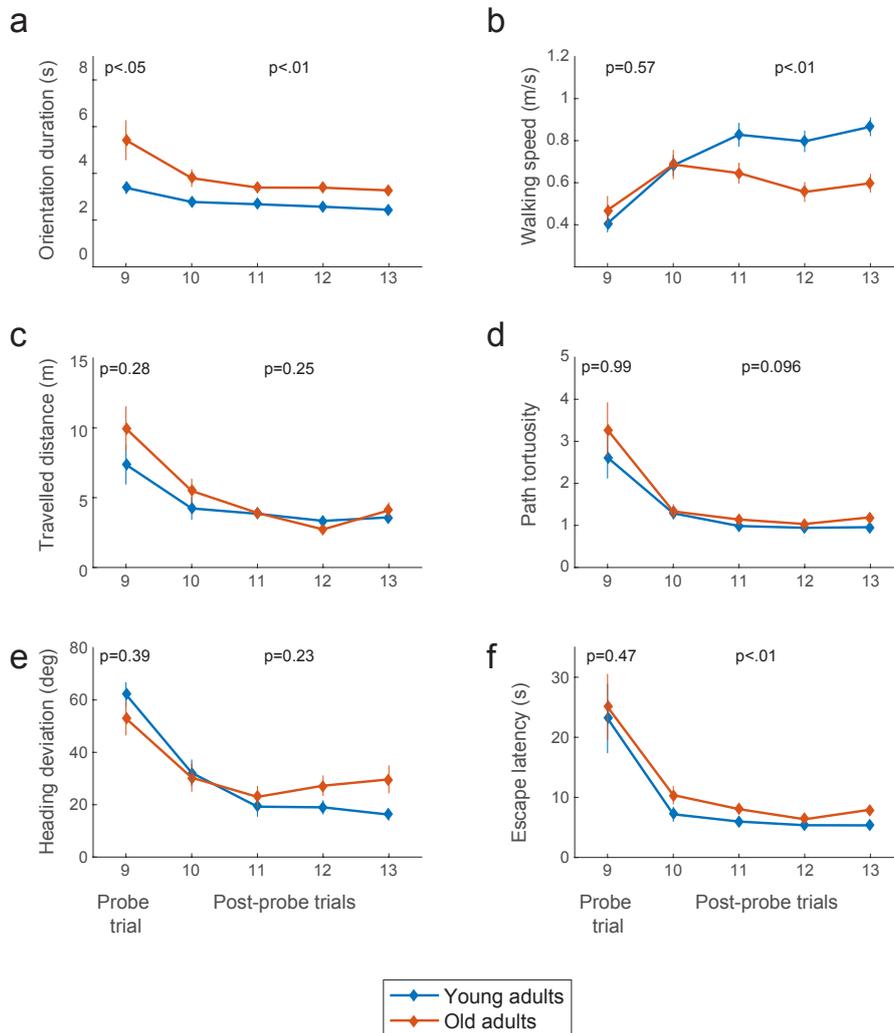
Supplementary Figure 1. Proportion of men and women that oriented according to landmarks and geometry on the first probe trial. No significant gender effect was observed with respect to cue preference ($\chi^2=1.43$; $p=0.23$).

Supplementary Figure 2



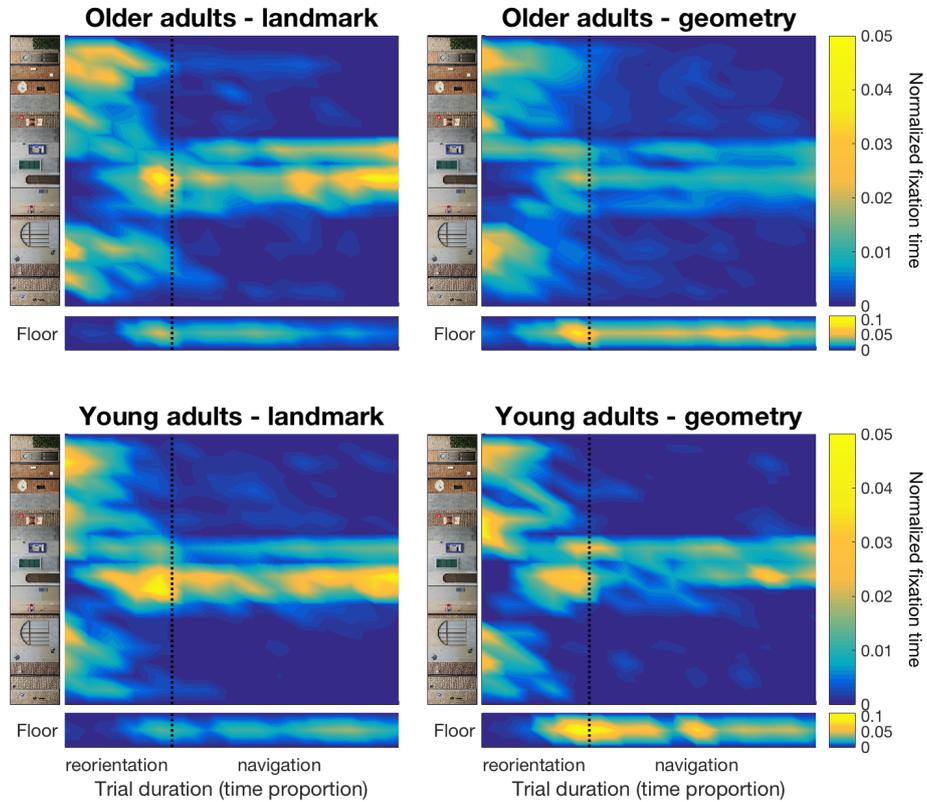
Supplementary Figure 2. Histogram of rotational errors during the learning phase. Most rotational errors (made by older participants only) occurred during the 2nd learning trial.

Supplementary Figure 3



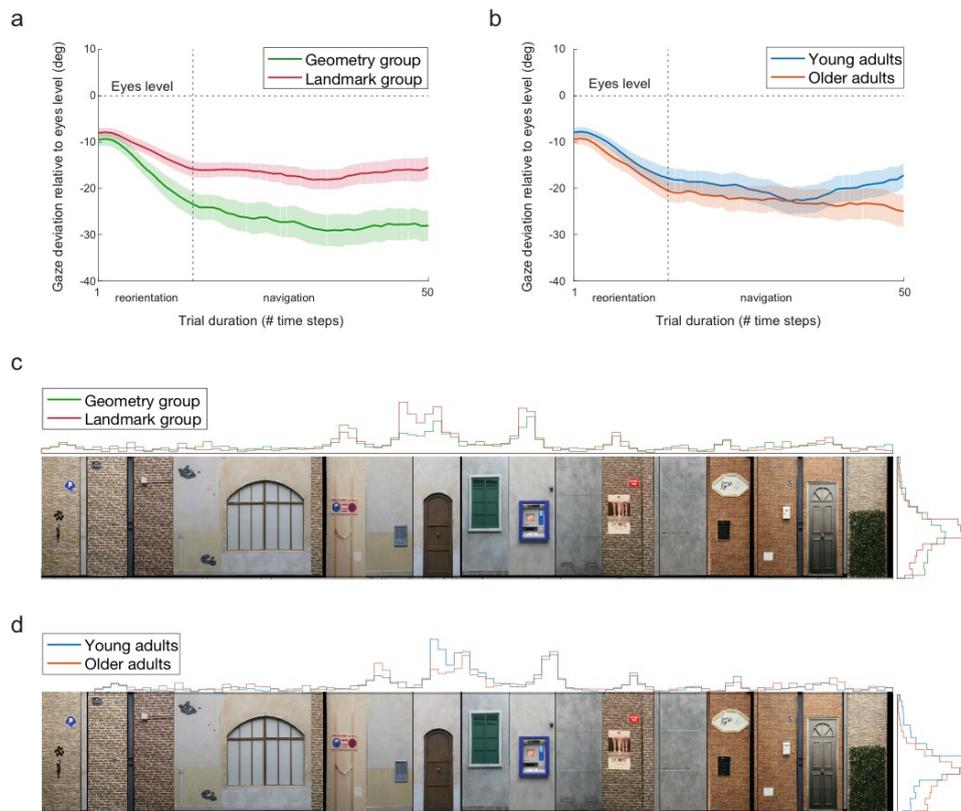
Supplementary Figure 3. Navigation performance during the probe (9th) and post-probe trials (10th to 13th) for young and older adults. P-values on the left correspond to the probe trial only, whereas p-values on the right correspond to data averaged over trial 10 to 13.

Supplementary Figure 4



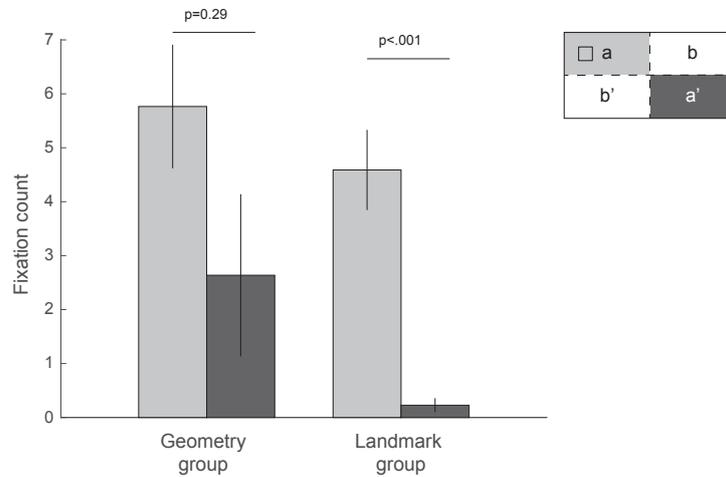
Supplementary Figure 4. Normalized fixation time spent on observing the panels and the floor of the environment during the learning phase. On average, during both orientation and navigation, subjects using landmarks gazed preferentially at panels, whereas subjects using geometry gazed preferentially at the floor.

Supplementary Figure 5



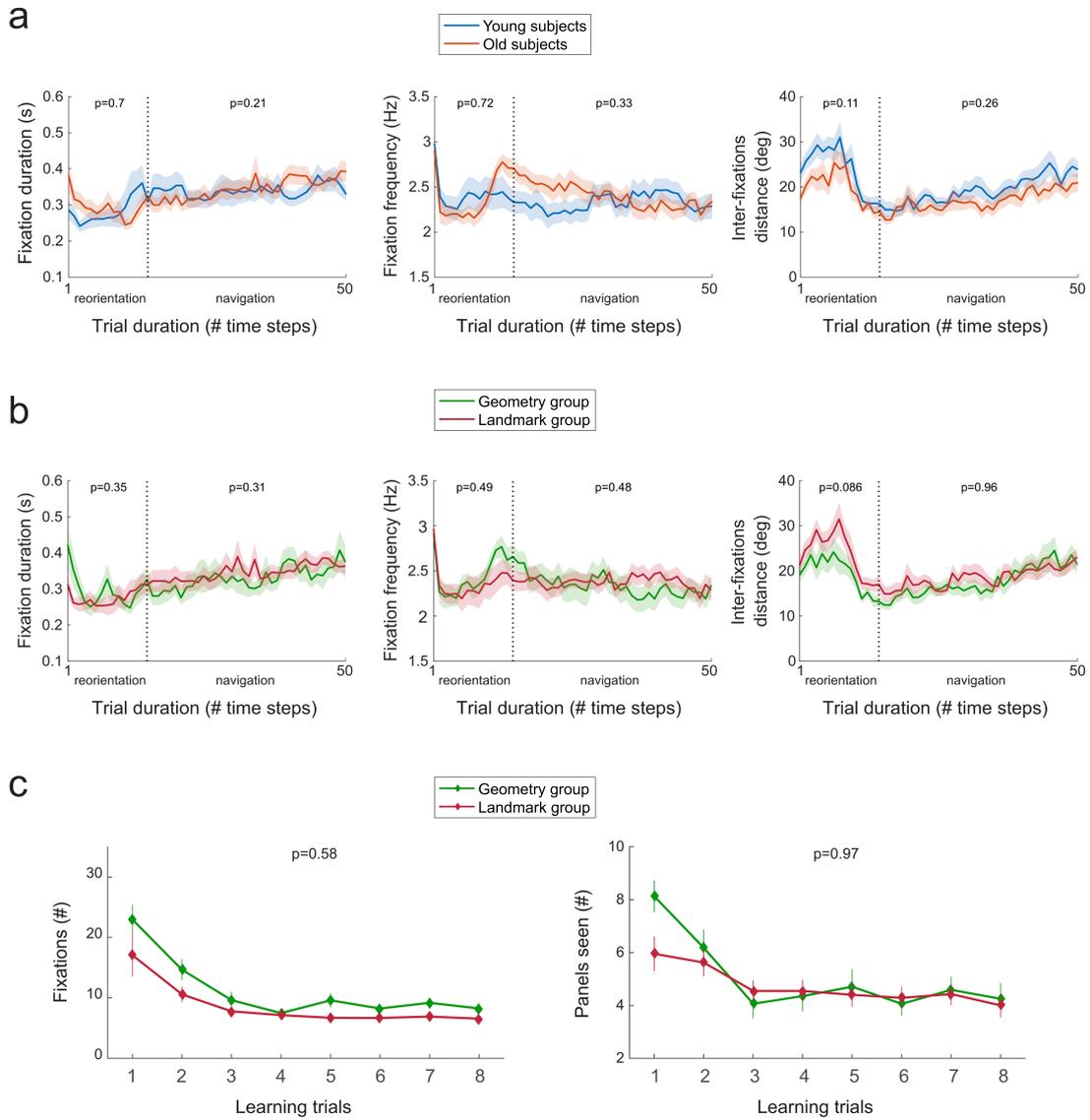
Supplementary Figure 5. (a) Cue preference did influence gaze dynamics (here in terms of azimuthal deviation with respect to eyes level averaged over the course of a trial), during both reorientation and navigation periods. (b) No significant effect of age was observed in terms of azimuthal gaze deviation. (c, d) Qualitative histograms summarizing the number of fixations across panels and latitudes, during the learning phase, for geometry versus landmark groups (c) and for young versus older participants (d).

Supplementary Figure 6



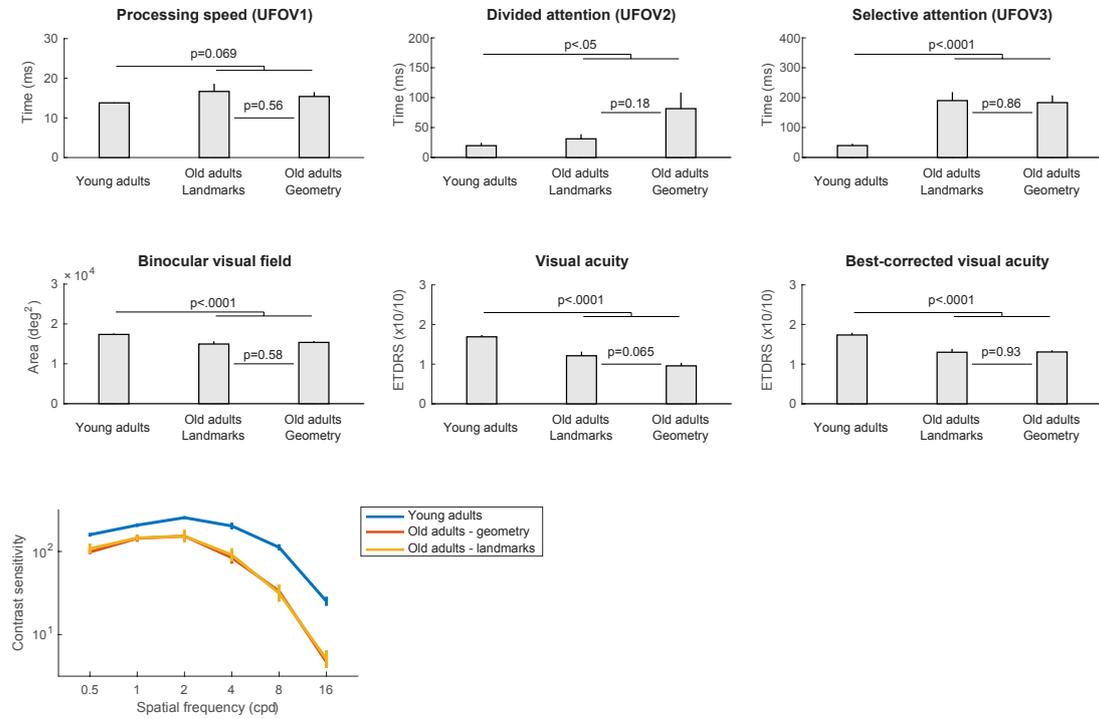
Supplementary Figure 6. Spatial distribution of fixations during the orientation period. Fixations produced by the geometry group were evenly distributed in areas **a** and **a'** (i.e., the goal quadrant and its geometrical symmetric quadrant, respectively), whereas the landmark group produced significantly more fixations in area **a** than in **a'**, according to the fact that wall features in the goal quadrant biased gaze dynamics in this group.

Supplementary Figure 7



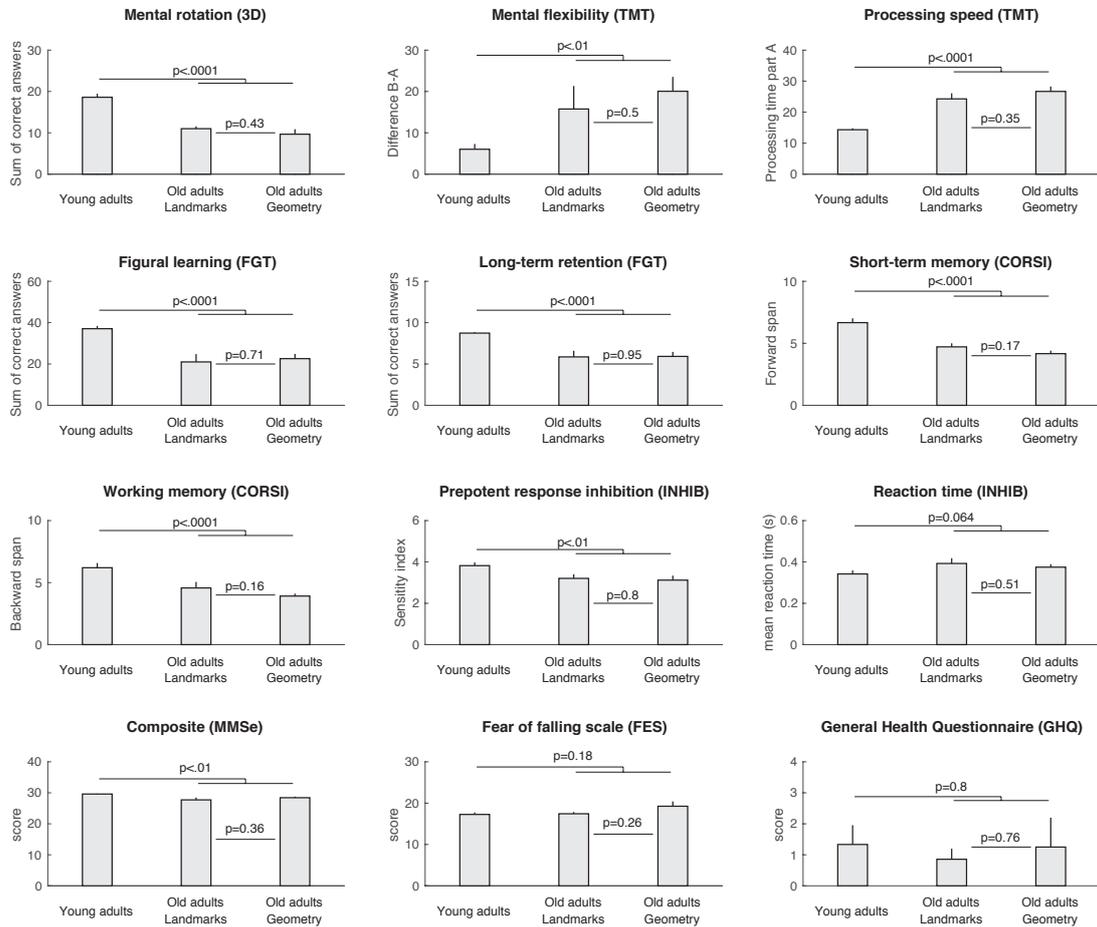
Supplementary Figure 7. (a,b) Fixation parameters (duration, frequency and inter-fixations distance) according to age and cue preference, respectively. Transparent areas correspond to the standard error of the mean. The dotted line delimits the orientation and navigation periods. (c) Number of fixations and number of panels seen by participants during the orientation period according to cue preference. There were 19 panels in total. Errors bars show the standard error of the mean.

Supplementary Figure 8

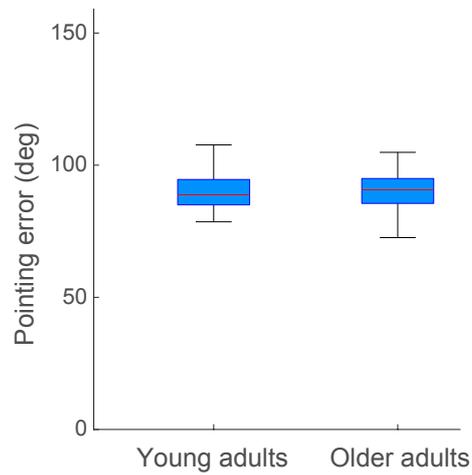


Supplementary Figure 8. Battery of visual tests used during the screening of the study population. Aging significantly affected all visuo-attentional functions, whether cue-preference did not. ‘cpd’ stands for circles per degree.

Supplementary Figure 9



Supplementary Figure 9. Battery of visuo-cognitive tests used during the screening of the study population. Aging significantly affected most cognitive assessment, except Fear of Falling and the General Health Questionnaire. Cue-preference did not correlate with any of the measured cognitive functions, except for the Perspective Taking/Spatial Orientation (Fig. 6b).

Supplementary Figure 10

Supplementary Figure 10. Mean pointing error of young and older adults post-disorientation procedure. Data are averaged over learning and test trials. The disorientation was efficient in both groups and led to an equivalent pointing error ($t_{(24)}=0.24$; $p=0.80$).

Supplementary Table 1

	Assessed function	Test/apparatus name and task
Visual screening	Binocular visual acuity	ETDRS chart at 2m distance, in scotopic condition, with subjects wearing their own optical correction.
	Best-binocular visual acuity	ETDRS charts at 2m distance, in scotopic condition, with the best optical correction.
	Binocular visual field	Perimeter Octopus 900 with constant luminosity and stimulus size (corresponding to the III ₂ in the Goldmann perimetry), in scotopic condition.
	Contrast sensitivity	Evaluating sensitivity thresholds binocularly for different spatial frequencies (0.5, 1, 2, 4, 8, 16 circles per degree) in photopic condition, with subjects' own optical correction.
	Divided visual attention	Useful Field of View (UFOV, Ball & Owsley, 1993): central (UFOV1) and peripheral visual discrimination task, without (UFOV2) and with (UFOV3) visual distractors.
Cognitive screening	Composite	Mini Mental State Examination (MMSE, Folstein, Folstein, & McHugh, 1975).
	Spatial working memory	Corsi block-tapping test: repeating spatial sequence of cubes forward and backward (Schuhfried, 2004).
	Visual memory	Figural Memory test: learning and short/long-term recalling of geometrical figures (Schuhfried, 2004).
	Mental rotation	3D test: mentally rotating cubes and imagining updated views (Schuhfried, 2004).
	Perspective taking	Perspective Taking/Spatial Orientation test: imagining position and facing direction relative to a two-dimensional array of objects and indicating the position of a third object (Hegarty & Waller, 2004).
	Mental flexibility	Trail Making test: alternating between sequences of letters and numbers (Schuhfried, 2004).
	Inhibition capacity	Go/no go task: responding to a frequent stimulus while inhibiting response to a rare one (Schuhfried, 2004).
	Fear of falling	Fear Efficacy Scale-International (FES-I, Tinetti, Richman, & Powell, 1990).
	Depression and anxiety	General Health questionnaire (GHQ, Goldberg & Hillier, 1979).
Supplemental Table 1. Battery of visual and cognitive tests used to screening/profiling our study population.		

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6.2 Spatial strategies: egocentric & allocentric navigation

6.2.1 Rationale

The objective of this second part is to understand how cue reliance impacts older adults' abilities to use egocentric and allocentric strategies. Indeed, in the previous section, we showed that older adults were more likely to use geometric cues than landmarks when navigating a real-world setting. This challenges the classical view for an *egocentric preference in aging* (Bohbot et al., 2012; Davis and Weisbeck, 2015; Driscoll et al., 2005; Wiener et al., 2012, 2013), given that standard paradigms that tested navigational strategies were exclusively dependent on the capacity of the subjects to use distal landmarks.

We adapted the Y-maze paradigm by introducing a geometric polarization to the maze to test spatial navigation strategies in a group of young and older adults. Additionally, because an egocentric preference has also been showed in development (Ruggiero et al., 2016), we added a group of children to the pool of the SilverSight adult cohorte. We used an immersive virtual reality (VR) head-mounted display (HMD) in this experiment in order to be able to manipulate geometric polarization and the position of distal landmarks. Although this type of HMD restricts the visual field extent to 145° diagonal, it is nevertheless more immersive than the desktop VR setups, as the participant experiences proprioceptive and vestibular inputs when navigating.

The first purpose is to replicate, with an immersive VR instead of desktop VR setup, previous evidence showing an egocentric preference when the performance is based on landmarks (Rodgers et al., 2012). Second, we tested whether introducing a geometric polarization could potentiate the use of allocentric strategies in our participants.

6.2.2 Methods

Participants. Seventy-nine subjects participated in this study: 29 children (range: 10-11 yrs, $\mu=10$, $\sigma=0.49$, 17 females, 12 males), 22 young adults (range: 23-37 yrs, $\mu=28$, $\sigma=4.28$, 13 females, 9 males) and 28 older adults (range: 67-81 yrs, $\mu=73$, $\sigma=3.90$, 17 females, 11 males) were included in this study. The adult participants were part of the SilverSight cohort population (~350 enrolled subjects) at the Vision Institute - Quinze-Vingts National Ophthalmology Centre, in Paris. The child participants were recruited in a primary school in the Paris area. All adult participants were voluntary and gave informed consent for inclusion based on the following criteria: *i*) corrected visual acuity of at least 7/10, or 5/10, in participants younger or older than 70 years, respectively; *ii*) a Mini-Mental State Examination score of 24 or higher; *iii*) no physical inability in terms of locomoting without assistance, and *iv*) no neurological condition. The clinical and functional assessment of adult participants involved: ophthalmological screening (e.g., optical coherence tomography, fundus photography), functional visual screening (e.g., visual acuity, visual field extent, contrast sensitivity, attentional field of view), otorhinolaryngological examination (e.g., audiogram, vestibular function), cognitive-neuropsychological assessment (e.g.,

visuo-spatial memory, mental rotation, executive functions), oculomotor evaluation (e.g., ocular fixation, saccadic control), and a static/dynamic balance assessment. A series of questionnaires were also administered to evaluate the quality of vision with respect to mobility (e.g., fear of fall). Participants habitually wearing far-vision lenses were encouraged to keep their glasses on during the experiment.

Material. The experiment with the adult participants was performed in the Streetlab platform at the Institute of Vision and in a school gymnasium with the child participants. The virtual reality (VR) environment was created using the Unity3D game engine (Unity Technologies) and displayed in a HTC VIVE headset equipped with a Tobii Pro VR binocular eye tracker. Participants were equipped with a VR capable backpack computer (VR One, MSI). As this computer is meant to be dedicated for VR usage, it has no screen and thus experiment control as well as monitoring were performed remotely. Our experimental software and the selected equipment allow the participant to move freely and explore the virtual environment with a feeling of immersion.

The real head position was tracked at 30 Hz by two laser emitters placed 9 m away from each other and at a height of 3 m allowing an experimental capture area of approximately 4.0 x 4.0 m. The HTC VIVE display had a nominal field of view of about 110° (approximately 90 ° per eye) through two 1080 x 1200 pixels displays, updated at 90 Hz. The pixel density of the display was about 12 pixels/degree. The Tobii eye-tracker recorded eye movements at a rate of 120 Hz.

We performed two calibration steps for the eye-tracking device before starting the experiment. The first one involved visualizing a projection of the subject's pupils position into the headset in order for the experimenter to reach the best eye-tracking measurement quality. This can be achieved by regulating the eye tracker camera positions, through the adjustment of the headset's position and the inter-pupillary distance. Second, the subject performed a nine-points calibration without moving their head. To ensure the quality of the calibration procedure, a validation of the same nine points was performed. Whenever the mean angular error of the calibration was above 3°, the calibration process was started over. Validation (and recalibration if required) was performed at the beginning, half-way through and at the end of the experiment. The material used with the child participants was the same as for adults, with the difference that we did not use the Tobii eye-tracking integration with the children.

Environments. The two mazes were composed of 3 corridors, with walls covered by a non-informative homogeneous texture. There were no shadows and the sky was homogeneous in order to prevent the subject from orienting based on the lighting condition. The height of the walls was adapted to be 5 cm taller than the subject's height, in order for all the subjects to have to exact same visual experience. In the **landmark condition**, the Y-maze had equiangular arms separated by 120° (fig. 6.1A). Each corridor was 66 cm large and 190 cm long. Three distal landmarks were placed outside of the maze, that is 10 m above the walls and 20 m from the center of the maze. These were a green star, a blue square and a red circle, each subtending a visual angle of 10° relative to the center of the maze. In the **geometric condition**, the geometric

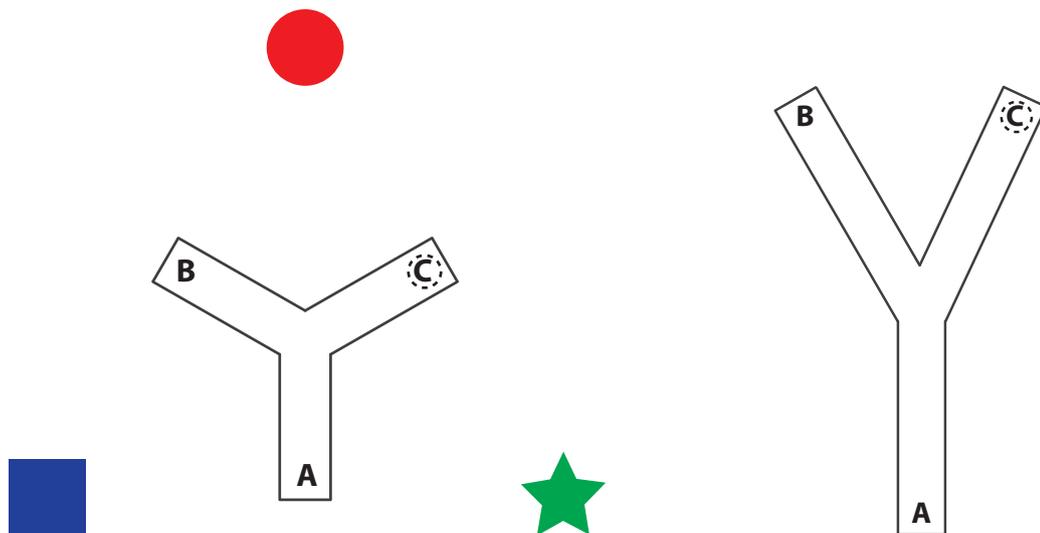


Figure 6.1 – Experimental conditions. In the landmark condition (left), the 3 arms of the maze were equally spaced by 120° and 3 distal landmarks (red circle, green star, blue square) surrounded the maze. In the geometric condition (right), two of the arms were spaced by 55° while the remaining two were separated by 155° . There were no distal landmarks in this condition. The goal location is indicated by the dashed circle. A, B, C represent the starting positions.

polarization of the maze was achieved by an anisotropic arrangement of the 3 arms, with the angle between arms being 155° for two sides and 50° for the last one. Each corridor was 66 cm large and 230 cm long. The corridors were longer in this condition to prevent the subject from seeing the end of corridors when starting from any location. There were no distal landmarks in this condition. Subjects were randomly assigned to the landmark or geometry condition but we ensured an equal distribution of gender throughout the two groups.

Task. During the course of the experiment, the subject was forbidden from walk through the virtual walls and to stand on tiptoes. The subject was disoriented before each trial. This procedure required the subject to hold the experimenter’s hands and be passively lead around the room with eyes closed. We controlled that this procedure was truly effective by asking the subject to try pointing towards the experimental computer. Once disoriented, subjects were positioned at one of four random starting positions facing the centre of the room, in a pseudo-random manner. At the end of each trial, the image displayed in the headset faded and the subject was instructed to stop walking and close their eyes. The experiment proceeded as follows:

1. **Exploration phase.** The experiment started with 3 exploration trials, each one lasting 60 seconds and starting from one of the three starting positions (fig. 6.1, areas A, B and C). There was no specific task during these trials but the participant was instructed to explore the whole environment. Whenever the subject did not explore one of the corridors, the experimenter gave a prompt by saying: "Make sure to explore the whole environment".
2. **Learning phase.** During each trial of this phase, the subject had to find a goal that

triggered a rewarding sound. The goal was located at the end of one corridor (fig. 6.1, area C with dashed line). The starting location (fig. 6.1, area A) was the same throughout the learning phase. The subject was instructed to navigate as directly as possible to the goal zone. The learning phase ended after 4 consecutive successful trials, which were defined as going directly to the goal zone without entering any other corridors.

3. **Testing phase.** The subject was instructed to return to the goal zone and warned that there would be no rewarding signal this time. The starting position during these trials was changed, unknown to the subject, and followed the same pseudo-random order across subjects. The predefined order of starting location areas was: B, A, A, B, A, B. Trials starting from position B were the probe trials.
4. **Debriefing.** At the end of the experiment, the subject had to indicate *i*) the shape of the maze they experienced among 3 different possibilities (a T-maze, a geometrically polarized Y-maze and an equiangular Y-maze), *ii*) the landmarks that they noticed during the experiment between 6 possibilities (blue square, yellow oval, green star, pink rounded-corner square, orange hexagon, red circle), *iii*) the position of the landmarks by drawing them on a top view of the maze and *iv*) the position of the rewarding zone by drawing it on a top view of the maze.

Data analysis. The strategy used by subject was determined by their trajectory during the 3 probe trials of the testing phase. Whenever the subject first entered the actual goal location (fig. 6.1, area C with the dashed line), they were classified as using an allocentric strategy for that particular trial. If they entered area A, the trial was classified as egocentric. We assessed the effect of age and the effect of our experimental conditions (landmark vs. geometry) on the probability of using an allocentric strategy, calculated for each subject.

6.2.3 Results

When considering the landmark condition (fig. 6.2, left), we found a significant effect of age, as the probability of using an allocentric strategy was significantly lower in children ($U = 149, p < 0.01$) and older adults ($U = 188, p < 0.05$), when compared to young adults. There was no difference between the performance of children and older adults ($U = 243, p = 0.86$). The probability of using an allocentric strategy thus formed an inverted U-profile when landmarks were the only source of spatial information.

For the geometric condition, we did not find any evidence for an inverted U-profile related to age. The performance of children did not differ from that of the young ($U = 171, p = 0.10$) and older ($U = 187.5, p = 0.71$) adults. Young and older adults' performance did not differ either ($U = 162, p = 0.07$).

When compared to the landmark condition, having a geometric polarization significantly increased the probability of using an allocentric strategy in children ($U = 156.5, p < 0.01$) and

older adults ($U = 198.5, p < 0.05$) but not in young adults (although approaching the level of statistical significance: $U = 97, p = 0.053$).

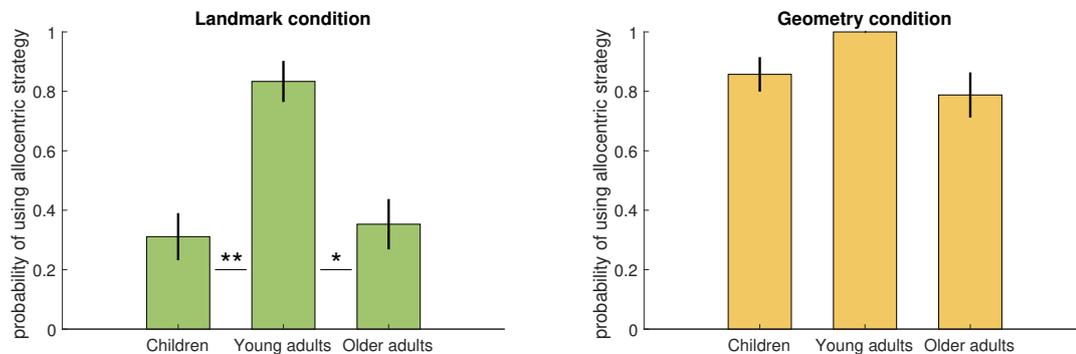


Figure 6.2 – Probability of using an allocentric strategy according to age. In the landmark condition (left), children and older adults were less likely to use the allocentric strategy, when compared to young adults. In the geometry condition (right), the three age groups were equally as likely to use an allocentric strategy. p -values for non-parametric two-sample tests: **** $p < 0.0001$; *** $p < 0.001$; ** $p < 0.01$; * $p < 0.05$.

6.2.4 Discussion

First of all, we replicated the results from Rodgers et al. (2012) showing that older adults are more likely to use egocentric strategies when navigating a Y-maze surrounded by landmarks. We furthermore add that this spontaneous preference is not related to sensory restriction due to desktop VR, given that older adults show this same preference with an immersive HMD, allowing both proprioceptive and vestibular information to be experienced during navigation. Nevertheless, some differences should be pointed out. Indeed the proportion of allocentric strategies used in the study of Rodgers were slightly lower than the current results both in older adults (Rodgers: 18%, current study: 35%) and more so in young adults (Rodgers: 54%, current study: 83%), likely indicating that the reliance on allocentric strategies was potentiated when proprioceptive and vestibular cues were experienced during navigation. Importantly, this holds true only in the case where distal landmarks were the only allothetic source of information available when facing the navigation decision. Another study assessed spatial strategy in older adults using a Y-maze surrounded by landmarks. Parizkova et al. (2018) found very different proportion of allocentric strategies in older adults (Parizkova: 61%, current study: 35%). However, landmarks in their experiment were placed at the very end of the corridors and could thus be used as beacons by the participants, likely explaining the differences.

Regarding development, we extend previous evidence by Bullens et al. (2010) showing a spontaneous preference for egocentric strategies in 10-year-old children. Again, the complex maze proposed by Bullens et al. did not contain any geometric polarization. Together, data across the lifespan confirm the classical inverted U-profile in the use of allocentric strategies, when the only cues available are distal landmarks.

When geometric cues could be used to define the allocentric goal position, the pattern of results changed drastically. The proportion of spontaneous use of allocentric strategies significantly increased in both children and older adults, but not in young adults. We have found that providing geometric cues eliminates age differences, although the ceiling effect observed in young adults shades these results. Altogether, these results suggest that the preference for an egocentric strategy observed in previous studies was actually conditioned by the sensory cues present in the environment rather than a strategic choice per se. Furthermore, these findings highlight the need for reframing the classical allocentric/egocentric dichotomy in order to integrate a landmark/geometry opposition that could better explain age-dependent navigation deficits.

In this experiment, our definition of egocentric or allocentric strategies were to use the body position or external elements as a reference to solve the task, respectively. However, we are aware that navigating to the goal position, as defined allocentrically, can nevertheless encompass different sub-processes varying in their allocentric/egocentric nature. Our hope is that these motion tracking data combined with eye-tracking will be valuable in understanding how the spatial decision is taken relative to the two types of cues and better situate this type of behavior on the egocentric to allocentric continuum. For instance, aligning one's self-view with the view experienced during the learning would be indicative of a rather egocentric kind of behavior whereas a quick decision after an explorative behavior at the start position, would be indicative of a more allocentric repositioning of the self relative to the cognitive map.

CONTRIBUTIONS TO EYE MOVEMENT CONTROL

This chapter presents the secondary contributions which evaluated the effect of aging on eye movement control under laboratory-based controlled conditions. Specifically, we assessed the effect of aging on fixation stability (sec. 7.1), fixational saccades (sec. 7.3) and regular (i.e. large) saccades (sec. 7.4) while proposing a new method for detecting small-size eye movements (sec. 7.2). Two journal papers originated from these works: the article *"Impact of healthy aging on ocular fixation stability"* has been submitted in INVESTIGATIVE OPHTHALMOLOGY AND VISION SCIENCE (IOVS) and second one, *"Unsupervised detection of microsaccades in a high-noise regime"* has been accepted in JOURNAL OF VISION and published in June 2018. The paper concerning the last part of this chapter (fixational saccades, sec. 7.3 and regular saccades, sec. 7.4) is in preparation.

7.1 Fixation area

7.1.1 Article 2: *Impact of healthy aging on ocular fixation stability*

The article below is characterizing the aging effect on ocular fixation stability considering that previous studies have provided inconsistent results. Specifically, we evaluate the influence of factors that have been under-estimated in the literature, such as how the data are cleaned for saccades and blinks before fixation stability being calculated or what techniques are used to estimate fixation stability. It also questions whether we are better or worse at fixating when optic flow conditions are experienced.

Impact of healthy aging on ocular fixation stability.

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Abstract

Ocular fixation stability corresponds to the capacity to maintain an object near the foveal region of the retina and is critical in many daily-life activities, as visual acuity decreases quickly from the fovea to more eccentric areas of the retina. Previous studies have given inconsistent results as to whether or not older adults were capable of maintaining their eyes on a fixation target. This study provides a systematic comparison of the effect of healthy aging on ocular fixation stability with particular attention to methodological issues (removal of blinks and saccades and estimation techniques, i.e. bivariate contour ellipse area or isoline) as well as an assessment of the potentially-challenging effect of optic flow conditions (i.e. the pattern of visual motion that projects to the retina due to the relative motion between an observer and the environment) on fixation stability. Our results showed that the age effect was critically dependent on the data-cleaning method and on the stability estimation techniques employed. Specifically, the age effect disappeared whenever saccades and blinks-related artifacts were accurately removed from the data. Additionally, fixation stability improved whenever visual stimuli were present in the visual field. However, this effect was not specific to the motion pattern of the optic flow.

Keywords: ocular fixation stability, aging, saccades, blinks, bivariate contour ellipse area, isoline, optic flow

Introduction

Ocular fixation stability corresponds to the capacity to maintain an object near the foveal region of the retina (Castet & Crossland, 2012). When attempting to fixate, our eyes

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are never completely still as oculomotor events such as slow drift, microsaccades and larger saccades constantly occur (Abadi et al., 2003; Rucci et al., 2007; Martinez-Conde et al., 2004). Fixation stability has a critical effect on vision and on many daily-life activities such as reading (Crossland et al., 2004; Falkenberg et al., 2007), given that visual acuity declines quickly from the fovea to more eccentric areas of the retina Jacobs (1979); Leigh & Zee (2015).

Fixation stability is influenced by a variety of intrinsic or extrinsic factors. Indeed, factors such as the type of fixation target, degree of immobilization of the head, the measuring instruments and methodology of quantification can affect stability (Castet & Crossland, 2012; Dunbar et al., 2010; Snodderly & Kurtz, 1985; Steinman et al., 1982; Thaler et al., 2013). Additionally, fixation stability (and eye movements in general) is altered in a number of pathologies such as macular diseases (Crossland et al., 2004), Alzheimer's disease (Kapoula et al., 2014) or schizophrenia (Gooding et al., 2000). Healthy aging can also cause a number of oculomotor changes (Peltsch et al., 2011; Sheynikhovich et al., 2018), however, very few studies have examined the consequences of aging on ocular fixation stability. Furthermore, these studies provided inconsistent results. Some studies found no age-related differences in ocular fixation stability (Kosnik et al., 1986, 1987; Crossland et al., 2008) whereas others reported larger fixation areas in older adults as compared to young adults (Cutini et al., 2014; Agathos et al., 2015; Morales et al., 2016).

Part of this discrepancy in the literature may be related to methodological differences. First, the measuring instruments varied across studies, with the use of microperimeter devices (Cutini et al., 2014; Agathos et al., 2015; Morales et al., 2016) revealing a significant age effect whereas this was not the case with the use of infrared eye-trackers (Kosnik et al., 1986, 1987; Crossland et al., 2008). This tendency may be explained by the fact that eye tracker devices allow for a more accurate removal of blinks artifacts and saccades whereas the sampling frequency of the microperimeter is not high enough to accurately detect saccades. Second, most of the studies used the bivariate contour ellipse area (BCEA) (Steinman, 1965) to quantify fixation stability. This method has been shown to be sensitive to outlying eye positions (e.g. eccentric saccadic movement) and furthermore makes the assumption of a Gaussian distribution of the data, an assumption that is often not respected with eye position (Castet & Crossland, 2012). Recommendations have been made for using outlier-resistant methods such as the isoline, which estimates fixation stability based on the density of data points and allows for multiple loci of fixation (Whittaker et al., 1988; Castet & Crossland, 2012). Thus, given that blinks, saccades and the use of the BCEA technique can potentially increase the measured ocular fixation area, the first objective of this study is to provide an systematic comparison of the effect of blinks/saccades removal and the two quantification techniques (BCEA and isoline) in order to understand whether age influences ocular fixation stability.

In more natural conditions, e.g. when we are walking in a structured environment, the patterns of optic flow projecting on the retina may challenge fixation stability as well. Indeed,

depending on the direction of gaze and travel, the generated retinal motion will be stabilized by ocular reflexes (e.g. the optokinetic reflex) (Lappe et al., 1998, 1999; Angelaki & Hess, 2005), that are suppressed whenever a visual anchor is available in the visual scene (e.g., when a person needs to fixate a target while walking (Lappe & Hoffmann, 2000; Williams et al., 2006; Wyatt et al., 1995)). The role of optic flow has been studied for many processes such as postural control, the perception of heading direction or obstacle avoidance (Warren et al., 1991, 1988; Warren, 2013; Angelaki & Hess, 2005; Lappe et al., 1999). Fixation stability under conditions of optic flow, however, has never been documented, to our knowledge. Laurens and colleagues (2010) have shown that visual tracking of a moving dot over a stationary background, a condition that generates retinal flow, had a stabilizing effect on posture (Laurens et al., 2010). We will test whether the same stabilizing effect applies to ocular fixation stability.

Given that possible age-related ocular stability impairments can lead to visual perception losses (Castet & Crossland, 2012), the overarching objectives of this study is to assess *i*) the effect of healthy aging on ocular fixation stability with particular attention to methodological issues (removal of blinks or saccades and estimation techniques, i.e. BCEA or isoline) and *ii*) the effect of optic flow conditions on fixation stability.

Methods

Participants

One hundred and nineteen adults (range: 21-83 yrs, $\mu=53$ $\sigma=21$, 74 females and 45 males) participated in this study. Among these, 6 participants were not able to complete the protocol due to difficulties in tracking the eye (cataract implants, wide ptosis) or discomfort during the task. This led to a total of 113 participants performing the fixation task. The participants were part of the SilverSight cohort population (~350 enrolled participants) at the Vision Institute - Quinze-Vingts National Ophthalmology Centre, in Paris. All screening and experimental procedures were in accordance with the tenets of the Declaration of Helsinki and were ethically approved by "CPP Ile de France V" (ID-RCB 2015-A01094-45, n. CPP: 16122 MSB). All participants were included based on the following criteria: *i*) corrected visual acuity of at least 7/10, or 5/10, for participants younger or older than 70 years, respectively; *ii*) a Mini-Mental State Examination score of 24 or higher; *iii*) able to ambulate freely without assistance, and *iv*) no neurological condition. The clinical and functional assessment of the participants involved: an ophthalmological screening (e.g., optical coherence tomography, fundus photography), a functional visual screening (e.g., visual acuity, visual field extent, contrast sensitivity, useful field of view), an otorhinolaryngological examination (e.g., audiogram, vestibular function), a cognitive-neuropsychological assessment (e.g., visuo-spatial memory, mental rotation, executive functions) and a static/dynamic balance assessment. A series of questionnaires were also administered to evaluate the quality of vision with respect to mobility (e.g., fear of falling). During the experiment, the participants wore

trial frames to achieve their best-corrected visual acuity, as blurring of the visual target has been shown to influence fixation stability (Ukwade & Bedell, 1993; Ghasia & Shaikh, 2015). We included an addition up to +1.75 dioptres to the refractive error to reduce the accommodation demands for the participant-screen experimental distance. All participants were recruited on a voluntary basis and gave their written consent before enrollment in the study.

Setup

The experiments were carried out at the Institute of Vision, in Paris. Eye movements were recorded with a monocular eye-tracker (Eyelink 1000, Tower mount, SR Research Ltd., Ontario, Canada, instrument noise: 0.01° RMS) on the dominant eye and at a 1000 Hz frame rate. Due to operating errors however, 9 of the 113 participants were recorded at 500 Hz. Psychophysics toolbox-generated stimuli (Cornelissen et al., 2002) were displayed on a screen (1280×1024 pixels, 60 Hz, 32 bits, RGB), placed 57 cm away from the participant's eye, at eye level. For this particular distance, the screen covered $30^\circ \times 38^\circ$ of visual angle.

Protocol

The experiment was performed in the dark and in head-fixed condition with a chinrest. The protocol included a fixation task and a saccade task, the later not being presented here. During the fixation task, participants had to fixate a central cross (figure 1F), which consisted of a bull-eye shaped target (Thaler et al., 2013), white on a black background, covering $0.6^\circ \times 0.6^\circ$ of visual angle. The fixation target was presented either alone (condition 1, fig. 1A) or superimposed on different optic flow patterns (conditions 2 to 4, fig. 1BCE). Optic flow patterns were generated by moving the observer (camera) through a volume of space filled with spheres. Each volume contained 1230 spheres. Three flow types were created: an expanding radial optic flow at a speed of 1.38 m/s (condition 2, fig. 1B); a tangential optic flow with a speed of 1.38 m/s (condition 3, fig. 1C); and an expanding radial optic flow with a speed of 6 m/s (condition 4, fig. 1D). A 5th control condition was added to the protocol whereby a static white noise was displayed (condition 5, fig. 1E). This condition allowed us to test if the presence of static spheres (and not the motion pattern of the optic flow) was sufficient to influence fixation stability. In this condition 200 spheres were displayed randomly on the screen. The size and lifespan of each sphere were random (1 to 7 pixels, 0.2 to 2 seconds, respectively). The protocol involved 10 trials for each of conditions 1-4, and 5 trials for the control condition 5, i.e. a total of 45 trials. Each trial lasted 32 seconds. The presentation order of trials and conditions was randomized across participants. A nine-point calibration was performed at the beginning of the experiment and after each break. Participants were encouraged to take breaks as needed. The entire session lasted approximately 90 minutes, breaks included.

The visual screening of the participants was performed before the experiments. It included, among others, measures of binocular best-corrected visual acuity (ETDRS chart

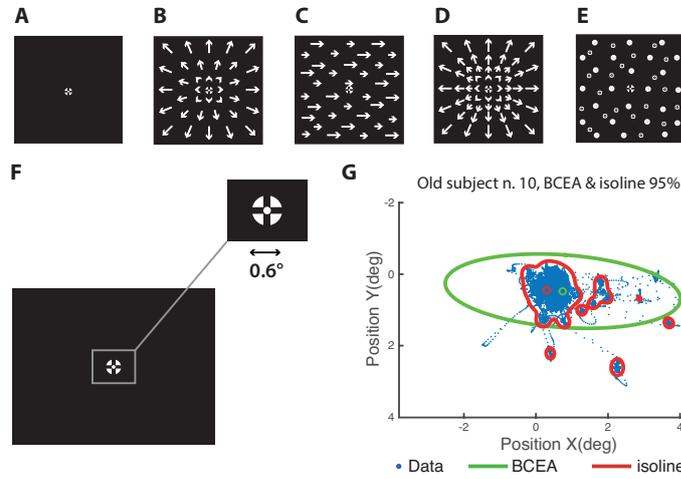


Figure 1. Ocular fixation task. (A) Condition 1: the fixation cross is presented on a homogeneous black background. (B) Condition 2: schematic representation of the radial optic flow (speed 1.38 m/s). (C) Condition 3: schematic representation of the tangential optic flow (speed 1.38 m/s). (D) Condition 4: schematic representation of the radial optic flow (speed 6 m/s). (E) Condition 5: schematic representation of white noise (no motion). (F) Fixation target used during the experiment. (G) Example of BCEA and isoline-based fixation stability estimation.

at 2m distance, in scotopic condition, with the best optical correction), binocular visual field (Perimeter Octopus 900 with constant luminosity and stimulus size, in scotopic condition) and visual attention (central [UFOV1] and peripheral visual discrimination task, without [UFOV2] and with [UFOV3] visual distractors). We report the performance on the UFOV task is expressed as the stimulus display time needed to perform the task, in milliseconds (Ball et al., 1993).

Data analysis

The first 2 seconds of recording were removed, as it corresponded to the period where the participant produced saccades to reach the target. Saccades and blinks were detected automatically by the Eyelink algorithm. Saccades (velocity threshold: $30^\circ/s$, acceleration threshold: $8000^\circ/s^2$, position threshold: 0.15°) and blinks (with additional removal of the 100 ms before and after each blink) could be removed or not before the ocular fixation stability was calculated. Whenever this cleaning process eliminated more than 50% of the data points, the entire trial was discarded. The eye position traces were then smoothed with a 2^{nd} order low-pass Butterworth filter with a 60 Hz cutoff frequency. The pupil size (in arbitrary units, (SR-Research, 2006)) was provided by the Eyelink system.

We considered two techniques to quantify fixation stability. The bivariate contour ellipse area (BCEA) calculates the ellipse that contains a given proportion of data according

to:

$$BCEA = 2k\pi\sigma_h\sigma_v(1-p^2)^{\frac{1}{2}}$$

where σ_h and σ_v are the standard deviation on the horizontal and vertical meridian, respectively, and p the product-moment Pearson correlation of both meridians. k is relative to the chosen probability:

$$P = 1 - p^{-k}$$

when k is equal to 1, the ellipse contains 63.2% of the data. In this experiment, we considered a P of 95%.

The isoline technique (Whittaker et al., 1988) consists in estimating a probability density function relative to a sample of data by using kernel density estimation:

$$\hat{f}_h(x) = \frac{1}{N} \sum_{i=1}^N K_h(x - x_i)$$

with K denoting the kernel, and h the Gaussian smoothing window size (or bandwidth). In this study, we empirically chose a bandwidth size of 0.125 and considered density levels corresponding to 95% of the data points. The area containing these data points is then calculated.

As shown in figure 1G, the BCEA method is more sensitive to eccentric eye positions than the isoline technique. The isoline-based area calculation is influenced solely by ranges where the density of eye position is high. On the other hand, the BCEA method encompasses areas where there are no actual eye positions recorded.

Statistics

Where applicable, data were preferentially analyzed by using paired or two-sampled t-tests. Normality of the data was verified quantitatively by visual inspection of Q-Q plots. When normality and homoscedasticity were dubious, we first employed a Box-Cox transformation to achieve normality and equalize variance (Osborne, 2010). If this procedure was ineffective, we used the non-parametric Wilcoxon signed-rank test and Friedman ANOVAs for paired samples and the Mann-Whitney test in case of independent samples. Partial correlations were computed between oculomotor and visual variables, controlling for the subject's age. Alpha level for statistical significance was set at $P < 0.05$.

For each analysis, we identified outlying participants based on Cook's distance method (Cook, 1977) and discarded any point over $4/n$ where n is the number of participants. The number of outliers can be inferred from the degree of freedom used for each statistical analysis. The age factor was either considered as a continuous factor (e.g. for linear regression) or as a categorical factor (with all participants under 40 or over 65 years old considered as "Young adults" or "Older adults", respectively) when needed.

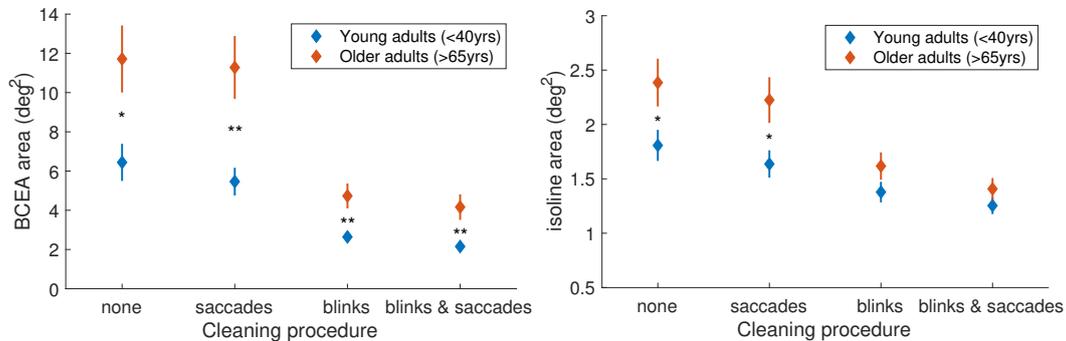


Figure 2. (A, B) Systematic comparison of the effect of saccades and blinks removal on the fixation area, for the BCEA and the isoline estimation techniques. p -value. **** $p < 0.0001$; *** $p < 0.001$; ** $p < 0.01$; * $p < 0.05$ for two-sampled t -tests. Error bars correspond to standard error of the mean.

Results

Influence of aging

In order to understand the effect of saccades/blinks removal, we performed a systematic comparison of removal across the two different techniques for estimating the fixation area (isoline and BCEA). All the analysis presented in this section were carried out on data collected during the condition 1, i.e. when the fixation target was presented on a homogeneous background.

We have found that the BCEA technique (fig. 2A) entailed larger fixation areas than the isoline (fig. 2B). Indeed, fixation areas quantified with a BCEA were up to 5 times larger than with the isoline method. These areas were implausibly large, especially when no cleaning method was applied. For instance, BCEA areas were up to 12° in older adults, which would represent 20 times the size of the fixation target. In addition, removing saccades had little effect on fixation area calculation whereas most of the variance was related to blink removal. This can be comprehended by the fact that saccades are very rapid eye movements. The saccade trace is thus associated with very low density of eye positions that does not critically influence area calculation.

When comparing the effect of age, we have found that older adults produced more saccades when attempting to fixate ($U = 2341, p < 0.0001$; fig. 3A) and those were larger in amplitude when compared to young adults ($U = 1321, p < 0.01$; fig. 3B). Blink rate was however comparable between the two age groups ($U = 1948, p = 0.26$; fig. 3C). On average, the age differences on the calculated fixation area were reduced (BCEA) and even disappeared (isoline) when saccades and blinks were removed from the data (cf. two-sampled t -tests on fig. 2AB). This was confirmed when examining the BCEA ($t_{(105)} = 2.1, p < 0.05$) and isoline ($t_{(100)} = 0.94, p = 0.35$) areas, cleaned for saccades and blinks, across all ages (fig. 4AB).

It seems that removing blinks in older, as compared to young adults' data, had a larger impact on the measured fixation area (cf. steepest decrease of the fixation area in older adults

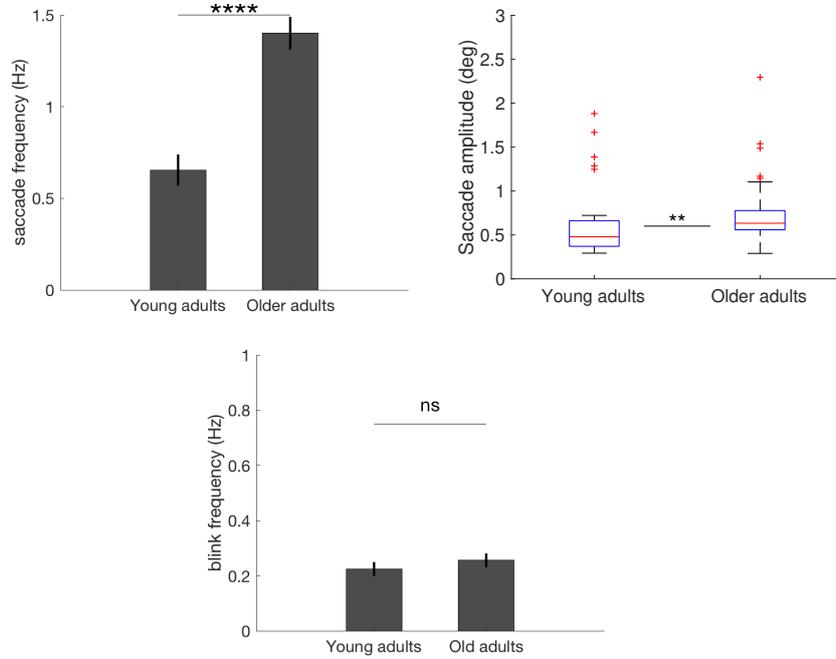


Figure 3. Older adults produced saccades that were more frequent (A) and larger (B) when attempting to fixate on the target. Blink rate was comparable between the two age groups (C). *p*-values: **** $p < 0.0001$; *** $p < 0.001$; ** $p < 0.01$; * $p < 0.05$. The mention 'ns' stands for not significant.

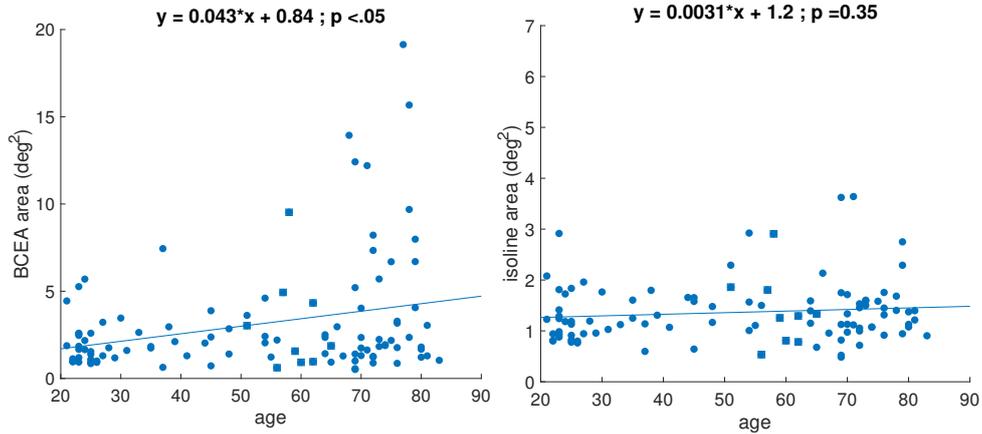


Figure 4. The age differences on the calculated fixation area were reduced (BCEA, A) and even disappeared (isoline, B) when saccades and blinks were removed from the data. The parameters for the linear regression with age and the associated *p*-value are indicated above the graphs. Participants identified by a square were recorded at 500 Hz, all other participants were recorded at 1000 Hz. Error bars correspond to standard error of the mean.

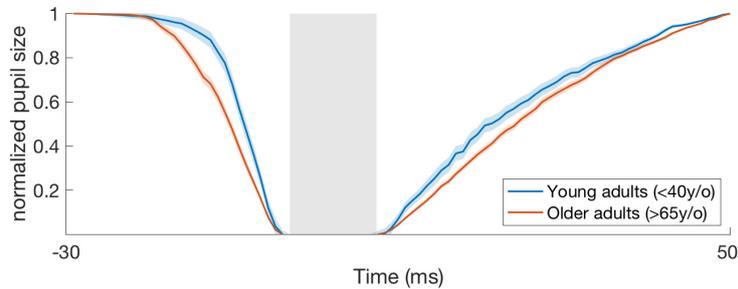


Figure 5. Spatio-temporal dynamics of a blink as estimated from the pupil size. Older adults had a different blink dynamic when compared to young adults as areas under the curve differ between the two age groups. The grey area represents a blink. The light colored areas correspond to standard error of the mean.

when removing only blinks, fig. 2AB). This result appears incoherent, at first glance, with the fact that young and older adults had a similar blink rate. An alternative hypothesis would be that the apparent larger effect of cleaning blinks in older adults is related to a different temporal dynamic of blinks in this group. To test this hypothesis, we considered the normalized pupil size around a blink period as a proxy of how rapidly the pupil will get masked by the eyelid. Consistent with our hypothesis, the eyelid masking velocity was slower in older adults relative to the young (fig. 5). This was confirmed by a statistical difference in terms of area under the curves, associated with each groups ($t_{(81)} = 2.27, p < 0.05$).

The question remains as to which technique (BCEA or isoline) should be considered when assessing fixation capacity. As highlighted by Castet & Crossland (2012), the BCEA technique is sensitive to outlying eye positions. For instance, whenever the participant trigger an unwanted saccade during the task, this will be associated with an excentric, fixation-related, eye positions. The BCEA will be highly influenced by these islands of fixation, unlike the isoline, which allows for multiple loci of fixation. An example of this issue can be seen on figure 1G, where the BCEA encompasses area where the density of eye fixation is null. Thus, because both young and older adults triggered some saccades when attempting to fixate and because isoline seems to be a better measure of fixation per se, we will thus prefer to quantify fixation area with the isoline, on data cleaned for saccades and blinks for all subsequent analyses.

We next considered whether the capacity to maintain a stable fixation was further influenced by factors intrinsic to the participant, such as visual acuity, attention capacity or fatigue during the experiment. We thus correlated our results to the visual function assessments that our participants performed before being included in this study and assessed potential fatigue-related effect by analyzing the variability of the fixation area for a particular trial and between trials.

Between (fig. 6A) and within-trial variability (fig. 6B) were similar for the two age groups. There was no effect of trials (fig. 6A) on the estimated fixation area for both young

(Friedman ANOVA, $\chi^2=10.84$, $p=0.28$) and older participants (Friedman ANOVA, $\chi^2=18.85$, $p=0.22$). The fixation area thus appears to be constant throughout the experiment and does not seem to be influenced by potentially accumulated fatigue. There was no within-trial difference between the two age groups when considering the area under the curves for each group ($U = 899$, $p=0.37$, fig. 6B). Over the course of the 30-second trial, the increase of the cumulative fixation area is steeper before 15 seconds than after. In trying to identify visual correlates of fixation stability, we computed partial correlations controlling for the age variance. We found that the measure of selective attention (useful field of view subtask 3: selective attention) significantly correlated with the size of the fixation area ($r=0.33$; $p<0.05$), indicating that the ability to maintain the eyes on a target is in part an attention-related process (fig. 6C). No other visual functions correlated with the fixation stability.

Influence of optic flow

Having established that the isoline method is a suitable measure of ocular fixation, we applied it to answer the novel question of how optic flow influences ocular fixation in young and older participants. To do so, we expressed performance under optic flow conditions as a change in ocular fixation area relative to the condition 1, as follows:

$$\frac{(\textit{Fixation area}_1 - \textit{Fixation area}_n)}{\textit{Fixation area}_1}$$

We found that conditions 2 to 5 lead to a shrinking of the fixation area, relative to condition 1 (one-sample t-tests against zero value for data averaged across conditions 2–5 in young adults: $t_{(36)}=2.63$, $p<0.05$ and old adults: $t_{(45)}=7.89$, $p<0.0001$, fig. 7). The shrinkage was larger in older adults when compared to young adults particularly in condition 3 (tangential flow: $t_{(76)}=3.68$, $p<0.001$) and condition 5 (control condition: $t_{(78)}=4.31$, $p<0.0001$). There was a significant effect of conditions in older adults (Friedman ANOVA, $\chi^2=13.29$, $p<0.01$) but not in young adults (Friedman ANOVA, $\chi^2=5.73$, $p=0.13$). However, the fact that we found no difference between optic flow conditions (averaged over condition 2, 3 and 4) and the control condition (condition 5) either in young ($W = 1078$, $p=0.73$) or in older participants ($W = 859$, $p=0.41$) seems to indicate that the decreased fixation area was not specific to the motion pattern in the optic flow conditions but rather to the presence of stimuli in the visual field, in general.

Discussion

This study provided a systematic comparison of the effect of *i*) data cleaning (for saccades and blink-related artifacts), *ii*) stability quantification techniques (BCEA and isoline) and *iii*) optic flow conditions on fixation area, in order to assess fixation stability modulation related to healthy aging. Our results show that the age effect was critically dependent on the cleaning method and on the stability estimation techniques employed. Fixation stability was

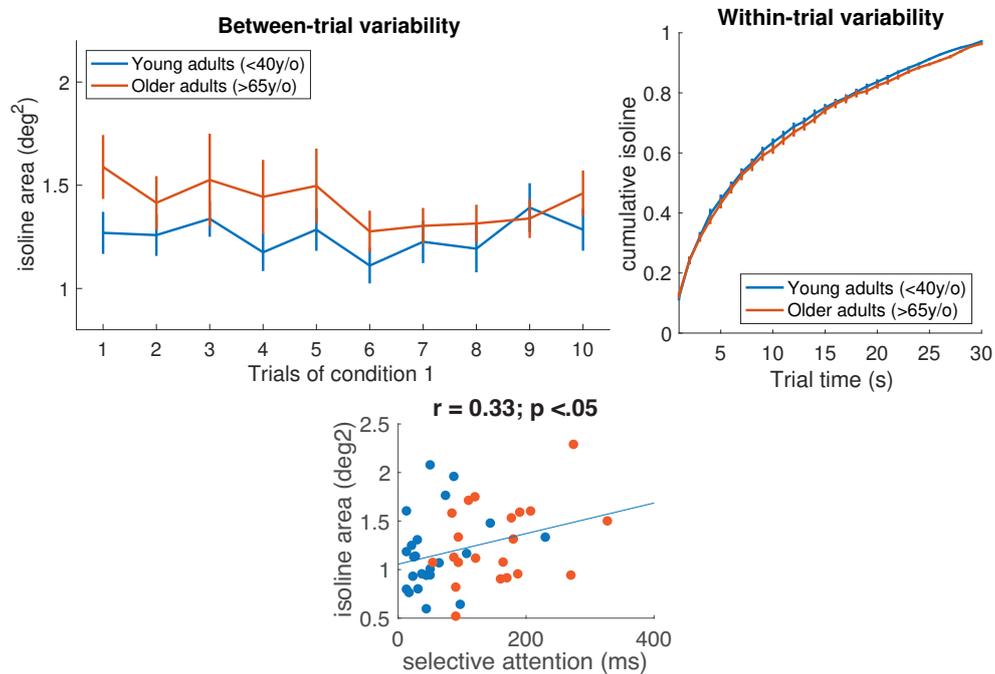


Figure 6. (A) Between and (B) within-trial variability on the isoline areas during condition 1: variability was similar between the two age groups. (C) Partial correlation between selective attention and isoline area: larger areas were associated with lower selective attention capacity (UFOV subtask 3), when taking out the aging variance. Error bars correspond to standard error of the mean.

further associated with the visual attention capacity of the participant but not with fatigue-related measures. Finally, fixation stability improved whenever visual stimuli were present in the visual field. This effect was not specific to the motion pattern of the optic flow.

Specifically, we have found that the aging effect on fixation stability disappeared whenever the data were accurately cleaned for remaining saccades and blinks-related artifacts. Saccades were more frequent and blink artifacts had a different dynamic in older adults. We believe that our results reconcile previous studies that have provided inconsistent evidence for the age-related influence on ocular fixation stability (Kosnik et al., 1986, 1987; Crossland et al., 2008; Cutini et al., 2014; Agathos et al., 2015; Morales et al., 2016), by proposing that the age effect is critically dependant on the cleaning/fixation estimation methods used. When the data were accurately cleaned and thus considering only pure fixation period, older adults were just as efficient as the young to maintain their eyes on the target. Both groups maintained their eyes on an area that was a little over twice the size of the fixation target (i.e. an area of approximately 1.5° on a target that represented 0.6° of the visual field). This was well within the size of the fovea, i.e. the central 2° of the visual field, where visual acuity is higher (Jacobs, 1979; Leigh & Zee, 2015). Accordingly, the fixation performance of both young and older adults, would be classified as stable, when considering Fujii's classification (Fujii

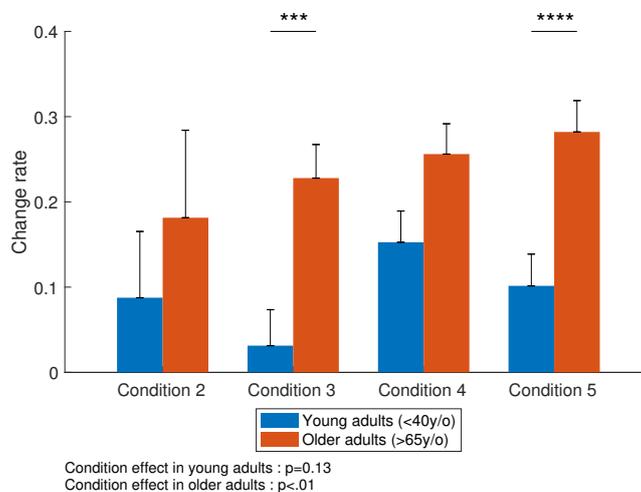


Figure 7. Effect of optic flow and control conditions, expressed relative to condition 1. Positive values indicate a smaller fixation area in optic flow and control conditions, relative to condition 1. All conditions led to a lower fixation area relative to the performance in condition 1, i.e. when the fixation cross is presented on a homogeneous background. This effect was larger in older adults. Stars on top of the graph indicate significance of two-sample t-tests with **** $p < 0.0001$; *** $p < 0.001$; ** $p < 0.01$; * $p < 0.05$. Error bars correspond to standard error of the mean.

et al., 2002). The BCEA entailed implausibly large fixation areas, especially when no cleaning method was applied. Indeed, the BCEA area could rise until approximately 12° , which would represent 20 times the size of the fixation target. This is related to the already-known sensitivity of this technique to outlying eye positions (Castet & Crossland, 2012; Steinman, 1965). Coherently with this, we have found that BCEA encompassed an area where eye position density was null. We would thus argue that the isoline technique should be used more frequently in future studies.

Whereas there is no doubt that blink-related artifacts must be considered and cleaned, fixation-related saccadic movements need more attentive consideration. Indeed, the saccadic movements produced during a fixation task could be either microsaccades, saccadic intrusion or larger illicite saccades. If microsaccades and saccadic intrusions (if small and not too frequent, Ciuffreda et al. 1983) are considered useful to vision by either counteracting visual fading (Martinez-Conde et al., 2006) or recentering the line of sight (Ko et al., 2010), the production of saccades during fixation is detrimental to vision, as they bring the object further from fovea. In our data, saccadic movements produced by young adults were mostly in the range of microsaccades (Poletti & Rucci, 2016), i.e. with a median amplitude of 0.5° . This is coherent with the previously reported increased rate and amplitude of saccadic intrusion (McGivern & Gibson, 2006; Herishanu & Sharpe, 1981; R. V. Abadi & Gowen, 2004) or illicite saccades (Beurskens & Bock, 2012) in older adults. On the other hand, the age-related impact on the rate of microsaccades has been poorly and inconsistently characterized (Gao et

al., 2018; Port et al., 2015). The systematic characterization of saccade-like movements was beyond the scope of the current paper however and the issue will be assessed by the authors in a future study.

Our results suggests that visual attention, and more precisely selective attention capacity, is related to the capacity of the participant to maintain a stable fixation on a centrally presented target. Specifically, a lower stability (and thus larger fixation area) was associated with lower attention capacities, even after controlling for the participants' age. In this test, the participant has to process two stimuli, one presented centrally, the other peripherally, in presence of visual distractors. Although the UFOV protocol is different to our fixation task in several respects, it nevertheless suggests, coherently with Agathos et al. (2015), that maintaining fixation over a long period of time involves attention-related mechanisms. On the other hand, fixation stability was constant and reproducible with regards to the number of trials, at least when considering the isoline estimation techniques. Coherently with previous evidences (Kosnik et al., 1986), this indicates that the fatigue accumulated from the repetition of trials does not influence fixation stability. Finally, the fact that the fixation area increases more linearly after 15 seconds of recording would suggest that the length of a trial can be restricted to roughly 15 seconds for an accurate assessment of fixation stability. While other visual functions, such as visual acuity, are likely to be contribute to a stable fixation (Ghasia & Shaikh, 2015; Alexander et al., 2018), our results argue against this, as no other visual measures were associated with fixation stability. This may be related to the fact that our participants were meticulously screened to exclude any potential visual impairment.

Finally, fixation stability was increased whenever visual stimuli were present in the visual field, and to a greater degree in older adults. This was, however, not specific to optic flow per se as the control condition, which does not contain any motion pattern, had a stabilizing effect just as well. We propose that this type of stimulation could be used by experimenters, whenever a stable fixation is required. Nevertheless, it is also possible that the fixation area measure is not sensitive enough to accurately assessed the effect on optic flow and that a finer grain eye movements analysis (microsaccades, drift) will help understand the impact of optic flow on eye movements (Laubrock et al., 2008; Piras et al., 2016).

As a conclusion, when considering pure fixation period, older adults were just as efficient as young adults in maintaining their eyes on a fixation target. However, older adults were more prone to produce saccadic movements when attempting to fixate. Whether this entails a detrimental effect on vision should be assessed in future studies, by adding a perceptual demand (e.g. adding a visual discrimination task) to the fixation task.

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7.2 Microsaccades detection

7.2.1 Article 3: *Unsupervised detection of microsaccades in a high-noise regime*

As highlighted in the previous section, we need to study finer-grain eye movements in order to understand more clearly the effect of aging and optic flow conditions on the oculomotor control.

Some technological issues must be surpassed beforehand. Indeed, video-based eye trackers are by far the most used in human studies (Irving et al., 2006; Port et al., 2015; Holmqvist et al., 2011). Pupil detection problems, caused by optical artifacts or eye-related disorders (e.g., miosis, ptosis; Salvi et al., 2006; Damasceno et al., 2015; Loewenfeld, 1979), often result in a high-frequency recording noise in these systems (Holmqvist et al., 2011). Because previous microsaccade detection methods are based on velocity thresholds, the presence of a high noise regime critically interferes with microsaccade detection by increasing the frequency of false positives that biases statistical analyses.

Here we propose a new technique, based on a clustering algorithm, that accurately detect saccades and microsaccades. Also very useful in the aging research, this method can be extended to other domains, as it outperforms other techniques in high noise regime but perform just as well otherwise. It is further more a simple and faster techniques that eliminate the need for time-consuming manual reprocessing or loss of candidates microsaccades.

Unsupervised detection of microsaccades in a high-noise regime

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Micromovements of the eye during visual fixations provide clues about how our visual system acquires information. The analysis of fixational eye movements can thus serve as a noninvasive means to detect age-related or pathological changes in visual processing, which can in turn reflect associated cognitive or neurological disorders. However, the utility of such diagnostic approaches relies on the quality and usability of detection methods applied for the eye movement analysis. Here, we propose a novel method for (micro)saccade detection that is resistant to high-frequency recording noise, a frequent problem in video-based eye tracking in either aged subjects or subjects suffering from a vision-related pathology. The method is fast, it does not require manual noise removal, and it can work with position, velocity, or acceleration features, or a combination thereof. The detection accuracy of the proposed method is assessed on a new dataset of manually labeled recordings acquired from 14 subjects of advanced age (69–81 years old), performing an ocular fixation task. It is demonstrated that the detection accuracy of the new method compares favorably to that of two frequently used reference methods and that it is comparable to the best of the two algorithms when tested on an existing low-noise eye-tracking dataset.

saccadic intrusions, fixational saccades, or microsaccades), drift, and tremor (Steinman, Haddad, Skavenski, & Wyman, 1973; Abadi, Clement, & Gowen, 2003; Collewijn & Kowler, 2008). During the last decades FEM research has gained a renewed interest due to the possible involvement in perception and attention (Engbert, 2006; Hafed, Chen, & Tian, 2015) and to neurophysiological evidence showing that neural activity is sensitive to different types of FEMs (Martinez-Conde, Macknik, & Hubel, 2000; Kagan, Gur, & Snodderly, 2008). While little functional significance has been attributed to tremor, multiple roles for drift and fixational saccades were suggested. These include error correction (Cornsweet, 1956; Poletti & Rucci, 2010), gaze relocation in high-acuity tasks (Ko, Poletti, & Rucci, 2010; Tian, Yoshida, & Hafed, 2016), enhancement of high-frequency content in input images (Kuang, Poletti, Victor, & Rucci, 2012), and prevention of image fading (Ditchburn, Fender, & Mayne, 1959; Martinez-Conde, Macknik, Troncoso, & Dyar, 2006, but see Collewijn & Kowler, 2008; Poletti & Rucci, 2010). In addition, eye movements, including microsaccades, have been linked with postural sway (Hunter & Hoffman, 2001; Jahn, 2002; Rolfs, Engbert, & Kliegl, 2004). In a more cognitive domain, timing of microsaccades has been associated with shifts in covert attention (Hafed & Clark, 2002; Engbert & Kliegl, 2003; Yuval-Greenberg, Merriam, & Heeger, 2014) and was shown to correlate with the task-induced cognitive load (Bonneh, Adini, Fried, & Arieli, 2011). Given these diverse functional roles of FEMs, eye movement analysis is often used as a diagnostic tool in clinical and aging research (Leigh & Zee, 2015). In particular,

Introduction

During visual fixation, the eyes produce small involuntary movements, called fixational eye movements (FEMs), which are conventionally separated into saccadic-like jumps (more generally referred to as

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changes in eye movement properties with respect to age-matched controls have been characterized in patients with age-related macular degeneration (Moller & Bek, 1998; Macedo, Crossland, & Rubin, 2011), glaucoma (Crabb, Smith, & Zhu, 2014), Parkinsonian disorders (Otero-Millan et al., 2011), and Alzheimer disease (Parkinson & Maxner, 2005; Kapoula et al., 2014).

The utility of FEM analysis in clinical and aging research critically depends on the availability of reliable detection methods for different types of FEMs. The quality and complexity of an appropriate detection method is in turn determined by the type of hardware and the associated quality of FEM recordings. While high precision eye trackers, such as those based on electromagnetic coils and dual-Purkinje images, are sometimes used in eye movement research (rarely in humans, Kagan et al., 2008; Poletti, Rucci, & Carrasco, 2017; more often in primates, Hafd et al., 2011), video-based eye trackers are by far the most used in human studies, including aging research (Irving, Steinbach, Lillakas, Babu, & Hutchings, 2006; Holmqvist et al., 2011; Port, Trimmerger, Hitzeman, Redick, & Beckerman, 2016). These eye trackers are readily available and easy to maintain, they do not require subjects to wear lenses, and they do not limit the visual field of recording (in contrast to some high-precision recording systems; Holmqvist et al., 2011), which are important practical constraints in aging research.

The dominating method used to estimate gaze direction in video-based systems consists in tracking the position of the pupil in a video recording of the eye. Pupil detection problems, caused by optical artifacts or eye-related disorders, often result in a high-frequency recording noise in these systems (Holmqvist et al., 2011). This is especially true for aged subjects, since “dropping eyelids” caused by fatigue or age-related abnormalities constitute a frequent phenomenon (Nyström, Andersson, Holmqvist, & van de Weijer, 2013; Damasceno et al., 2015). Such a high-frequency noise leads to inaccuracies of microsaccade detection methods that are based on velocity thresholds, since these thresholds are usually chosen depending on the velocity distribution in the sample (Engbert & Mergenthaler, 2006; Otero-Millan, Castro, Macknik, & Martinez-Conde, 2014). A substantial amount of high-frequency noise leads to an excessively elevated threshold value, leading to a massive loss of microsaccades and hence potentially biased statistical analyses. More recently, Bayesian methods were developed for (micro)saccade detection that are not based on velocity thresholds but assume a particular generative model for saccades and Gaussian noise sources (Daye & Optican, 2014; Mihali, van Opheusden, & Ma, 2017).

In this paper we propose a new (micro)saccade detection method, based on an unsupervised clustering

approach, that can effectively separate fixational microsaccades from high-frequency recording noise. The accuracy of the method is assessed on a new labeled dataset consisting of experimental recordings from aged subjects. The method is compared with previous methods in terms of performance and practical use, and finally, a procedure for tuning its main free parameter from the experimental data is proposed.

Methods

Data collection

Eye-position data were recorded monocularly from 14 subjects aged 69–81 years (75.27 ± 4.25). The participants were recruited as part of the Silversight cohort study (Vision Institute, Paris, France) and they were ascertained to have no visual, audio-vestibular, neuropsychological, or cognitive losses. Subjects with refractive errors larger than $+4.00\delta$ or lower than -4.00δ , astigmatism larger than 1δ , visual acuity lower than 8/10 (0.1 logMAR), or dissociate phoria larger than 6δ were excluded. The clinical screening was ethically approved by the “CPP Ile de France,” and it was carried out under medical supervision at the Clinical Investigation Center of the Quinze-Vingts Ophthalmologic Hospital, Paris.

The EyeLink 1000 (SR Research Ltd., Ontario, Canada) static tower-mounted video-based eye tracker with forehead and chin rest was used for recordings at 1-kHz frequency and manufacturer-stated spatial resolution $<0.01^\circ$ (root-mean-square). Subjects were asked to fixate a bull’s-eye-shaped target ($0.6^\circ \times 0.6^\circ$ of visual angle) at the center of computer screen ($1,280 \times 1,024$ pixels, 60 Hz, 32 bits, RGB) located 57 cm in front of the subject, covering $30^\circ \times 38^\circ$ of visual angle. A 9-point calibration procedure was performed at the beginning of each session for all subjects. The experiments were performed in the dark and throughout the recording subjects wore trial frames to ensure their best corrected visual acuity for this particular eye-screen distance. To reduce accommodative demands, between $+1$ and $+1.75\delta$ was added to the refractive error. Five sessions were performed per subject, 10 trials per session. Each trial lasted 32 s, resulting in 26.66 min total recording time per subject.

In order to quantify the performance of our microsaccade detection method and compare it to other methods, second trials of all experimental sessions were manually labeled, giving rise to five labeled traces per subject. All traces were labeled independently by three experts (including M.B. and C.W.), who marked all microsaccade-like events as either “microsaccade,”

“ambiguous event,” or “artifact.” These labels were then combined into a final labeled dataset by the majority vote, resulting in 5,049 labeled microsaccades, 480 ambiguous events, and 38 artifacts in total.

In addition, the performance of the algorithm was comparatively assessed on an existing labeled dataset provided by M. Rucci (Active Perception Laboratory, University of Rochester). This dataset included two-dimensional traces from four young subjects (22–31 years old) performing a fixation task similar to the one used in our experiment (each subject performed 16–90 fixation trials, 12–15 s each). Monocular recordings at 1 kHz were conducted using a high-resolution Dual-Purkinje eye tracker system.

Preprocessing and event detection

Raw recording data for each subject consisted of horizontal and vertical coordinates of the eye in degrees of visual angle, along with the corresponding time-stamps (in milliseconds). The data from all sessions/trials were stacked into one matrix (per subject) with three columns $[\vec{t}, \vec{x}, \vec{y}]$ (this is not a necessary step as the algorithm can work with traces from a single trial, provided that they include a sufficient number of microsaccades; see Discussion). Parts of the trace corresponding to a 200-ms period around blink events, automatically detected by the EyeLink software, were removed as an obvious source of noise. Due to the presence of blinks and concatenation of multiple trials, the combined data traces exhibited artifactual jumps in the x and y traces. These jumps were removed by aligning data traces independently for the horizontal and vertical components. No other data preprocessing was performed.

To detect velocity peaks as candidate microsaccade events, the horizontal and vertical velocity components were calculated from eye position recordings using 11-point average

$$v_x = \frac{\sum_{i=1}^5 (x_{n+i} - x_{n-i})}{30\Delta t} \quad (1)$$

and similarly for the vertical component v_y , with $\Delta t = 1$ ms (Engbert & Kliegl, 2003). This is equivalent to smoothing the position by a triangular normalized Bartlett window (of size 12) and then differentiating (Otero-Millan et al., 2014). Velocity smoothing using this method was very close to smoothing using Savitzky-Golay differentiation filters of second order (filter size 11; Nyström & Holmqvist, 2010).

Following the well-known detection procedure proposed by Engbert and Kliegl (2003), separate velocity thresholds η_x and η_y were computed for the horizontal and vertical components using a multiple (λ) of median SD estimator:

$$\eta_{x,y} = \lambda \left[\langle v_{x,y}^2 \rangle - \langle v_{x,y} \rangle^2 \right] \quad (2)$$

where $\langle \cdot \rangle$ denotes the median value of the argument. These thresholds define an ellipsoid in the velocity space, such that any velocity point lying outside the ellipsoid corresponds to a high-speed event in the trace. The time point corresponding to such an event was considered as the time of a candidate microsaccade. The value of λ controls the initial separation between the potential microsaccades from noise, and was shown to produce the best results with empirically defined values set to 5 or 6 (Engbert & Kliegl, 2003; Engbert & Mergenthaler, 2006). In our algorithm we used a permissive value $\lambda = 5$ to detect most of the velocity peaks, under the constraint that consecutive peaks are separated by at least 30 ms. In addition, peaks with unnaturally high velocity (1000°/s) were discarded.

If the noise level is low and microsaccades are the only events with a relatively high speed, then microsaccades can efficiently be detected as sequences of high-speed events (Engbert & Kliegl, 2003; Engbert & Mergenthaler, 2006). However, in a high-noise regime such a procedure can result in large number of false positives, as any sequence of sufficiently high-speed events is taken to be a microsaccade, without consideration of the actual velocity profile. Note that in contrast to the Engbert and Kliegl’s method, candidate microsaccades in our algorithm are single peaks in the velocity profile, rather than event sequences, eliminating one free parameter (i.e., the minimal duration of the candidate microsaccade). Moreover, while λ is considered as a free parameter in the Engbert and Kliegl’s method, it is fixed to the relatively low value in our algorithm, since it is only used to implement initial selection of candidate events. A higher value of this parameter will result in a lower sensitivity of the algorithm (i.e., its ability to detect a true microsaccade), since it limits the number of candidate events even before noise removal. A lower value will result in a large number of candidate events without further increasing the sensitivity, since a vast majority of the microsaccades is detected at this value at low noise. Separation of putative microsaccades from noise is performed as a next step of the algorithm.

Correlation-based unsupervised clustering

Once velocity peaks were determined, feature vectors were constructed by concatenating absolute velocity along horizontal and vertical dimensions in the interval $[-\Delta p, \Delta p]$ around each candidate peak ($\Delta p = 50$). The feature vectors can be easily extended to also include position and acceleration data around the peak (see Results) without any changes to the algorithm. The unsupervised clustering is performed in the high-

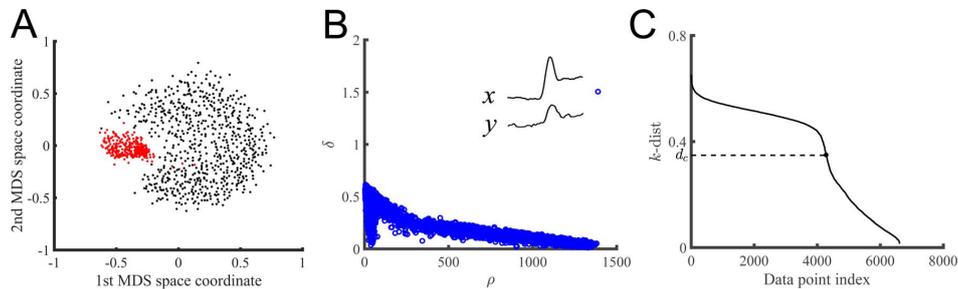


Figure 1. Unsupervised clustering in the correlation feature space. (A) A multidimensional scaling (MDS) representation of candidate microsaccades. Each dot corresponds to a feature vector. A cluster on the left (shown by the red dots) represents potential microsaccades that are highly correlated and thus lie close to each other in the correlation space. Noise events are less correlated with microsaccades and between themselves and thus form a low-density cloud of points (shown by the black dots). Note that the visible distance between the points on the plot does not reflect the true distance, as the feature vectors are projected onto the MDS plane. (B) The decision graph represents candidate microsaccades (small circles) as points in $\delta\rho$ space. The cluster center is detected as the point with the largest product $\delta\rho$ (the outlier in the upper-right part of the plot). Inset: The position trace of cluster center (i.e., the prototypical microsaccade). (C) The characteristic distance d_c is chosen as the point of the fastest increase of the k -dist curve. This value is used to separate microsaccades from noise, giving rise to the color labeling in (A).

dimensional (i.e., of dimension $2\Delta p + 1$ in the case of velocity-based features) space using a recently proposed fast density-based clustering method (Rodríguez & Laio, 2014). This method estimates, for each data point i , its local density ρ_i and the nearest neighbor distance δ_i between this point and its closest point having a higher density. Cluster centers are then determined as widely separated points of highest density—that is, points with large values of ρ_i and δ_i .

Calculation of both of these measures is based on the distance matrix, whose components are pairwise distances d_{ij} between feature vectors. Our method uses a correlation-based distance metric:

$$d_{ij} = 1 - r_{ij} \quad (3)$$

where r_{ij} is the Pearson correlation between the two vectors. This distance corresponds to the cosine of the angle between the two vectors (in the case of centered data) and hence does not depend on the vector lengths. Since microsaccades are events with a stereotyped shape but generally different amplitudes, the correlation distance is well suited to detect them. A high correlation between two data points (e.g., between two microsaccades) corresponds to the correlation distances close to zero, whereas a low correlation (e.g., between a microsaccade and a noise event) gives $d_{ij} \approx 1$. The space spanned by all pairwise distances between feature vectors is limited to the volume of maximal size 2, in which all microsaccades are expected to form a tight cluster, while noise events are expected to lie far from the cluster center (Figure 1A). The number of clusters may be higher than 1 depending on the chosen features (see Results).

Given the distance matrix, a local density of each point (i.e., the feature vector corresponding to a

candidate microsaccade) is estimated using a smooth Gaussian kernel:

$$\rho_i = \sum_j \exp\left(-\frac{d_{ij}^2}{d_c}\right) \quad (4)$$

where d_{ij} the distance between data points i and j , and d_c is a parameter determining a characteristic distance between feature vectors in the data set (see the following section for the proposed procedure of estimation of this parameter based on the data). The nearest neighbor distance is computed as (Rodríguez & Laio, 2014):

$$\delta_i = \min_{j: \rho_j > \rho_i} d_{ij}. \quad (5)$$

A plot of δ_i as a function of ρ_i for all data points for one sample subject shows an example of the decision graph, with a clearly separated cluster center (Figure 1B). The cluster center (i.e., a prototypical microsaccade) is determined automatically as the data point with the largest product $\rho_i\delta_i$. In the case of multiple clusters, a corresponding number of points with the largest product $\rho\delta$ is determined, and each point in the dataset is assigned to the same cluster as its closest neighbor with a higher local density (Rodríguez & Laio, 2014). This clustering approach is not iterative; it is thus fast compared to classical algorithms such as k -means, and it does not suffer from related overfitting problems.

Separating microsaccades from noise

With the proposed correlation-based distance metric, noise events are those that are far from (i.e., uncorrelated with) the prototypical microsaccade of a

given subject. We thus label a data point as noise if it is farther than a characteristic distance d_c from its nearest neighbor with a higher density. The value of d_c is determined based on the density of the microsaccade cluster as follows. First, the density profile of the data is estimated using a sorted k -dist graph (Ester, Kriegel, Sander, & Xu, 1996). Namely, for each data point, we calculate the distance (Equation 3) to its k th nearest neighbor with $k = 4$ (we checked that values $k = 1, \dots, 5$ produce similar results). These distances are then sorted in the descending order, giving rise to the curve that reflects the density distribution of the data points (Figure 1C). The data points with largest indices (corresponding to the lowest k -dist values) are those located near the cluster centers. As the data point index decreases, there is a sharp increase in the associated k -dist value, indicating a fast decrease in the density. We set the characteristic distance d_c to the k -dist value corresponding to the point of the steepest decrease in density (i.e., the fastest change in the k -dist curve), which is in turn calculated as the maximum of the derivative of the k -dist function. The derivative is estimated using Savitzky-Golay differentiation filters of fourth order (filter size was set to 10% of the number of data points to smooth out noise). Depending on the size of the dataset, other methods can be used to detect the maximum of the derivative, including semi-automatic approaches. Thus, distances between neighboring data points are (a) smaller than d_c for data points close to the cluster center; (b) approximately equal to d_c near the border of the cluster (i.e., when its density drops fast); and (c) larger than d_c far from the clusters, since noise events have lower local density (i.e., noise events are less correlated between each other than microsaccade events).

Note that in our algorithm, in contrast to the microsaccade clustering algorithm based on k -means (Otero-Millan et al., 2014), no separate cluster is assigned to noise. Rather, noise events are those that are far from the microsaccade center (although not necessarily close to each other; Dave, 1991). This essentially means that no specific assumptions are made about noise, apart from it being different from microsaccades.

Receiver operating characteristic analysis

Receiver operating characteristic (ROC) analysis was used to compare the performance of our method against methods proposed by Engbert and Kliegl (2003) and Otero-Millan et al. (2014), referred in the following as EK and OM methods, respectively. For the EK algorithm (Version 2.1 written in MATLAB), the λ parameter varied from 3 to 15, with minimal duration of microsaccade fixed to 6. The OM algorithm

(Version 1.1, downloaded from <http://smc.neuralcorrelate.com/sw/microsaccade-detection/>) does not have free parameters, since it automatically detects the best separation between the microsaccade cluster and noise cluster in a chosen low-dimensional feature space. Therefore, when showing ROC curves, we indicate the performance of this method by a point corresponding to the optimal performance, instead of a curve.

While manual labeling provides a way to quantify the number of true positives, false positives, and false negatives, the number of true negatives is arbitrary, since any point in time can be considered as a nonmicrosaccade event (Otero-Millan et al., 2014). Therefore this analysis cannot be used to give an absolute measure of the method's performance in terms of its specificity. However, it is valid to compare different methods at an arbitrarily fixed true negative rate. We thus set the number of true negatives for each subject equal to the total number of microsaccades for that subject (as detected by the experts). This changes the interpretation of the horizontal axis of the ROC curve, labeled *adjusted false positive rate* in the figures. While in the classical ROC analysis, the false positive rate equals to 0.5 when the number of false positives is equal to the number of true negatives, the same value of the adjusted rate corresponds to the case when the number of false positives equals the number of true microsaccades executed by the subject.

An implementation of the algorithm using MATLAB (version R2016b; MathWorks, Natick, MA) is available at <https://github.com/sheynikh/msdetect>.

Results

Detection of (micro)saccades in a high-noise regime

To illustrate the ability of the algorithm to detect fixational microsaccades, we show in Figure 2A and B samples of position and velocity traces from two subjects with different noise levels. While microsaccades can be relatively easily discerned by eye in the position trace in both subjects, saccade detection from the velocity trace becomes more difficult when the noise is higher. Specifically, high-frequency bouts in the velocity trace make a simple threshold-based approach unreliable. While making a few errors, the new algorithm is not vulnerable to this type of noise, as it considers the shape of the signal around velocity peaks as feature vectors. Nevertheless, the higher noise level resulted in a lower performance in this particular example (i.e., decrease in the true positive rate from 0.99 to 0.85, and increase in the adjusted false positive

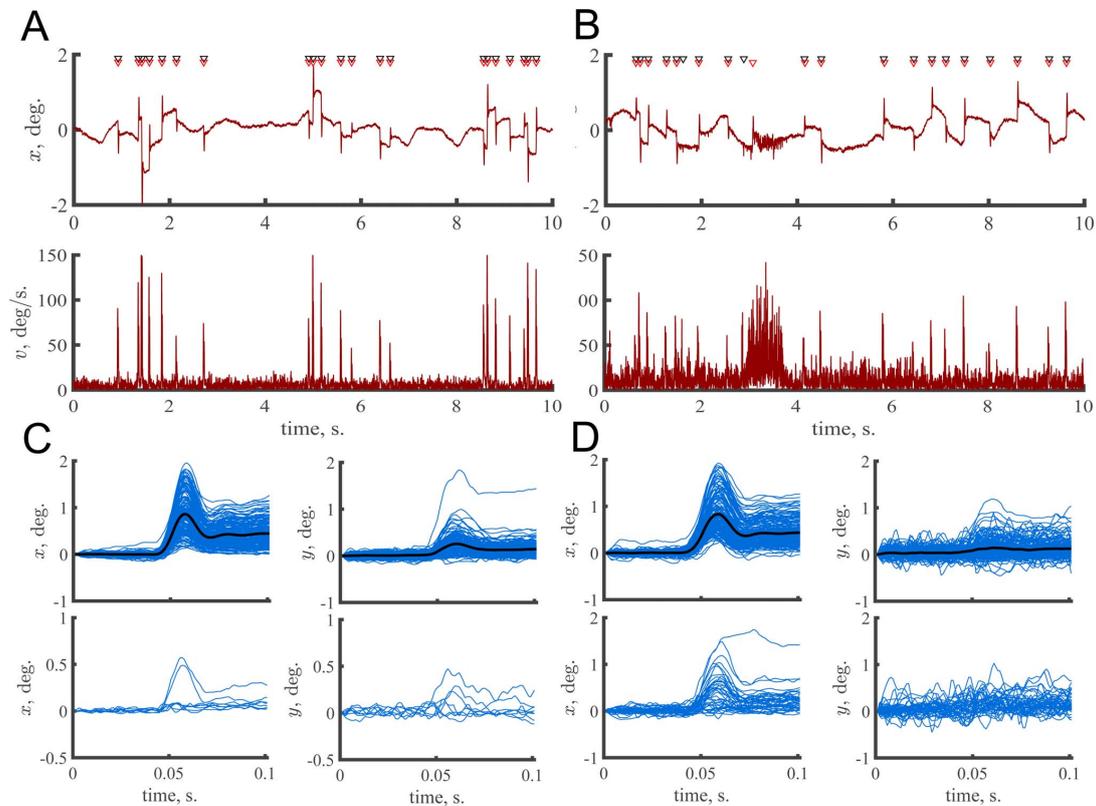


Figure 2. Example traces and extracted microsaccades. (A–B) Horizontal position (top) and velocity $v = \sqrt{v_x^2 + v_y^2}$ (bottom) during 10-s recording period for two different subjects. Microsaccades detected by the algorithm and manually labeled microsaccades are shown by the black and red triangles, respectively. (C–D) Shape of the microsaccades detected by the algorithm in the two subjects across all labeled trials. Top: Horizontal (left) and vertical (right) eye coordinate for correctly detected microsaccades (true positives). Mean microsaccade shape is shown by the black line. Bottom: Horizontal (left) and vertical (right) eye coordinate for false positives. Note the change in vertical scale. Only saccades with amplitude $< 2^\circ$ are shown for clarity.

rate from 0.04 to 0.16). Plots of microsaccade shapes show that almost all microsaccades in these two subjects were horizontal with a strong overshoot (Figure 2C and D, top row), while false detections mostly corresponded to low-amplitude peaks in velocity (Figure 2C and D, bottom row).

We compared the accuracy of the new microsaccade detection method with that of the EK and OM methods using ROC analysis. The analysis was performed on the manually labeled portion of the data recorded in aged subjects and shows that the new method offers a better balance between sensitivity (i.e., true positive rate) and specificity (i.e., adjusted true negative rate), compared to the two previous methods (Figure 3 and Table 1). Per-subject performance at a chosen value of the free parameters shows also that the new method offers an advantage over the EK method in terms of specificity (i.e., it has a smaller false positive rate, Wilcoxon $p <$

10^{-6}), and over the OM method in terms of sensitivity (i.e., it has a higher true positive rate, Wilcoxon $p < 10^{-5}$). Although the EK method had a higher mean sensitivity, compared to the new algorithm, it also had a much larger number of false positives. The number of false positives did not differ between the new method and the OM method.

In a video-based, pupil-corneal reflection system, gaze direction is estimated on the basis of the relative position of the pupil and the corneal reflection centers. Either the pupil or the corneal reflection may be (partially) covered by dropping eyelid or downward pointing eyelashes (often referred to as partial blinks) leading to a repetitive misestimation of the reflection center positions (Damasceno et al., 2015). In addition, the pupil or the corneal reflection can be confused with other optical object in the image of the eye, caused by uncontrolled light sources, glasses, contact lenses, or a

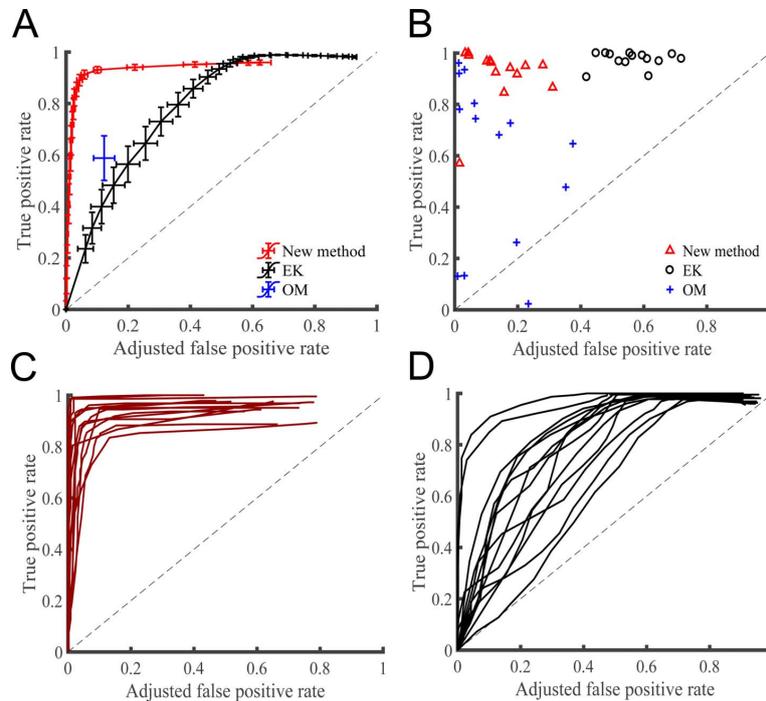


Figure 3. Performance comparison of the EK (in black), OM (in blue), and the new microsaccade detection method (in red) using eye recordings from aged subjects. (A) Average ROC curves (\pm SEM) across subjects for the three methods. Since the OM method has no free parameters, its average performance is shown by a point. (B) Each symbol corresponds to the performance of the method (in the ROC space) applied to the eye-tracking data of one subject. For the EK method (small circles) $\lambda = 6$, while for the new method (triangles) the parameter is chosen automatically, separately for each subject, using the estimation procedure described in Methods. Performance of the OM method is shown by the crosses. (C–D) ROC curves for all subjects resulting from the new method (C) and the EK method (D).

clinical condition of the subjects (Nyström et al., 2013). The partial blinks or optical artifacts cause repetitive errors in eye tracking, resulting in high-frequency oscillations in the recordings. The usual method of dealing with high-frequency noise consists in removing parts of the trace before and after a detected blink event (since partial blinks often, but not always, occur just before or after normal blinks), as well as in removing the parts of the trace that are accompanied by fast changes in pupil size (e.g., when the pupil is repetitively confused with another optical object of a different size).

To see whether trace filtering based on pupil size improves the microsaccade detection performance in our data, we removed parts of the trace 200 ms before and after time points in which pupil size changed faster than 20 units per millisecond (Otero-Millan et al., 2014; filtering based on blink detection was applied during preprocessing, see Methods). This standard blink- and pupil-based filtering approach led to the loss of about 20% of recorded data (including about 20% of true recorded microsaccades, as estimated from labeled data, Figure 4A). Moreover, the performance of the

	Precision	Sensitivity	Adjusted FPR	Youden's index
EK	0.43 ± 0.09	0.97 ± 0.03	0.56 ± 0.09	0.41 ± 0.09
OM	0.76 ± 0.27	0.59 ± 0.32	0.12 ± 0.13	0.47 ± 0.38
New method	0.85 ± 0.10	0.92 ± 0.11	0.14 ± 0.09	0.78 ± 0.14

Table 1. Performance comparison of the EK, OM, and the new microsaccade detection method. *Notes:* Precision = the fraction of true microsaccades as labeled by the experts among all events detected as microsaccades by the algorithm; Sensitivity = true positive rate; Adjusted FPR = adjusted false positive rate (see Methods); Youden's index (or informedness) = performance index corresponding to the height above the chance line in the ROC space, see text for details.

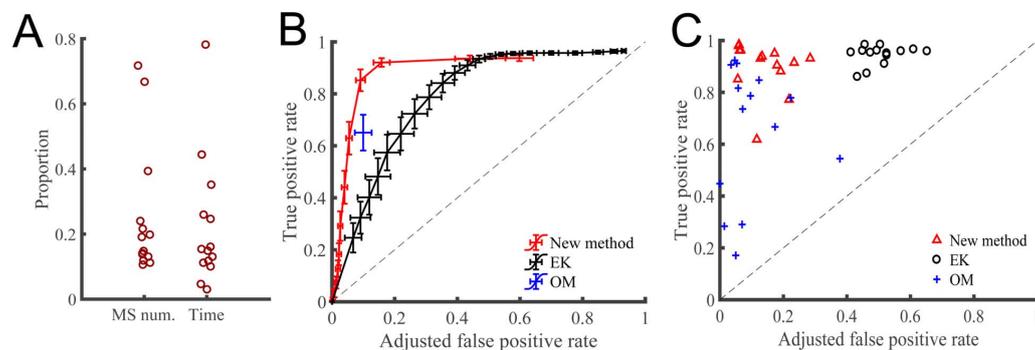


Figure 4. Performance comparison of the EK, OM, and the new micro-saccade detection method on prefiltered data. (A) Per-subject data loss due to prefiltering. The loss is measured by the proportion of true micro-saccades (*MS num.*) and the proportion of recorded time (*Time*) removed during prefiltering of the original data. (B–C) Mean ROC curves \pm SEM (B) and per-subject performance (C) for the three methods.

new method was still better than that of the other two methods, even though the filtering step actually decreased the accuracy of the new method (probably due to the loss of data, cf. Figures 3A and B and 4B and C). These results suggest that, first, the high-frequency recording noise in our data is not always associated with partial blinks and changes in pupil size and, second, that the proposed method appears to be resistant to noise that cannot be accounted for by standard noise-removal procedures. Moreover, the proposed method does not require the application of these procedures for efficient micro-saccade detection.

Detection of micro-saccadic FEMs in low-noise regime

We next verified whether the difference in performance between the three methods is caused by specific noise properties rather than other possible reasons. We thus compared the performance of the three methods on a dataset from a different study, in which eye tracking was performed using a high-precision double-Purkinje-image (DPI) system with a much lower level of recording noise (Poletti et al., 2017; see Methods). Under these conditions, the performance of the new method was similar to that of the OM method, and both of these methods outperformed the EK method (Figure 5A and B). This result suggests that the method proposed here is more efficient than the two previous methods in the high-noise regime, while its performance is comparable to the OM method for low-noise data. In agreement with the above considerations about possible high-frequency optical artifacts in video-based eye-tracking systems, we found a significantly higher probability of high-speed events in our data as compared to DPI recordings, suggesting the presence of

high frequency noise (Figure 5C). These high-frequency oscillations are sometimes accompanied by oscillations in pupil size (e.g., when the pupil is partially occluded by eyelid or eyelashes), but this is not always the case (e.g., when the oscillations are caused by errors in the detection of corneal reflection).

Preliminary assessment of Bayesian detection methods

Daye and Optican (2014) proposed a Bayesian detection of (micro)saccades, based on a generative model for the velocity signal, subject to motor and measurement Gaussian noises. In their algorithm, jumps in velocity that correspond to saccades are detected as abrupt changes in velocity distribution, quantified by the variance γ of the ratio of velocity distributions predicted on successive time steps. If the assumptions of the model are not violated and the two noise parameters are well chosen, the application of the method results in a strong decrease of noise, after which saccades can be detected by thresholding. Because of the stochastic nature of Bayesian prediction, several passes of the algorithm are required, after which candidate micro-saccades are grouped together, or discarded, based on three heuristic grouping parameters. In total, at least six parameters have to be suitably chosen to ensure correct detection. Figure 6A shows a γ -plot corresponding to the velocity trace from Figure 2B for noise parameters adjusted by hand. Even though the noise is strongly reduced, the issue of the threshold assignment and the choice of grouping parameters remains. While it is possible that some parameter values could result in a high-detection performance, the choice of these parameters on a per-subject basis is a problem that makes practical application of this

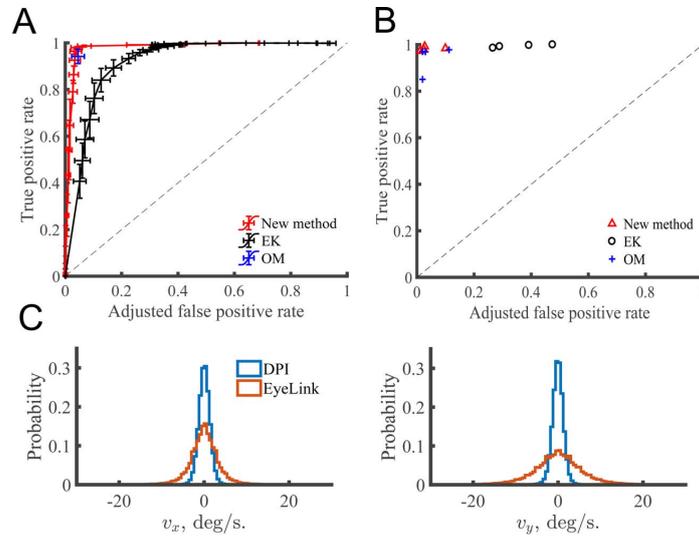


Figure 5. Performance comparison of the EK, OM, and the new microsaccade detection method on low-noise DPI data. (A–B) Mean ROC curves $\pm SEM$ (A) and per-subject performance (B) for the three methods. (C) Velocity distributions in the horizontal (left) and vertical (right) components of eye traces, recorded in the current study (orange) and using a DPI eyetracker (blue).

method and its comparison with our algorithm difficult.

More recently, Mihali et al. (2017) proposed a Bayesian approach for microsaccade detection that

uses a more elaborate generative model for saccade generation by assuming a piecewise-linear velocity profile for microsaccades, and Gaussian motor and measurement noises. In their algorithm, motor and

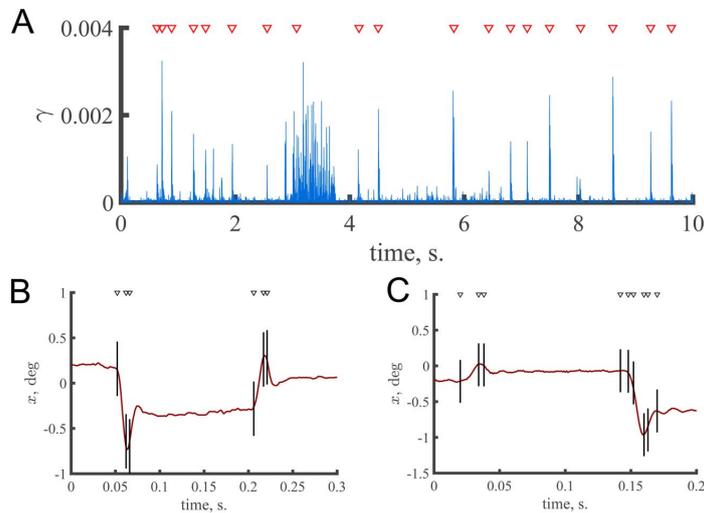


Figure 6. Application of Bayesian methods for microsaccade detection. (A) Noise reduction in the velocity signal shown in Figure 2B as a result of the algorithm proposed by Daye and Optican (2014). Parameter values: $N=200$, $m=10$, $\Omega=0.1$, $\xi=5$, $\lambda=0.005$ (see Daye & Optican, 2014, for details). Four additional parameters need to be specified to extract microsaccades from the denoised trace. Manually labeled microsaccades are shown by the red triangles. (B–C) Microsaccades detected by the algorithm proposed by Mihali et al. (2017). Several events are detected (shown by the black triangles and vertical black lines) for each true microsaccade, both for the data from video-based eye-tracker (B) and DPI eye tracker (C).

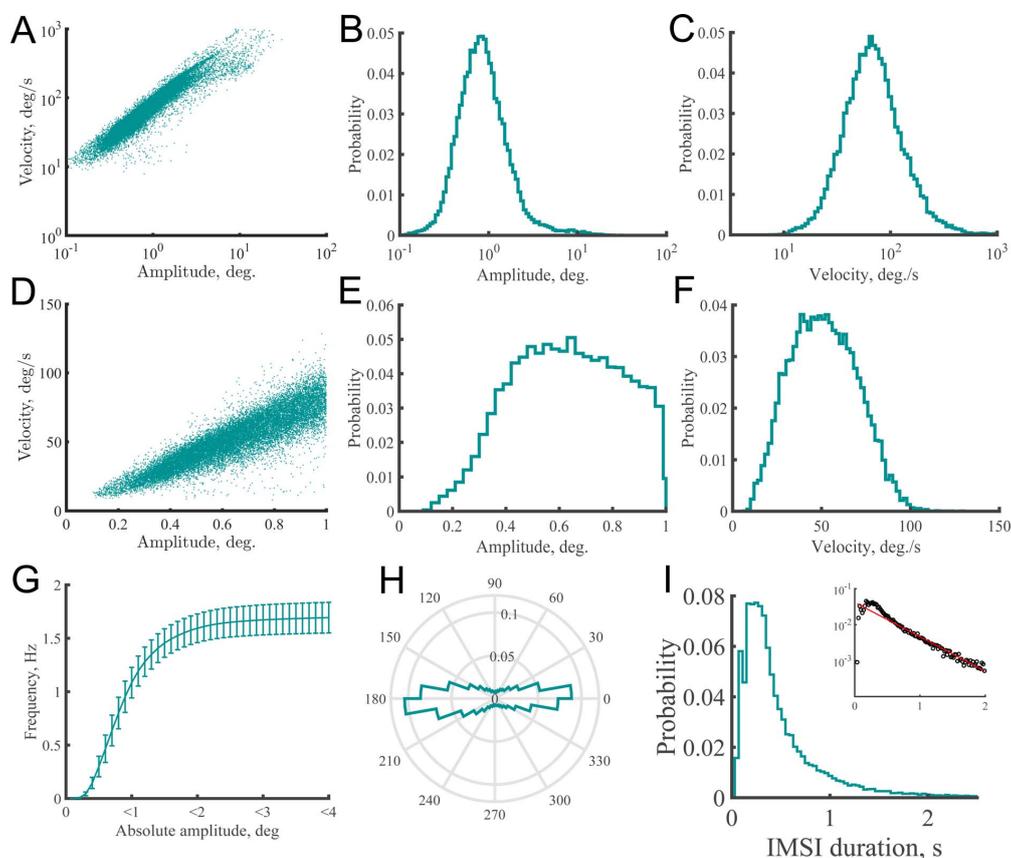


Figure 7. Case study: Analysis of (micro)saccade properties in aged subjects. (A–C) Main sequence (A), normalized amplitude (B), and velocity (C) distributions. (D–F) Main sequence, amplitude, and velocity distributions for saccades smaller than 1° in amplitude. (G) Saccade frequency as a function of amplitude. (H) Normalized distribution of saccade directions in polar coordinates. (I) Normalized distribution of IMSI. Inset: The same data with a logarithmic vertical axis and linear regression fit (red line).

measurement noise variances are estimated from the data and it is shown that the performance is not very sensitive to other adjustable parameters, controlling prior distributions for microsaccade frequency and duration. Unfortunately, the application of this method to our data resulted in a variable number of detected events for each true microsaccade, resulting in a high number of false positives (several examples are shown in Figure 6B and C). This problem is potentially related to the fact that our recordings were performed with the default setting of the EyeLink eye tracker parameter “Heuristic filter” (“on”) that enables online trajectory smoothing (see “Caveat” in Mihali et al., 2017). While it is possible that grouping of detected events based on their number or time lags might solve the problem, the choice of these additional parameters based on the data remains an open problem.

Case study: Properties of fixational saccades and microsaccades in aged subjects

Analysis of fixational saccades extracted from our recordings (including labeled and unlabeled data) in aged subjects, shows that they follow a so-called main sequence—that is, exhibit a high linear correlation in logarithmic coordinates (all saccades: $r = 0.94$, $p < 10^{-6}$; saccades smaller than 1° : $r = 0.9$, $p < 10^{-6}$; Figure 7A and D). Mean ($\pm SEM$) amplitude (Figure 7B and E) and velocity (Figure 7C and F) of fixational saccades were equal to $1.13^\circ \pm 0.01^\circ$ and $85.11^\circ/s \pm 0.39^\circ/s$, respectively, with a mean frequency of 1.69 ± 0.15 Hz. Microsaccade frequency was below 1 Hz on average (Figure 7G). A vast majority of fixational saccades had a larger horizontal component (Figure 7H), independently of their amplitude. This analysis can be compared to a previous study that addressed saccades and micro-

saccades in subjects with ages between 60 and 70 years old (as a part of a larger cohort of younger subjects; Port et al., 2016). In their visual search task (“Where’s Waldo” puzzles) Port et al. (2016) observed similar saccade frequencies, but higher amplitudes and mean velocities, as well as a large subset of saccades with a vertical bias. These differences can be attributed to the differences in the task requirements, since stimulus characteristics during visual search influence the spatial distribution of visual fixations (Najemnik & Geisler, 2008).

The distribution of inter-microsaccade-intervals (IMSI) in our recordings suggests that microsaccade generation in aged subjects can be described by a Poisson process, since distribution of IMSI is approximately exponential (Engbert & Mergenthaler, 2006). The peak of the distribution (at ≈ 300 ms) occurs earlier than what has been observed in younger subjects (Engbert & Mergenthaler, 2006), indicating a higher frequency of an underlying periodic component of microsaccade generation process.

Feature and parameter sensitivity analysis

The choice of feature space, in which candidate microsaccades are represented, can influence the detection accuracy of an algorithm. Appropriately reducing the size of the feature vector can often result in a faster and more accurate detection procedure, while an overly restricted set of features results in low sensitivity. A useful property of the proposed algorithm is that it is flexible with respect to the choice of features. In particular, the feature space can be easily reduced—for instance, to treat either the horizontal or vertical velocity components—or it can be extended to include position and acceleration data. Such changes in the feature space do not require any modification of the algorithm (apart from changes in the input data). To illustrate the flexibility of the algorithm with respect to the choice of features, we assessed its detection accuracy when the feature space was reduced to include only the horizontal (x) component of the velocity traces. Since the vast majority of microsaccades in the fixation task have a nonzero component along the horizontal direction (Figure 7D), such a reduction of the feature space is expected to increase the detection rate (since an approximately constant nonzero y amplitude during a horizontal microsaccade leads to a decreased signal-to-noise ratio of the microsaccade velocity signal). Reducing the input data to only include the horizontal velocity component indeed resulted in a better detection performance (Figure 8A and B). To test whether adding position and acceleration data can further improve the detection performance, and to illustrate the ability of the algorithm to work with multiple clusters, the feature space was

extended to include full position, velocity, and acceleration data along the horizontal component. Since the shape of a microsaccade in the positive x direction is inverted with respect to the negative one, the clustering step results in two clusters in the feature space (Figure 8C and D). Such an extension of the feature space did not result in any further improvement in accuracy (in fact it slightly decreased the sensitivity of the algorithm, see Figure 8A), thus indicating that velocity profile contains most of the information useful for microsaccade detection. Note that for all the tested feature combinations the performance of the algorithm was better than that of the two other methods (Figure 8B).

Even if the feature space is appropriately chosen, the detection accuracy is further determined by the decision threshold. We thus studied the sensitivity of the performance to the choice of the free parameter—that is, the characteristic distance d_c between microsaccade candidates in the correlation feature space. For each subject, the ROC-optimal value of the parameter corresponds to the point with the maximal Youden’s index, given by the difference between the true positive rate and the (adjusted) false positive rate (Youden, 1950). We thus estimated the drop in the Youden’s index due to an incorrectly estimated d_c value (Figure 9A and B). An underestimation of d_c by about 0.05 or an overestimation by about 0.1 (in units of correlation distance, $0 < d_c < 2$) resulted in the drop in performance by about 10% on average, even though it is different from subject to subject (Figure 9B). To assess the efficiency of our proposed estimation procedure for the value of the free parameter, we quantified how close the estimated value was to the ROC-optimal value (Figure 9C). Thus, our procedure for the choice of d_c based on cluster density overestimates the optimal value by about 0.04, leading to the corresponding performance drop of only about 2.1% on average.

Finally, in order to assess the detection performance with respect to the microsaccade size, we estimated the precision (i.e., the probability that a detected microsaccade is a true microsaccades, according to manual labels) and sensitivity (i.e., the true positive rate) of the algorithm as a function of the (absolute value of) microsaccade amplitude. The new algorithm was as precise as the OM method, but with a considerably higher sensitivity (Figure 10). Compared to the EK method, our detection algorithm was considerably more precise, and was also more sensitive for fixational saccades with amplitudes under 1° .

Discussion

Most of existing microsaccade detection methods are based on the identification of high-speed events in the

CHAPTER 7. CONTRIBUTIONS TO EYE MOVEMENT CONTROL

Journal of Vision (2018) 18(6):19, 1–16

Sheynikhovich, Bécu, Wu, & Arleo

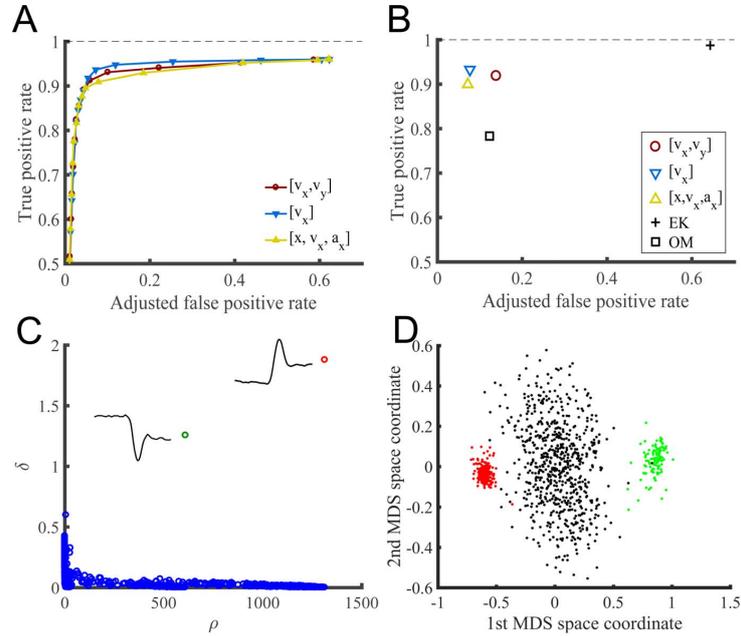


Figure 8. Flexibility of the algorithm with respect to the choice of the feature space. (A) Average ROC curves for the new method when the feature vectors were composed of two velocity components (red circles); of only the horizontal velocity component (blue triangles); and of horizontal position, velocity and acceleration (yellow triangles). (B) Average (across subjects) performance of the new method with different features (see [A]) in comparison with the EK method (black cross) and the OM method (black square). The value of d_c for the new method was chosen using the procedure described in Methods. For the EK method $\lambda = 6$. (C) Decision graph for the same subject as in Figure 3 when the feature vectors included position, velocity, and acceleration data. The two cluster centers correspond to prototypical microsaccades in opposite directions. (D) MDS representation of the candidate microsaccades after clustering and separating noise events for the same subject (red and green dots correspond to two clusters in [C]).

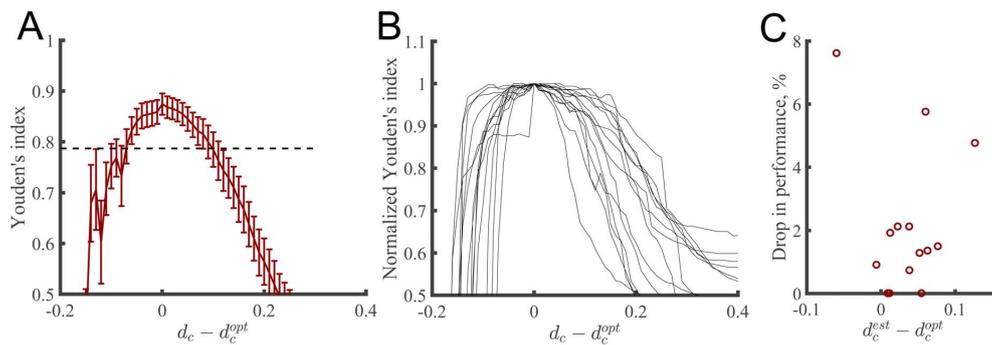


Figure 9. Sensitivity of the new method to the choice of the free parameter. (A) Youden's index ($\pm SEM$ across subjects) as a function of d_c estimation error. The optimal parameter value d_c^{opt} is the parameter value corresponding to the maximal Youden's index (calculated based on the labeled data and different for each subject). Dashed line: 10% drop in the average Youden's index from its maximum. (B) Each curve shows Youden's index as a function of d_c estimation error for one subject, normalized to a maximum value of 1. (C) Drop in performance (measured by the relative decrease in Youden's index) as a function of the error $d_c^{est} - d_c^{opt}$, where d_c^{est} is produced by the estimation procedure proposed in Methods (separately for each subject). Each circle corresponds to one subject.

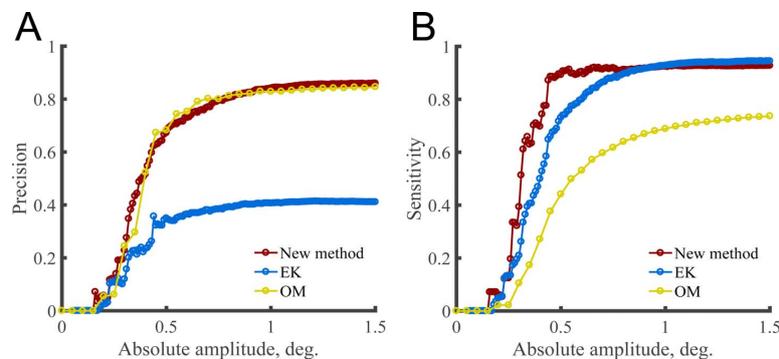


Figure 10. Detection performance of the new method as a function of microsaccade size. (A) Precision (i.e., the fraction of true labeled microsaccades among all events detected as microsaccades by the algorithm) as a function of the absolute value of the microsaccade amplitude for the OM (yellow), EK (blue), and the new method (red). (B) Sensitivity (i.e., the true positive rate), as a function of the amplitude.

velocity and acceleration profiles of recorded eye position as a function of time (Holmqvist et al., 2011). To separate candidate microsaccades from noise, either a single velocity-based threshold can be chosen (Engbert & Kliegl, 2003; Holmqvist et al., 2011) or a set of manually chosen features of velocity and acceleration profiles can be used to construct a feature space. In this feature space, noise and microsaccades are assumed to form separate clusters that can be detected using standard machine-learning techniques such as K-means (Otero-Millan et al., 2014). These detection methods rely on the assumption that all high-speed events are microsaccades or that statistical properties of noise can be captured by a small number of velocity- and acceleration-based features. However, these assumptions may not hold true depending on the age of the subjects or their clinical condition with respect to visual functions. High-frequency events caused by optical artifacts can have very different statistics depending on the origin of the noise, which may be the reason for the relatively inadequate performance of previously developed methods when applied to our data. The method of microsaccade detection proposed in this paper can take into account all available information (e.g., position, velocity, and acceleration) around each candidate microsaccade, and it makes use of a recently developed fast clustering algorithm by Rodriguez and Laio (2014) to determine microsaccade clusters. Importantly, the proposed method does not make any assumptions about noise properties, the only requirement being that noise events be sufficiently different from a typical microsaccade. This method is shown to work better than the EK and OM methods with noisy data, and it eliminates the need for data preprocessing based on pupil size, thus avoiding a considerable amount of data loss. It is therefore suitable for (semi)automatic microsaccade detection for

a large number of subjects and/or experimental conditions, and a high amount of variability between the subjects due, for instance, to differences in age or clinical conditions.

More recently, Bayesian methods for microsaccade detection were proposed that assume a particular generative model of saccade generation, and the performance of these methods depends on how close the model accords with reality. Moreover, computational tractability of these models often requires Gaussian noise assumptions. When either the generative model or Gaussian noise assumption is not adequate, these methods may fail. In addition, the generative model, noise, and priors are controlled by parameters that have to be, ideally, determined based on the data. The assessment of performance of these methods can be difficult in practice since a method's failure might be caused by any of the above issues and an advanced mathematical background is required to understand how to address a particular issue. An advantage of these methods is that they are not data-hungry and they work equally well on large and small datasets (given that the generative model and parameters are suitably chosen). Feature-based clustering methods, like the one proposed in the present work, are in contrast conceptually simple and usually faster, but in order to work reliably they need a dataset with a sufficient number of microsaccades to form a cluster. In our analysis this was the case even when working only with labeled trials (160 s total time per subject). The problem of insufficient number of microsaccades can easily be detected from the decision graph (see Figures 1B and 8C), where it would correspond to the absence of outliers for microsaccade clusters.

While our method is proposed in the context of aging research, it is not limited to the age-related ocular noise. Indeed, any type of noise can in principle be

considered as the only requirement for successful detection of (micro)saccades is that they have a stereotyped shape (independent of amplitude). In particular, this algorithm can be suitable (but has not been tested) for eye recordings performed with head-mounted eye trackers (Holmqvist et al., 2011). We note, however, that the initial choice of microsaccade candidates based on the EK method assumes approximately zero velocity between saccades, as is the case for head-fixed ocular fixation tasks. This assumption may not be correct during other oculomotor tasks, such as smooth pursuit, or in freely moving subjects, as in these conditions eyes may move with a high velocity between saccades (Daye & Optican, 2014). In this case, a single velocity threshold may be inadequate to detect initial saccade candidates. This issue, however, can be resolved by using saccade-detection methods adapted to smooth pursuit (e.g., Daye & Optican, 2014) in the initial event detection phase (with a permissive setting of parameters to ensure high sensitivity), and then subjected to unsupervised clustering to ensure high precision.

We have shown that our algorithm can detect saccades based on position, velocity, acceleration, or a combination of (subsets of) these features. The quality of a particular feature set with respect to microsaccade detection can be judged from decision graphs, in which a clear separation of the microsaccade cluster(s) from the rest of the points normally correspond to a high detection performance. While in our experimental study we used monocular recordings, binocularity is an important property of genuine saccades (Engbert & Kliegl, 2003; Collewijn & Kowler, 2008). Although not tested, extending the feature set by binocular recording traces can further improve the detection performance of our method.

We propose an automatic procedure for the estimation of the single free parameter, based on the approximated density profile of the data. This procedure assumes that microsaccades form the densest cluster in the correlation space, and so the border of the cluster is detected using the fastest drop in the density. If the recording period is too short, or a too low number of microsaccades occurred, this assumption may not hold true, resulting in the failure of the automatic estimation procedure. In that case an experimenter intervention may be required to choose a suitable smoothing of the k -dist curve, so that the drop in density can be detected (once per subject). Alternatively, the experimenter can manually choose the d_c value that corresponds to the fastest density drop by visual inspection of the k -dist graph. As our analysis shows, an overestimation of this value by as much as 0.1 will not result in a substantial drop in performance.

As a case study, we applied the detection method to investigate the impact of natural aging of fixational

microsaccade characteristics. While a substantial number of studies addressed the influence of age on saccades, only one study, to our knowledge, specifically examined saccades with amplitudes under 0.5° (Port et al., 2016). In this study, seven subjects aged between 60 and 66 were assessed as a part of a larger cohort that included 343 subjects, most of whom were children and adults under 30 years old. The results of this study suggested a slight but significant increase of the frequency and peak velocity of microsaccades with age, although the efficiency of their detection method (an ad hoc modification of the EK algorithm) with respect to older subjects in the cohort is not clear. The present study thus complements these previous findings in subjects older than 69 years and demonstrates that the proposed algorithm can reliably detect microsaccades of sizes up to 0.2° from video-based recordings in the presence of high-frequency noise.

Overall, the proposed method for the detection of (micro)saccades is noise-resistant, fast, and flexible with respect to the choice of features and it does not require manual data preprocessing. This method can be applied to detect other events with a stereotyped shape in eye-tracking data and provides an estimation procedure for the per-subject choice of the free parameter. This method compares favorably to other existing methods in a high-noise regime and it can be useful in aging and clinical research involving video-based eye trackers.

Keywords: eye tracking, microsaccades, unsupervised clustering, aging, noisy data

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7.3 Fixational saccades

7.3.1 Rationale

Given that we now have an accurate method for detecting small saccadic movements, the objective of this part is to characterize the impact of healthy aging on microsaccades and square-wave jerks (SWJ), as it has been surprisingly poorly and inconsistently studied. We will pay attention, in doing so, to the classical definition of genuine microsaccades and SWJ.

By measuring fixational saccades in a large sample of participants, with an age profile that is above what has been done in previous studies, we seek to provide normative data in aging. Given that *i*) abnormalities in microsaccade properties are often used to characterize ophthalmological and cognitive disorders, and *ii*) older adults are often taken as control group for these age-related diseases, these descriptive results will be useful in many domains of research.

Finally, we will try to understand influence of optic flow conditions on fixational saccades in order to complement previous studies and our own results on fixation area (sec. 7.1.1). Indeed, a directional bias (in the form of a "micro-optokinetic reflex") has been observed in the direction opposite to a lateral visual motion (Laubrock et al., 2008; Piras et al., 2016). We will test whether fixational saccades are biased in the direction opposite to the flow (i.e., inward) under a radial flow condition, when the direction of travel and direction of gaze coincide.

7.3.2 Methods

General method. The participants, setup and protocol used for this section are identical to those presented in the section "*Fixation area*" (sec. 7.1.1).

Detection of saccadic movements. The saccades produced during our fixation task were detected according to the method presented in the section "*Microsaccades detection*" (sec. 7.2.1). Although this method was initially dedicated to the detection of microsaccades, it can nevertheless detect saccades of any amplitude. The classical relationship between amplitude and peak velocity of saccades, the "main sequence", can be seen on figure 7.1. There was a strong correlation ($r=0.72$, $p<0.001$) between the two properties. Although most of the observed events were in the range of microsaccades, some larger saccades occurred as well, albeit less frequently. In this study, we use the term "fixational saccades" for any saccadic movements produced during the fixation task. Where appropriate, we characterized genuine microsaccades according to two upper thresholds: a permissive threshold (any saccade smaller than 1° ; Martinez-Conde et al., 2009) and a restrictive threshold (any saccade smaller than 0.5° ; Poletti and Rucci, 2016). We detected 189063 candidate saccades across all subjects and all trials. Among these, we discarded any saccades smaller than 0.03° (0.006%). This lower threshold corresponds to 3 times the instrument's spatial resolution of 0.01° (SR-Research, 2006; Poletti and Rucci, 2016). This leads to a final sample of 187923 saccadic movements.

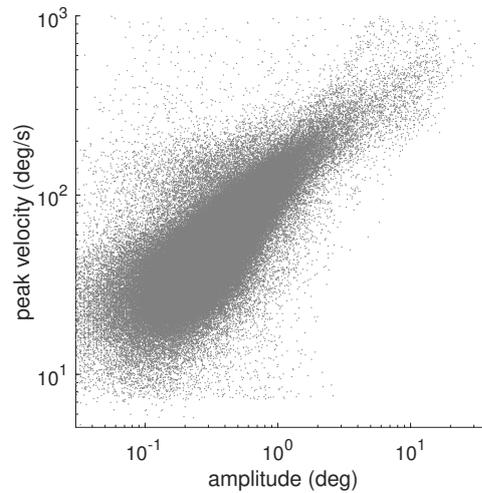


Figure 7.1 – Main sequence of the detected fixational saccades. Double-logarithmic representation of the relationship between amplitude and peak velocity of saccades.

Data analysis. Given that one of our objectives is to test whether microsaccades are directed inward in radial optic flow conditions, we estimated the center toward which fixational saccades are directed using a maximum likelihood approach. We first assumed that saccade directions θ from an initial position (x, y) are distributed according to a von Mises distribution (an analogue of the Gaussian distribution for circular data):

$$f(\theta | \mu, \kappa) = \frac{e^{\kappa \cos(\theta - \mu)}}{2\pi I_0(\kappa)}$$

where the mean direction μ of saccades is towards the unknown fixation center (x_0, y_0) :

$$\mu = \arctan \frac{y_0 - y}{x_0 - x}$$

and κ is the concentration parameter. The likelihood function was then obtained as a product of von Mises distributions, corresponding to all saccades from a given trial and subject. The maximum of likelihood function with respect the three unknown parameters x_0, y_0 and θ was determined numerically using simplex search method of Lagarias et al. (1998), implemented by a `fminsearch()` function in Matlab (Mathworks, version R2018b).

Statistics. Where applicable, data were preferentially analyzed by using paired or two-sample t-tests. Normality of the data was verified quantitatively by visual inspection of Q-Q plots. When normality and homoscedasticity were dubious, we used non-parametric Wilcoxon signed-rank test and Friedman ANOVAs for paired samples and the Mann-Whitney test in case of independent samples. Circular data were analyzed with a MATLAB toolbox for circular statistics (Berens, 2009). Alpha level for statistical significance was set at $P < 0.05$. The Bonferroni correction was used when multiple comparison were needed.

For each analysis, we identified outlying subjects based on the distance method by Cook (1977) and discarded any point over $4/n$ where n is the number of subjects. The number of outliers can be inferred from the degree of freedom used of each statistical analysis. The age factor was either considered as a continuous factor (e.g., for linear regression) or as a categorical factor (for non-parametric testing, with "Young adults" being any subject under 40 years old and "Older adults" any subject over 65 years old) when needed.

7.3.3 Results

7.3.3.1 Age effect, condition 1

The age-related influence was first assessed by estimating saccade amplitude and peak velocity for all events detected across the 10 trials of condition 1, i.e., when the fixation target is presented on a homogeneous black background. There was a shift in the distributions associated with older as compared to young adults, suggesting a modulation of fixational saccade properties with advancing age (fig. 7.2, top graphs). Specifically, the median amplitude ($F_{(105)} = 4.01, p < 0.001$) and median peak velocity ($F_{(104)} = 5.01, p < 0.0001$) of fixational saccades were higher in older adults, compared to young adults (fig. 7.2, bottom graphs).

In accordance with previous studies, we found that the saccades produced during attempted fixation were concentrated on the horizontal axis (fig. 7.3). The direction of the distribution was heterogeneous in both young adults (omnibus test: $m = 6359, p < 0.0001$) and older adults (omnibus test: $m = 11373, p < 0.0001$). The concentration on the horizontal axis seemed higher in older adults when compared to the young.

As can be seen in figure 7.2, a number of fixational saccades exceed the amplitude thresholds generally used to define genuine microsaccades. The aging effect on saccade frequency we found was unsurprisingly modulated by such thresholds. Indeed, when considering all *fixational saccades*, older adults show a significant increase in saccadic frequency ($F_{(99)} = 4.68, p < 0.001$, fig. 7.4, top left). On the other hand, microsaccade frequency, as defined by the *permissive threshold* show no significant age effect ($U = 1570.5, p = 0.58$, fig. 7.4, top right). Finally, when considering the *restrictive threshold*, older adults produced fewer genuine microsaccades ($U = 2003, p < 0.001$, fig. 7.4, bottom). Altogether, these data show that the aging effect found on frequency is critically dependent on the thresholding method used.

We next seek to characterize the occurrence of square-wave jerks (SWJ) in aging. At first sight, the fact that fixational saccades are more frequent and large in older adults fits well with a higher occurrence of SWJ in this population, given that the probability of forming a SWJ (thus increasing saccadic frequency) is higher for large microsaccades (Otero-Millan et al., 2011a, 2013). To verify this prediction, we analyzed the properties of pairs of fixational saccades, with the hypothesis that, if forming a square-wave jerk, pairs of consecutive saccades should be more likely to *i*) be separated by a temporal delay between 200 and 400 ms *ii*) have a similar amplitude

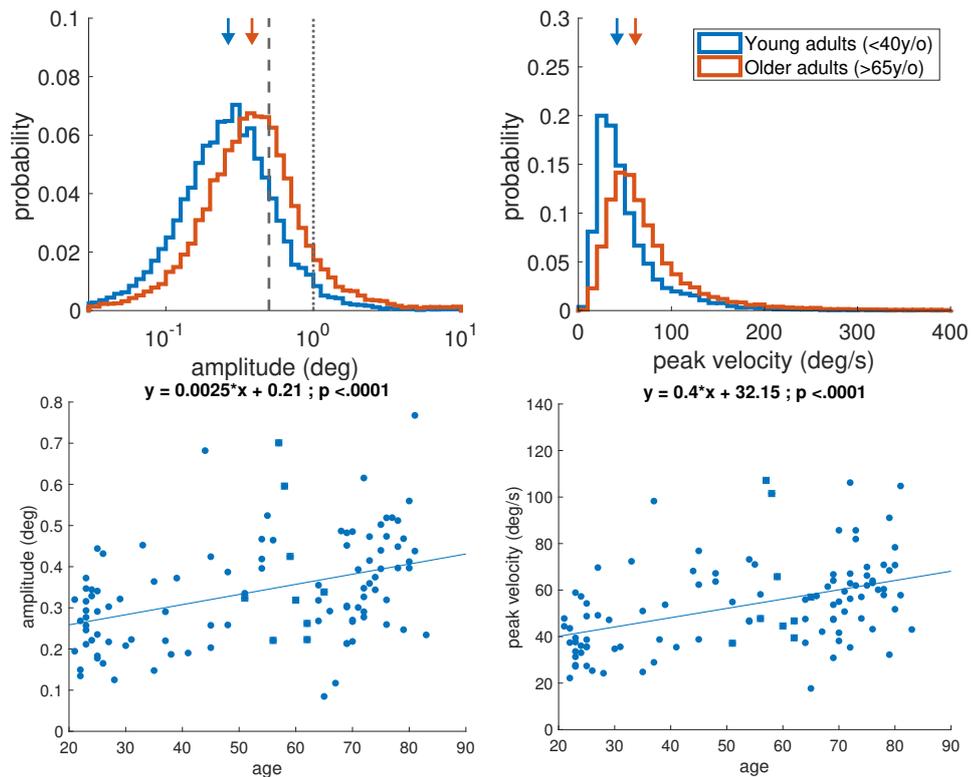


Figure 7.2 – Amplitude and peak velocity of fixational saccades. Distributions (top) and median (bottom) of fixational saccade amplitude (left) and peak velocity (right), according to age. Older adults show an increase in fixational saccade amplitude and peak velocity. Colored arrows indicate the median associated with each age group. The dashed and the dotted lines indicate the restrictive and the permissive upper threshold of genuine microsaccades, respectively. The parameters for the linear regression with age and the associated p -value are indicated above the graphs. Subjects identified by a square were recorded at 500 Hz, all other subjects were recorded at 1000 Hz.

and *iii*) an opposite direction (Abadi et al., 2003; Abadi and Gowen, 2004). This would be the case specifically for a large initial microsaccade.

The distribution of time differences between pairs of successive saccades (fig. 7.5A) were different between the two age groups (two-sample Kolmogorov-Smirnov test: $D^* = 0.10, p < 0.0001$). The kurtosis was larger in older adults (kurtosis = 72.46) when compared to young adults (kurtosis = 59.69), thus indicating a more peaked distribution in older adults. Additionally, the probability that pairs of saccades be separated by 200 to 400 ms tended to be higher in older adults when compared to young adults ($t_{(83)} = 1.86, p = 0.06$). The distributions of amplitude differences (fig. 7.5B) were also different between the two age groups (two-sample Kolmogorov-Smirnov test: $D^* = 0.05, p < 0.0001$), but this time the distribution of saccade amplitude differences in young adults (kurtosis = 219.93) was more peaked than that of older adults (kurtosis = 96.71). For angular differences between pairs of saccades (fig. 7.5C), both distributions had the same mean direction ($F = 1.42, p = 0.23$), centered around 180° . The distribution of angular differences in

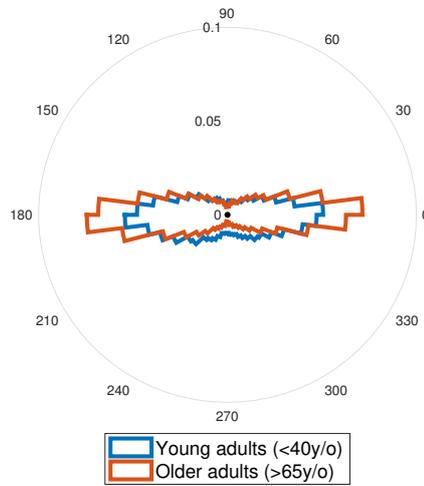


Figure 7.3 – Fixational saccade direction. Microsaccade directions are concentrated on the horizontal axis in both age groups.

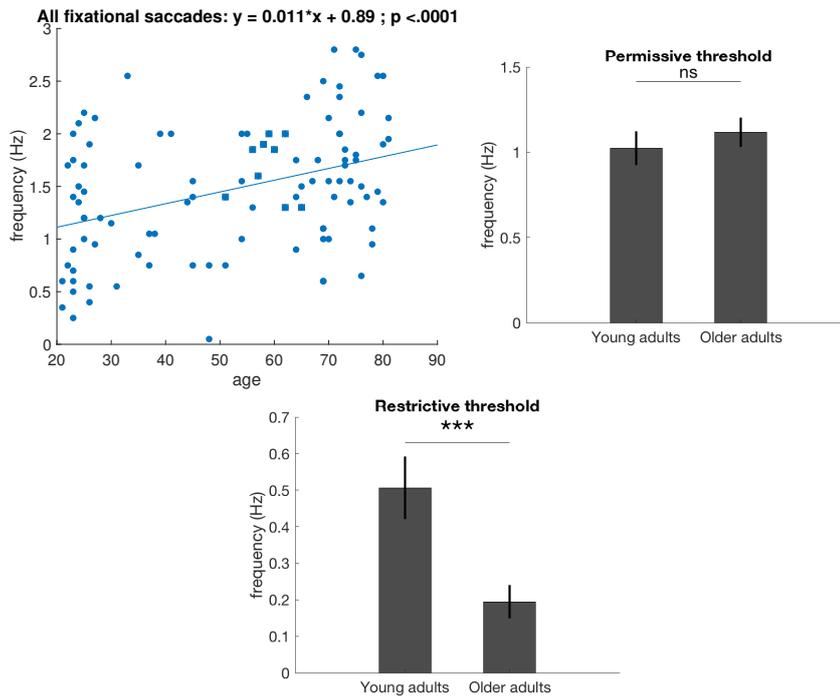


Figure 7.4 – Aging effect on fixational saccade frequency when considering all fixational saccades (top right), microsaccades as defined by a permissive (top left) or restrictive (bottom) threshold. The parameters for the linear regression with age and the p -values for non-parametric two-sample tests are indicated above the graph: **** $p < 0.0001$; *** $p < 0.001$; ** $p < 0.01$; * $p < 0.05$. Subjects identified by a square were recorded at 500 Hz, all other subjects were recorded at 1000 Hz.

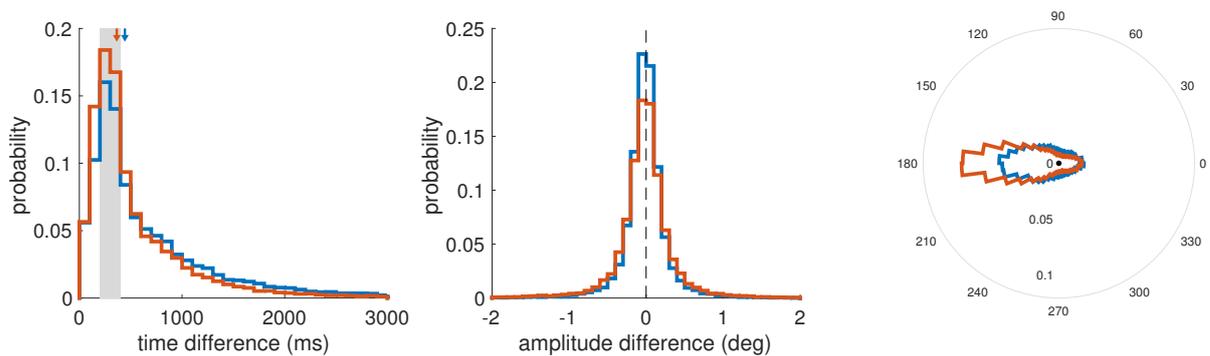


Figure 7.5 – Properties of pairs of consecutive fixational saccades. Time (left), amplitude (middle) and angular (right) differences between pairs of consecutive saccades. If forming a square-wave jerk, pairs of microsaccades should be separated by a temporal delay between 200 and 400 ms, indicated by the shaded area on A. Colored arrows indicate the median associated with each age group. They should have a similar amplitude, the dashed line representing a theoretically ideal case where two consecutive microsaccades have an equal amplitude on B. Finally, pairs should have an opposite direction, i.e., being clustered around 180° on C.

older adults was however more peaked around the mean direction (Fisher kurtosis = 2.05) than that of young adults (Fisher kurtosis = 1.09).

Finally, coherent with our hypothesis, it appears that large initial saccades were associated with a successive saccade with a delay between 200 and 400 ms and with an opposite direction (supp. fig. 7.9). Although these preliminary data need further studies, including the determination of associated statistics, they seem coherent, nevertheless, with a potential increased frequency of SWJ in older adults: pairs of fixational saccades in older adults were more likely to adhere to the temporal delay and direction classically defining SWJ. This appears to be the case especially when large saccades occur, coherent with the definition of SWJ.

7.3.3.2 Optic flow effect, *conditions 2-5*

The influence of the different optic flow conditions on fixational saccade frequency can be appreciated in figure 7.6. There was a significant effect of the condition both in young (Friedman ANOVA: $\chi^2 = 45.11, p < 0.0001$) and older adults (Friedman ANOVA: $\chi^2 = 63.51, p < 0.0001$). Post-hoc comparisons on ranks with an additional Bonferroni correction (Pereira et al., 2015) were carried out for each group (supp. tab. 7.1). Overall, the condition effect found with the Friedman ANOVA was mainly related to the condition 1, leading to a higher saccade frequency, compared to all other conditions, in both age groups. The only exception was condition 3 (tangential optic flow) which was associated with a higher fixational saccade frequency when compared to other optic flow conditions in young adults only.

There was almost no influence of the experimental conditions on saccade amplitude (supp. fig. 7.10) and peak velocity (supp. fig. 7.11), with the exception, again, of condition 3 (tangential optic flow) which was associated with larger saccades (supp. tab. 7.2), and greater peak velocities

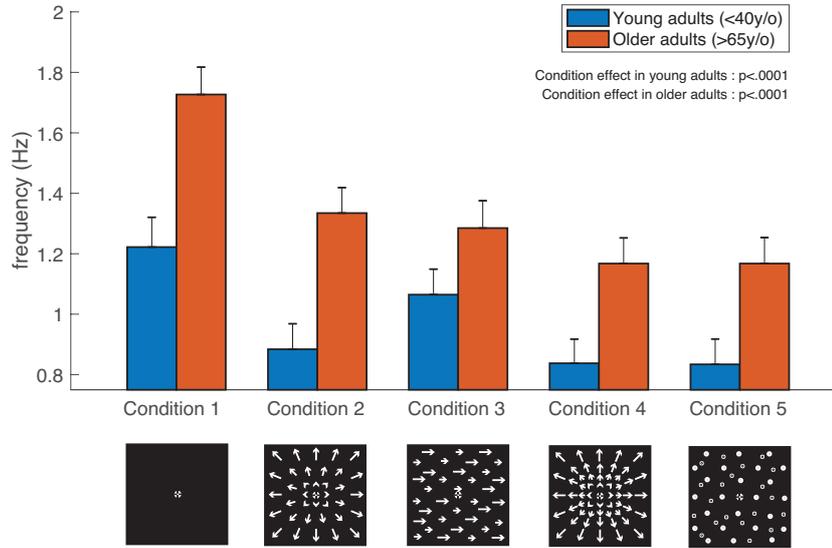


Figure 7.6 – Influence of optic flow on fixational saccade frequency. Data were averaged over the trials of each condition. Error bars correspond to the standard error of the mean. Condition effects correspond to a Friedman ANOVA associated with each age group.

(supp. tab. 7.3), in both groups. These effects were stronger in young adults.

We next wondered how the optic flow conditions affected fixational saccade direction. Fixational saccades in the radial flow conditions (conditions 2 and 4) and the control condition (condition 5) were clustered on the horizontal axis, just as in condition 1, with no preferred direction (Fig. 7.7). There was a directional bias in the tangential flow condition (condition 3) as more fixational saccades were directed to the left, i.e., in the direction opposite to optic flow, thus resembling an optokinetic reflex (Fig. 7.7).

We next wanted to test whether fixational saccades in the radial flow conditions (conditions 2 and 4) were directed inward, i.e., toward the probable center of fixation (which would correspond to the optic flow’s focus of expansion) or whether they were directed outward. To do this, we estimated the probable center toward which saccades were directed (see Methods 7.3.2) and then calculated the angular distance between each fixational saccade and the probable center. Under these circumstances, saccades were directed inward, i.e., to the probable center, when the mean angle of the distribution of angular distances ($\bar{\alpha}$) is equal to 0° and outward when $\bar{\alpha}$ is equal to 180° . We used a one sample test on the mean angle (Berens, 2009) with the following hypothesis:

$$H_0 : \bar{\alpha} = \bar{\alpha}_0$$

$$H_1 : \bar{\alpha} \neq \bar{\alpha}_0$$

where $\bar{\alpha}_0$ is a constant against which the data are compared. The test was performed by verifying whether $\bar{\alpha}_0 \in [CI_1, CI_2]$, with CI_1 and CI_2 being the lower and upper confidence intervals on the population mean $\bar{\alpha}$, at a 0.05 significance level. Note that the values of $\bar{\alpha}_0$, CI_1 and CI_2 are given in radians.

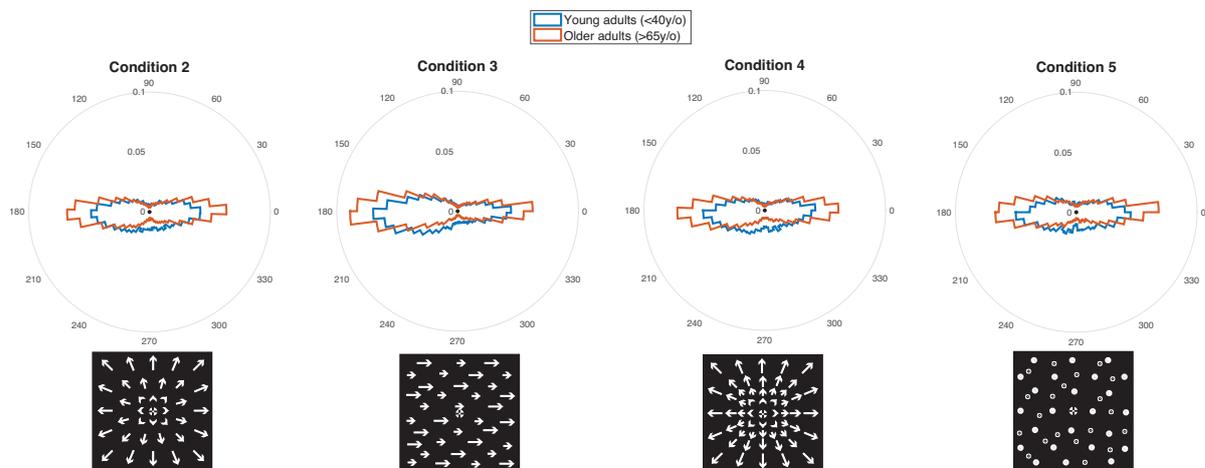


Figure 7.7 – Influence of optic flow on fixational saccade direction. Fixational saccades were clustered on the horizontal axis with no apparent preferred direction in the radial optic flow conditions (conditions 2 and 4) and in the control condition (condition 5). The tangential optic flow condition (condition 3) triggered more saccades to the left, thus resembling an optokinetic reflex.

We found that angular distances during both condition 1 (baseline condition, fig. 7.8) and condition 5 (control condition, supp. fig. 7.12) seem to be directed outward (condition 1: $3.11 \in [3.08, 3.15]$ and condition 5: $3.03 \in [2.85, 3.21]$). On the other hand, the distribution of angular distances during condition 2 (radial flow at low speed) seems bimodal and slightly more oriented toward 0° than the equivalent distribution during condition 1 (fig. 7.8). Statistically however, we could reject that $\bar{\alpha}_0$ was centered on 0° (condition 2: $3.08 \in [2.81, 3.35]$). When considering the condition 4 (radial flow at high speed), fixational saccades were directed inward, i.e., toward the center (condition 4: $-0.25 \in [-0.71, 0.21]$).

7.3.4 Discussion

The main objectives of this section were to characterize the effect of *i*) aging and *ii*) optic flow conditions on fixational saccade properties during a fixation task. Overall, we have found a global increase in all the fixational saccade properties with advancing age. Optic flow conditions influenced saccade statistics, notably by orienting saccades in the direction opposite to the flow.

There was a clear shift in the whole spectrum of fixational saccades with advancing age. When attempting to fixate, older adults produced saccades that are characterized by a higher frequency, amplitude and peak velocity, compared to young adults. What would be the reason for such an age-related shift? Several interpretations are plausible. First, a detrimental interpretation with respect to aging is that advancing age is associated with a higher instability in the oculomotor system. For instance, neural aberrations in frontal brain areas involved in the control of saccade generation and inhibition have been found in older adults (Pa et al., 2014). This overactivity was associated with a poor capacity to inhibit unwanted saccades. Given that microsaccades are

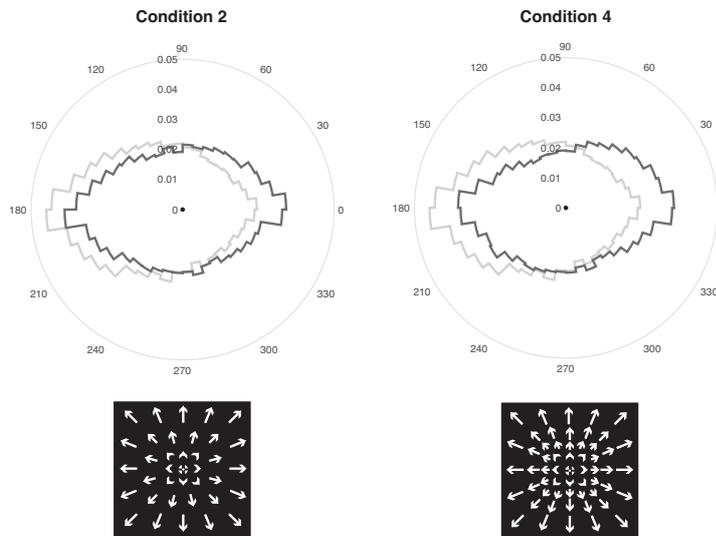


Figure 7.8 – Directional bias in the radial optic flow conditions. A distribution clustered on 0° is indicative of fixational saccades going toward the center of fixation whereas a distribution centered on 180° indicates outward saccades. The distribution of saccades during condition 1 is indicated in light gray, for comparison.

subject to some form of voluntary control (Steinman et al., 1967), a higher fixational saccade frequency could be indicative of a failure to inhibit unwanted fixational saccades, as has been observed for large, voluntarily controlled, saccades (Peltsch et al., 2011; Abel and Douglas, 2007). Since no perceptual task was associated with our fixation task, we can not say whether this age-related shift in saccade properties positively or negatively impacts vision. Additional experiments are required in order to understand the origins of these age-related changes. A second, more positive interpretation, is viewing this shift as a compensatory adaptation of the oculomotor system to age-related changes in the visual system. Indeed, it has been suggested by McCamy et al. (2012) that larger and more frequent microsaccades can be useful in restoring foveal vision. This could be due to the fact that large microsaccades are likely to bring the neuronal receptive fields to an uncorrelated region of the stimulus. Interestingly, the size of receptive field populations within the foveal region were shown to increase in healthy older adults (Brewer and Barton, 2014). It could thus be hypothesized that the oculomotor system adapts, by increasing microsaccade amplitude, so as to counteract changes in the visual system, such as e.g., increased receptive field size.

Our results suggest that the characterization of fixational saccade properties in the literature can be biased depending on the threshold chosen for saccade detection. For instance, Port et al. (2015) used a permissive upper threshold (1°) when studying microsaccades in older adults. They found a small, but significant, increase in microsaccade frequency. In our experiments, when using the same threshold as in the study of Port et al., our results do not confirm their conclusion, derived from a very small sample of older subjects ($n=7$ for subjects with age between 60 and 66 y.o.). Our results are in agreement with Gao et al. (2018) who found no effect of age

on microsaccade frequency. However, since the exact value of the threshold they used to detect microsaccades is not clear, it is difficult to draw definite conclusions based on the comparison of the two studies.

The observed increase in fixational saccade size, peak velocity and frequency in older adults can correspond to an increase in SWJ occurrence in this group, but we did not study this question in detail. The fact that older adults were more likely to produce a returning saccade within the temporal delay generally associated with SWJs is an indication that this suggestion may be correct. A deeper analysis could involve using a detection method to classify eye movement into SWJ and isolated microsaccades (Otero-Millan et al., 2011b), however, such a classification algorithm requires setting multiple thresholds (e.g., for the amplitude, timing, distance and direction of events constituting a potential SWJ). As discussed above, the choice of these thresholds can bias potential conclusions concerning age-related differences.

In our optic-flow studies, we have observed a significant decrease in fixational saccade frequency in conditions 2-5, relative to the condition 1, in which the fixation cross was displayed on a homogeneous background. The fact that this effect was observed both during the optic flow conditions and the control condition (white noise, that did not contain any motion pattern) suggests that it does not depend on the motion pattern contained in the visual flow.

In contrast to the observed independence of the microsaccade rate on specific motion patterns, our results show that fixational saccade direction is strongly affected by the type of optic-flow presented. When experiencing a tangential motion pattern (condition 3), participants produced eye movements resembling a small-sized optokinetic reflex (OKR), with microsaccades directed in the direction opposite to the flow. These data are consistent with other studies (Laubrock et al., 2008; Piras et al., 2016), suggesting a presence of resilient optokinetic processing despite the presence of a visual anchor (e.g., a fixation target). Interestingly, saccades were more frequent and larger during tangential flow in young adults, leading to the suggestion that they are more sensitive than older adults to this type of visual stimulation.

Finally, we observed that in all conditions except condition 3, fixational saccades were aligned with the horizontal axis. It is not completely clear why microsaccades and, more generally, saccadic intrusions, are predominantly horizontal in humans (Otero-Millan et al., 2011b). Though, the fact that fixational saccades are horizontal does not indicate whether these are directed to the fixation target (i.e., inward) or whether they are directed outward. To address the latter issue, we estimated the center of the saccade target distribution and found that fixational saccades were more likely directed to the center in the radial flow condition (conditions 2 & 4). This was especially true during the high-speed condition (condition 4). On the contrary, saccades were directed outward when no motion pattern was present (conditions 1 and 5). However, the observed effects were small, with a high heterogeneity in the distribution of directions, suggesting a rather weak influence of the type of optic flow pattern on the direction of fixational saccades. More generally, our results are in agreement with the idea that fixational saccades both introduce (e.g.

in conditions 1 and 5) and correct (e.g. in conditions 2 and 4) fixational errors (Engbert and Kliegl, 2004; Rolfs, 2009).

7.3.5 Supplementary information

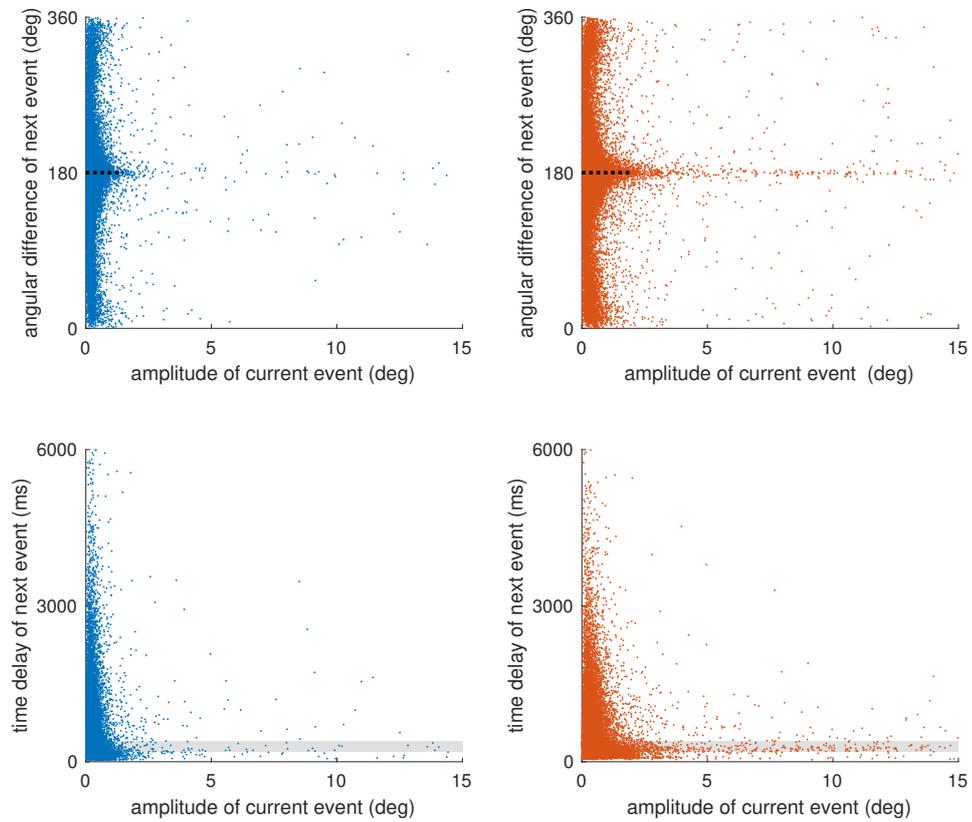


Figure 7.9 – Properties of fixational saccade pairs as a function of the amplitude of the first event. Large saccades seem followed by a saccade in opposite direction (dashed line centered on 180° and in-between the 200 – 400 ms delay window (shadowed area).

YOUNG ADULTS			
condition a	condition b	estimate	p-value
1	2	1.6	<0.0001
1	3	0.39	1
1	4	1.6	<0.001
1	5	2	<0.0001
2	3	-1.2	<0.01
2	4	-0.029	1
2	5	0.33	1
3	4	1.2	<0.01
3	5	1.6	<0.001
4	5	0.36	1
OLD ADULTS			
condition a	condition b	estimate	p-value
1	2	1.6	<0.0001
1	3	1.8	<0.0001
1	4	2.2	<0.0001
1	5	2.7	<0.0001
2	3	0.16	1
2	4	0.64	0.8
2	5	1.1	<0.05
3	4	0.47	1
3	5	0.92	0.11
4	5	0.45	1

Table 7.1 – Statistical effect of the experimental conditions on fixational saccade frequency.

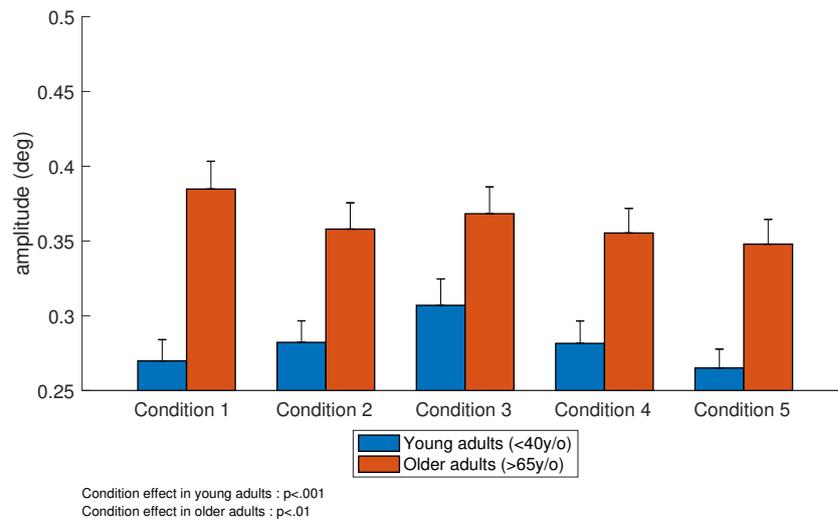


Figure 7.10 – Influence of optic flow on fixational saccade amplitude. Data were averaged over the trials of each condition. Error bars correspond to the standard error of the mean. Condition effects correspond to Friedman ANOVA associated with each age group.

YOUNG ADULTS			
condition a	condition b	estimate	p-value
1	2	-0.44	1
1	3	-1.5	<0.001
1	4	-0.35	1
1	5	-0.18	1
2	3	-1.1	<0.05
2	4	0.088	1
2	5	0.26	1
3	4	1.2	<0.05
3	5	1.4	<0.01
4	5	0.18	1

OLD ADULTS			
condition a	condition b	estimate	p-value
1	2	0.56	1
1	3	0.22	1
1	4	0.46	1
1	5	1.3	<0.01
2	3	-0.34	1
2	4	-0.098	1
2	5	0.76	0.3
3	4	0.24	1
3	5	1.1	<0.05
4	5	0.85	0.15

Table 7.2 – Statistical effect of the experimental conditions on fixational saccade amplitude.

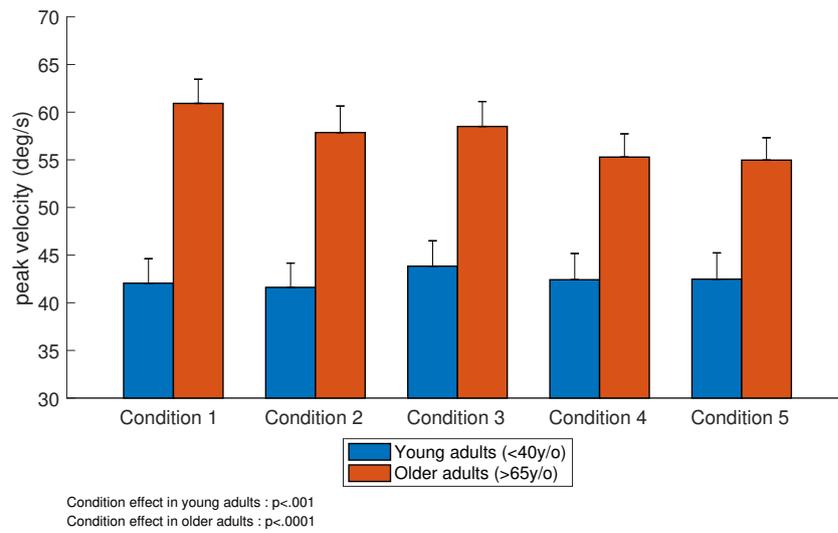


Figure 7.11 – Influence of optic flow on fixational saccade peak velocity. Data were averaged over the trials of each condition. Error bars correspond to the standard error of the mean. Condition effects correspond to Friedman ANOVA associated with each age group.

YOUNG ADULTS			
condition a	condition b	estimate	p-value
1	2	0.47	1
1	3	-1.1	<0.05
1	4	0.24	1
1	5	0.41	1
2	3	-1.6	<0.001
2	4	-0.24	1
2	5	-0.059	1
3	4	1.4	<0.01
3	5	1.5	<0.001
4	5	0.18	1
OLD ADULTS			
condition a	condition b	estimate	p-value
1	2	1.4	<0.001
1	3	0.45	1
1	4	1.4	<0.001
1	5	1.6	<0.0001
2	3	-0.9	0.087
2	4	0.071	1
2	5	0.29	1
3	4	0.98	<0.05
3	5	1.2	<0.01
4	5	0.21	1

Table 7.3 – Statistical effect of the experimental conditions on fixational saccade peak velocity.

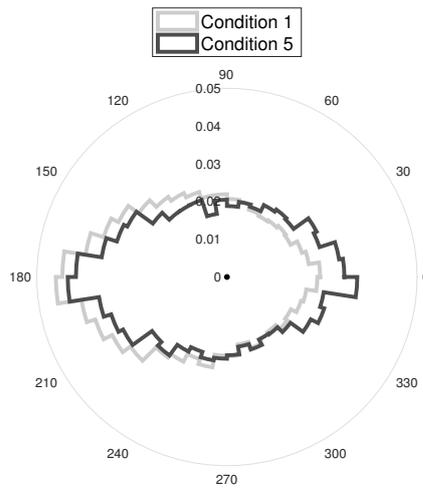


Figure 7.12 – Inward/outward fixational saccades for condition 5 (white noise). A distribution clustered on 0° is indicative of fixational saccades going toward the center of fixation whereas a distribution centered on 180° indicates outward saccades. The distribution of saccades during condition 1 is indicated in light gray, for comparison.

7.4 Regular saccades

7.4.1 Rationale

The purpose of this section is to characterize regular saccades in the participants of the SilverSight cohort. The effect of aging on regular saccade generation and inhibition has been well characterized: older adults are impaired in inhibiting an unwanted saccade, as measured by the anti-saccade task (Peltsch et al., 2011; Abel and Douglas, 2007) and they produce saccades with a reduced temporal and spatial precision (higher saccadic latency and lower accuracy on the pro-saccade task, Peltsch et al., 2011; Irving et al., 2006). The influence of aging on peak velocity is still inconclusive with some evidence of no age-related differences (Huaman and Sharpe, 1993; Munoz et al., 1998; Shafiq-Antonacci et al., 1999) and other reports showing a decrease in saccadic peak velocity (Moschner and Baloh, 1994; Abel et al., 1983).

The objectives are to *i*) replicate previous data on a large sample of participants, *ii*) try to resolve the inconsistency of reports on the effect of age on saccadic peak velocity and *iii*) search for associations between oculomotor and visual functions in aging.

7.4.2 Methods

Participants and Material. The participants, setup and protocol used for this section are identical to those presented in the section "*Fixation area*" (sec. 7.1.1).

Protocol. The experiment was performed in the dark and under head-fixed conditions using a chinrest. During the experiment, the subjects wore trial frames to achieve their best-corrected visual acuity. We added up to +1.75 dioptre to the refractive error to reduce accommodative demands. The protocol included pro- and anti-saccade tasks that were performed together with the fixation task, described in section 7.1.1. The order of the tasks was randomized between subjects. The entire session lasted approximately 90 minutes, breaks included. A nine-point calibration was performed at the beginning of the experiment and after each break. Participants were encouraged to have a break when needed.

During the pro-saccade task, the participant was instructed to look as fast as possible towards a target appearing in the periphery, whereas in the anti-saccade task, the participant had to look as fast as possible at the opposite position relative to the target. At the beginning of each trial, a fixation cross appeared at the center of the screen. After 3 seconds, the fixation cross disappeared and the target was displayed for 1.5 seconds after a 200 ms gap (fig. 7.13A). The fixation cross consisted of a bull-eye shaped target (Thaler et al., 2013), white on an evenly black background, covering $0.6^\circ \times 0.6^\circ$ of visual angle. The target was a white square covering $0.34^\circ \times 0.34^\circ$ of the visual field. In the pro-saccade task, the target appeared at 8 possible positions (fig. 7.13B). The distance between the fixation point and the target was of 10° for positions 2, 4, 6, 8, and of 14° for positions 1, 3, 5, 7. Each position was tested 10 times, for a total of 80 saccades. In

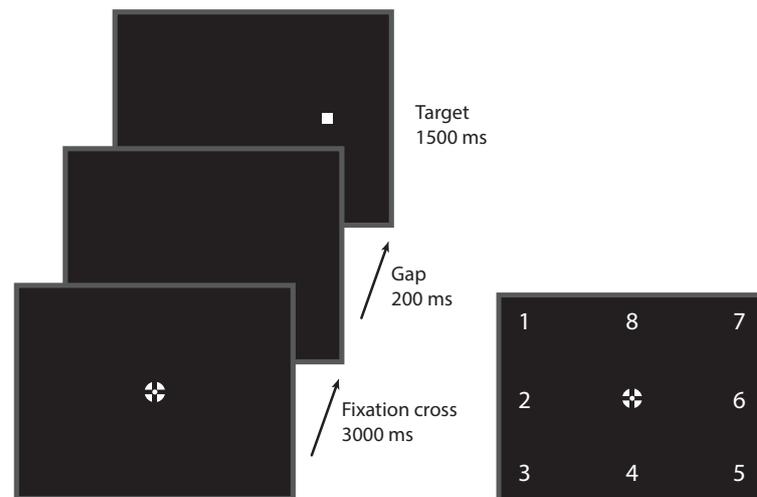


Figure 7.13 – Saccadic task. (Left) At the beginning of each trial, the fixation cross appeared at the center of the screen. After 3000 ms, the fixation cross disappeared and the target was displayed for 1500 ms after a 200 ms gap. (Right) During the pro-saccade task, the target could appear at 8 possible positions. The participant was instructed to look as fast as possible towards the target. In the anti-saccade task, the target appeared at positions 2, 4, 6, 8. The participant had to look as fast as possible towards the opposite position relative to the target.

the anti-saccade task, the target appeared at positions 2, 4, 6 and 8 only. A total of 40 randomized anti-saccades were carried out. Participants did 3 practice trials for the pro-saccade task and 6 practice trials for the anti-saccade task. These practice trials could be reiterated if necessary.

The visual screening of the participants was performed before the experiments. It included measures of binocular best-corrected visual acuity (ETDRS chart at 2m distance, in scotopic condition, with the best optical correction), binocular visual field (Perimeter Octopus 900 with constant luminosity and stimulus size, in scotopic condition) and visual attention (central [UFOV1] and peripheral visual discrimination task, without [UFOV2] and with [UFOV3] visual distractors, Ball et al., 1993). We report the performance on the subtask 3 of the UFOV only, expressed as the stimulus display time needed to perform the task, in milliseconds.

Data analysis. Saccades were automatically detected by the Eyelink algorithm (detection thresholds: velocity above $30^\circ/s$, acceleration above $8000^\circ/s^2$, position drift above 0.15°). Variables of interest for pro-saccades were the saccadic latency (i.e., the temporal delay between target appearance and saccade onset), the saccadic gain (i.e., the ratio between the saccade amplitude and the real distance between the fixation cross and the target) and the angular error of the saccade (angular difference between the triggered saccade and the position of the target). Because the peak velocity of a saccade is dependent on its amplitude (Bahill et al., 1975), we analyzed peak velocity by binning saccades according to different amplitudes (bin width: 2°). We also analyzed the fixation area covered by eye positions when the subject was fixating on the central fixation cross. We discarded the first second of recording for this analysis and used the isoline

estimation technique to estimate the fixation area (density level: 95%, bandwidth size: 0.125¹).

The variable of interest for the anti-saccades task is the proportion of inhibition errors. An error in the anti-saccades paradigm corresponded to a saccade towards the target rather than in the opposite direction. We analyzed parameters for the first saccade produced after target appearance. However, we discarded any anticipatory saccades (latency lower than 80 ms) and potential microsaccades (saccades smaller than 1°) from our data.

We report the effect size for every ANOVA on the age factor as an η^2 , calculated as a ratio between the sum of squares of the effect and the total sum of squares. We computed partial correlations between oculomotor and visual variables, controlling for the subject' age.

7.4.3 Results

We have found a significant effect of age on saccadic latency ($F_{(99)} = 6.6, p < 0.0001, \eta^2 = 0.31$, fig. 7.14A), saccadic gain ($F_{(99)} = -5.33, p < 0.0001, \eta^2 = 0.22$, fig. 7.14B) and the angular error of the produced saccade ($F_{(97)} = 2.32, p < 0.05, \eta^2 = 0.05$, fig. 7.14C). Older adults had a higher latency, a lower gain and a higher angular error indicating that spatial and temporal precision of saccades decreased with age. On the other hand, age had no effect on the fixation area produced before saccade triggering ($F_{(95)} = 0.87, p = 0.38, \eta^2 = 0.008$, fig. 7.14D), nor on the saccadic peak velocity for none of the studied bins (all $p > 0.05$, fig. 7.14E). Older adults were also less capable of inhibiting a saccade as they had a higher rate of error on the anti-saccade task ($F_{(102)} = 3.8, p < 0.001, \eta^2 = 0.13$, fig. 7.15).

There was no significant partial correlation between the oculomotor variables (saccadic gain, latency and inhibition error) and visual functions (best-corrected visual acuity, visual field extend, visual attention, fig. 7.16).

7.4.4 Discussion

Overall, we have reproduced the classical effect of aging on regular saccade generation and inhibition. Older adults' saccadic latency and accuracy were lower and saccadic inhibition was less efficient, when compared to young adults. This is in accordance with previous evidence (Peltsch et al., 2011; Abel and Douglas, 2007; Fischer et al., 1997; Irving et al., 2006; Warren et al., 2013).

In our large sample of participants, we did not observe any age effect of saccadic peak velocity, coherent with previous studies (Huaman and Sharpe, 1993; Munoz et al., 1998; Shafiq-Antonacci et al., 1999). However, it has been suggested by others that the age modulation on peak velocity may be evident only for large saccades, i.e., exceeding 20° (Moschner and Baloh, 1994; Abel et al., 1983). Given that we had saccades no larger than 16-18°, it is possible that we did not have the opportunity to observe this phenomenon.

¹More information about this estimation technique can be found in section 7.1.1.

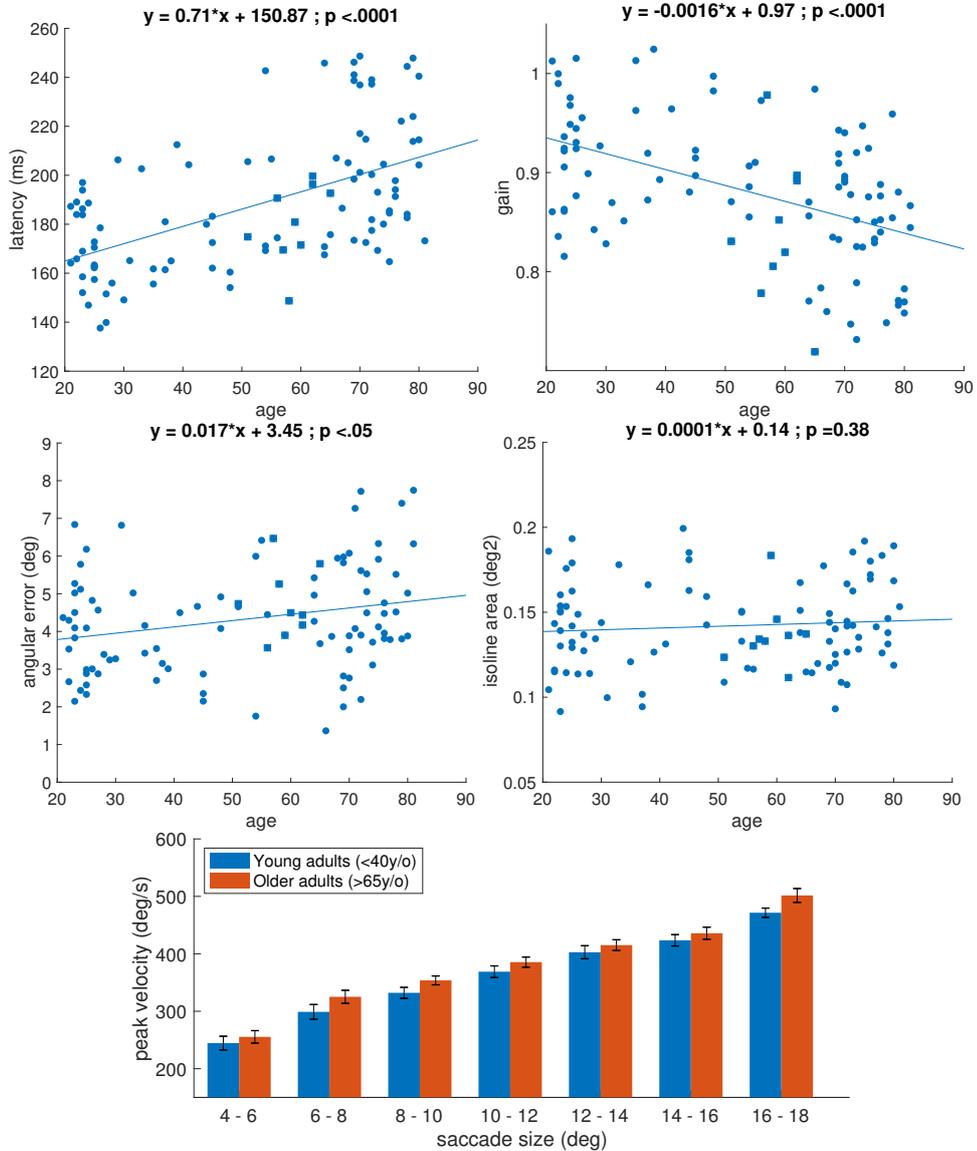


Figure 7.14 – Properties of regular saccades during the pro-saccade task. Latency (top left), gain (top right), angular error (middle left), isoline area (middle right) and peak velocity of saccades binned into different saccade amplitudes (bin width: 2°, bottom). Age had a significant effect on latency, gain and angular error of the saccades. However, there was no effect of age on the fixation area covered before the production of the saccade nor on the saccade peak velocity, regardless of its amplitude. Data were averaged across all conditions and trials. The parameters for the linear regression with age and the associated p -value are indicated above the graphs in A, B, C and D. p -values: **** $p < 0.0001$; *** $p < 0.001$; ** $p < 0.01$; * $p < 0.05$. Participants identified by a square were recorded at 500 Hz, all other participants were recorded at 1000 Hz. Error bars correspond to standard error of the mean.

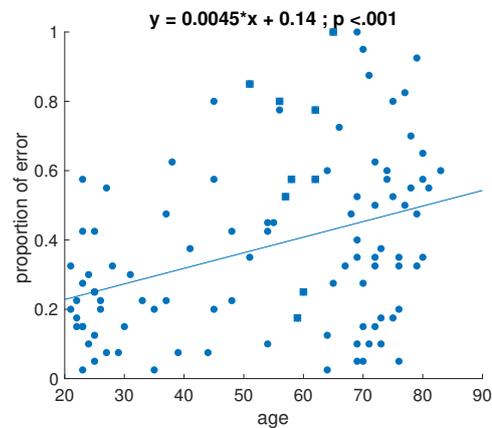


Figure 7.15 – Proportion of error during the anti-saccade task. An error in this task corresponds to the production of a saccade towards the target, instead of in the opposite direction. Data were averaged across all conditions and trials. The parameters for the linear regression with age and the associated p -value is indicated above the graph. p -values: **** $p < 0.0001$; *** $p < 0.001$; ** $p < 0.01$; * $p < 0.05$. Participants identified by a square were recorded at 500 Hz, all other participants were recorded at 1000 Hz. Error bars correspond to standard error of the mean.

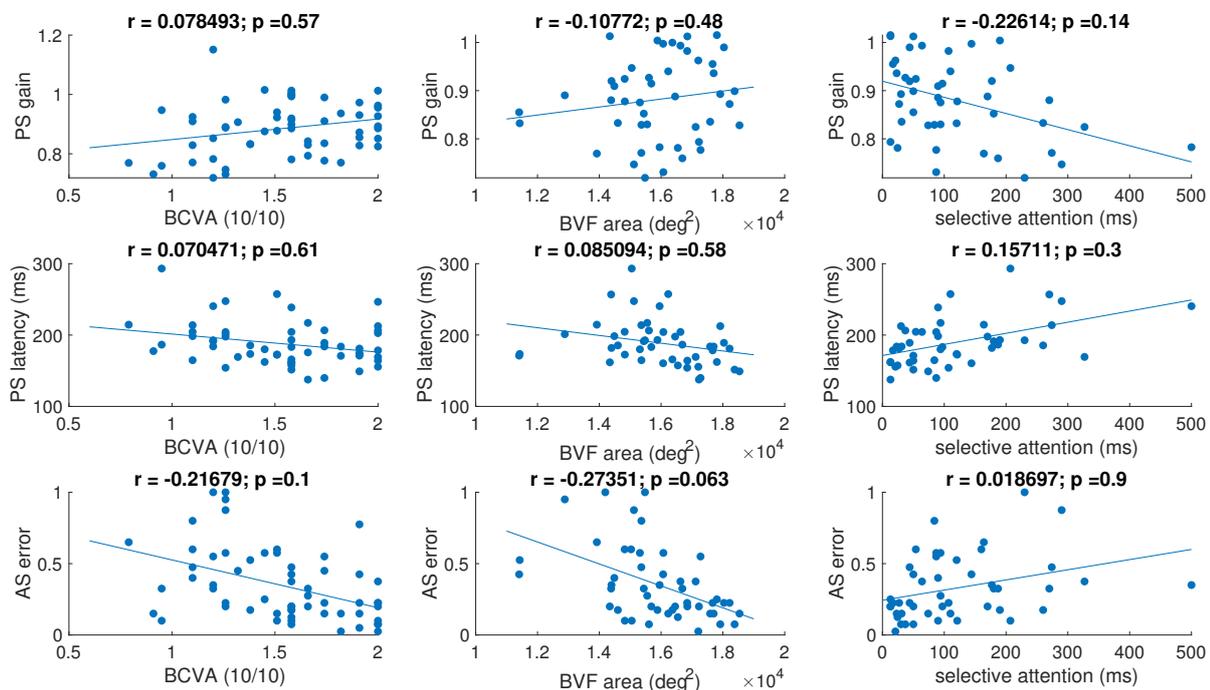


Figure 7.16 – Partial correlations between oculomotor and visual variables. On top of each graph is indicated the coefficient of the partial correlation controlling for the participant' age and the p -value associated. PS = pro-saccade, AS = anti-saccade, BCVA = binocular best-corrected visual acuity, BVF = binocular visual field.

What are the factors likely to explain the decreased latency and accuracy of reflexive saccades in aging? Several interpretations have been given in the literature. A lower temporal and spatial precision of saccades in aging can be linked with visual deficits (i.e., increased visual thresholds, poor target localization), extraocular muscle dysfunction or (sub)cortical degeneration with age (Yang et al., 2006; Warren et al., 2013; Huaman and Sharpe, 1993). Concerning the visual influences, the fact that *i*) all participants had a visual acuity better than 8/10 *ii*) performed the task with their best optical correction and an addition that reduced accomodative demands and finally *iii*) the lack of any correlation between oculomotor performance and visual functions, does not support this interpretation. Additionally, the fact that we did not find any effect of age on the fixation area (as estimated by an isoline) likely indicates that the decreased precision of saccades is not related to an instability of the eye during the period preceding saccade generation.

Saccadic inhibition was less efficient in older adults. This deficit is interpreted as an evidence of frontal hypofunction in aging (Raz et al., 2005). For instance, a decrease in saccadic inhibition capacity has been shown to correlate with gray matter atrophy in the frontal lobes and with deficits in measures of executive functions in older adults (Mirsky et al., 2011). Contrary to previous studies (Peltsch et al., 2011; Fischer et al., 1997), however, we did not find that automatic processes (saccade generation) were less impacted by age than voluntary ones (saccade inhibition), given that the effect size associated with inhibition error (in the AS task) were lower than those observed for saccadic precision (in the PS task). This could indicate that frontal integrity in our sample of older adults was well preserved, as compared to other samples in the literature. The fact that we payed attention to exclude cognitively impacted subjects from the Silversight cohort fits well with this interpretation.

Part III

GENERAL DISCUSSION

8.1 Discussion on aging & spatial cognition

8.1.1 Achievements

Our main objectives regarding the impact of aging on spatial cognition were to *i*) understand what type of spatial cues older adults relied on to anchor their spatial representations, and *ii*) what is the impact of cue preference on the use of egocentric and allocentric strategies in aging. Overall, our results suggest an age-related spatial reorganization where representations are spontaneously anchored by geometric cues with advancing age. Importantly, these age-related changes were demonstrated in an ecological environment. The type of environment, the number of landmarks and general properties of visual cues were similar to those experienced in real life. Participants were free to move and to naturally explore this real, yet controlled, environment. One of important conclusions from our results is that older adults might not be as bad navigators as previously thought if available geometric cues provide unambiguous spatial information. Indeed, we showed that older adults, similarly to children, were as efficient as young adults when using allocentric strategies, provided that their preferred cue (i.e., geometry) was available at the time of navigation decision. When landmarks were the only source of allothetic information, older adults preferred an egocentric strategy potentially due to its lower cognitive load.

8.1.2 Implications

Scientific impact. The results of this work contribute to a vivid debate on the consequences of aging on spatial cognition and, more generally, on the impact of geometric cues in guiding behavior in many species, including humans (Lester et al., 2017; Cheng et al., 2013). More specifically,

our findings fill the gap in the knowledge of the relative influence of landmark versus geometric information in aging, a question that has received little attention so far. The scientific implication of two aspects of this work can be highlighted. First, our results challenge a long-standing hypothesis that older adults have a spontaneous preference for egocentric strategies (Colombo et al., 2017; Bohbot et al., 2012; Davis and Weisbeck, 2015; Driscoll et al., 2005). Although our observations do not exclude that this interpretation of previous results is correct, we show that the preference for egocentric strategies was almost always observed under quite specific experimental conditions, i.e., when only landmarks provided useful cues for navigation. In the light of our findings, age-related changes in cue preference may offer a novel explanation for the observed age-related differences in spatial navigation strategies. That is, the preference for geometric cues (observed on the reorientation paradigm) may critically determine how allocentric and egocentric strategies are employed by older adults. There is thus a need to rethink the allocentric/egocentric dichotomy by integrating other dimensions (such as spatial cue processing), allowing for a better understanding of age-related consequences on spatial navigation. Second, regarding the effect of gender, it was proposed that women relied more on landmarks as compared to men during spatial navigation (Sandstrom et al., 1998; Saucier et al., 2002). Our results in ecological-like conditions do not confirm these data, as we did not find any association between cue preference and gender.

Technological implications. From a technological viewpoint, our results stress the need for studying spatial navigation in natural conditions by either building a real environment or using immersive mobile virtual reality (VR). Despite the fact that immersive VR may alter the way people interact with the environment, e.g., due to the reduction of the field of view, our experiments confirmed the validity of this tool in replicating previously reported age-related tendencies in spatial navigation. However, we note that some behavioral responses recorded with our immersive VR had some differences as compared to computer screen based observations. For example, we found a relatively more frequent use of allocentric strategies in *young* adults solving the Y-maze task as compared to the previous desktop study by Rodgers et al., 2012. Importantly, we found that immersive VR was well tolerated by all older participants, suggesting that it can be a useful tool in aging studies. The crucial advantage of immersive mobile VR relative to desktop VR consists in enabling the subject to experience the full sets of idiothetic cues (e.g., proprioceptive and vestibular), which is critical for spatial learning and for integrating visual information with head and body movements. The advantage of this setup relative to real-world testing is the possibility to easily control environmental cue appearance and position as well as to perform cue manipulations that are impossible to do in real life. For instance, studying how morphing of geometric cues by manipulating the aspect ratio of the room may affect spatial behavior, is feasible in a VR environment. Additionally, because VR experiments generally require less time relative to real experiments, it is possible to test a larger sample of participants, which can be beneficial to the understanding of inter-individual differences in navigation.

Societal payoff. Wayfinding deficits have a tremendous impact on older adults autonomy and well-being, including such aspects as: decreased social interactions (Simon et al., 1992); decreased mobility and driving; and increased avoidance of unfamiliar environment (Burns, 1999). Furthermore, getting lost is frequently associated with frustration and anxiety (Chiu et al., 2004). Physical and social isolation can in turn diminish the quality of life community-dwelling older adults and increase the cognitive decline in this population (Hertzog et al., 2008; Lindenberger, 2014). As shown by Lövdén et al. (2012), cognitive training based on navigation in a complex maze had protective effects on both navigation performance and hippocampal integrity against age-related loss. In their protocol, they did not distinguish between landmarks and geometry, which were both present in the virtual city they used. Our results suggest a potential benefit of cognitive training that can favor the use of geometry or that is aimed at a rehabilitation of the use of landmarks in older adults. They also suggest that navigating in environments that are poorly polarized in terms of geometry can represent an additional cognitive effort in older adults and therefore participate in spatial disorientation and anxiety in this population.

8.1.3 Raised questions & future studies

Why do older adults preferentially use geometric cues to reorient and navigate in space? In other terms, what is wrong with landmarks? We have identified several non-exclusive interpretations that we discuss below.

1. The "adaptive-combination model" states that reorientation is flexible and that preferential use of spatial cues depends on the weight associated to each cue. The weight is based on the perceived reliability, validity, salience, or prior experience with the cue (Newcombe and Ratliff, 2007, 2008). When interpreted in relation to this model, our results may suggest a relative change in the associative weight of landmarks vs. geometry occurring across lifespan. In our reorientation/conflict paradigm, we did not manipulate reliability, validity, salience or size of cues. All landmarks were visually salient and they covered all the walls of the enclosure. Additionally, geometry and landmarks were equally stable and they were both valid in indicating the goal position during spatial learning. During the probe trial (with a rotated landmark configuration), young adults searched for the goal position by using the landmark array, whereas older adults reoriented and navigated by using the geometry of the room. Intriguingly, the behavioral response of older adults is somewhat reminiscent of the primacy for geometry in young children (Hermer-Vazquez et al., 2001), although our experimental protocol was different. One possibility is that ontological experience, acquired through lifetime, changes the weight associated with landmark or geometry information. For instance, the primacy for geometry in children has been linked to the fact that children are more exposed to geometric enclosures than open-field distal landmarks during childhood (Newcombe and Ratliff, 2007), whereas young adults had acquired more experience where landmarks were useful in indicating locations

(Newcombe and Ratliff, 2008). This type of age-related changes in navigational habits is difficult to test in humans but has received support from animal studies showing that the rearing environment critically influences how spatial cues are used (Twyman et al., 2013). It can be speculated then, that the primacy of geometry in older adults is associated with a perceived increase of landmark instability with advancing age. It is not clear, however, what changes in navigation habits (e.g., lower exposition to distal landmarks) or acquired knowledge (e.g., landmarks are more changing over time than geometry) would lead to this decreased weight accorded to landmarks in older adults.

2. A second possible interpretation is that there is a failure, in older adults, in anchoring their "cognitive map" with respect to landmarks. Although our reorientation experiments show that landmarks are not completely disregarded by older adults, older adults express a clear decline in performance when forced to use landmarks, and they are not capable of using them to encode a goal position allocentrically. It could be hypothesized that older adults fail to associate landmarks to directions on their cognitive map or that they fail to use landmarks to determine their heading. These hypotheses are supported by the fact that older adults were impaired in inferring the directions associated with landmarks in the Perspective Taking test. On the other hand, one could also suggest that because landmarks are not properly bound to the cognitive map, they cannot help identifying allocentric positions (e.g., that of a goal). That landmarks are not efficiently bound to the spatial representations in older adults is supported by some surprising comments made by older adults during informal interviews after the reorientation experiment. When asked whether they noticed a change in the second phase of the reorientation experiment (i.e., after the rotation of the whole landmark configuration), many older adults responded negatively. Moreover, one participant had the (wrong) impression that panels were changed before each trial of the learning phase. Testing these hypotheses by using classic experimental paradigms, such as the reorientation paradigm, the Y-maze, or the MWM might be difficult. We are therefore developing a novel paradigm to effectively dissociate the encoding of directional information *per se* from the encoding of information about the goal position. For instance, varying the position of landmark or geometric information from proximal (i.e., to indicate position) to distal/infinite (i.e., to indicate allocentric direction), could be useful for this purpose.
3. A third possibility is that processing of geometry is less cognitively demanding as compared to landmarks. Thus, the observed preference for geometry in older adults might be the result of a 'cognitive resource saving policy'. If this were true, one would expect geometry-related choices to be associated with a more efficient navigation. In addition, one might expect a lower performance of subject relying on geometry subjects in cognitive tests. Conversely, cue preference (for landmarks or geometry) was not associated with differences in navigation efficiency in our experiments. Participants were just equally rapid in making

their navigation decisions to navigate to the goal, independently from the type of preferred cue. Moreover, older adults that preferred geometric cues did not differ in terms of memory capacity, attention and executive functions from older adults preferring landmarks. The only exception is the Perspective Taking test, the results of which may be more related to difficulties in landmark processing than in cognitive decline.

4. A fourth possibility is that: *i)* the processing of geometric cues is mediated by a different sub-network of brain areas with respect to the processing landmarks; and *ii)* the sub-network related to geometric processing is better preserved in aging. More experiments are thus required in order to *i)* differentiate the brain areas implicated in geometry vs. landmark processing in humans, and *ii)* characterize age-related cortical and sub-cortical dysfunctions potentially explaining the preference for geometry observed in our experiments. To address these issues, the Y-maze experiment realized during this project is being currently replicated by using fMRI in our laboratory (by S. Ramanoel).
5. Finally, a last interpretation could be that age-related, low-level constraints, such as fear of falling, age-related lowering of the head or potential kyphosis, would bias older subjects to look at the ground, which in turn, could result in the preference for geometry. This interpretation is unlikely, at least in our experiments, as shown by our postural and gait analysis (see Article 1, and sec. 6.1.1).

Is there an inverted-U shape profile of landmark processing across the lifespan? The preference for geometric cues in the reorientation paradigm was shown in children under the age of 6 (Hermer-Vazquez et al., 2001). Subsequent studies found that in certain situations, such as in large rooms with distal landmarks, children are capable of using landmarks to distinguish the correct corner from its rotationally symmetric one (Newcombe et al., 2005; Learmonth et al., 2008). In relation to our results, it is an interesting question whether, even if capable of using landmarks, children prefer geometry when searching for the goal position. An experimental study addressing this question (i.e., a replication of the reorientation paradigm in ecological conditions) is ongoing in our laboratory. If this is indeed the case, these data would suggest a symmetry of spatial cue processing across the lifespan, and, more specifically, an inverted-U shape profile of landmark processing. An indication that this hypothesis might be correct comes from our study in the Y-maze (see also Bullens et al., 2010). If this interpretation is correct, it predicts that children younger than 10 y.o. (i.e., the age of children in our experiments) would use landmark-based allocentric strategies less often, while they would use geometry-based allocentric strategy in the same proportion as in our data (see Hermer and Spelke, 1994, 1996; Hermer-Vazquez et al., 2001). At the other end of the curve, our hypothesis predicts that in a population older than ~75 y.o. on average (i.e., older than participants in our experiments) the proportion of subjects preferring geometry in the reorientation paradigm would increase, whereas the proportion using allocentric strategies based on landmarks in the Y-maze would decrease.

What about pathological spatial cognitive aging? Alzheimer's disease (AD) is a neurodegenerative condition associated with neuronal pathology, manifested as intraneuronal formation of tau and β -amyloid proteins, first appearing in brain areas such as the entorhinal cortex and the hippocampus (Braak et al., 2011). AD is characterized by memory and spatial orientation deficits (Henderson et al., 1989), and by devastating spatial navigation impairments (Cushman et al., 2008; Parizkova et al., 2018). Spatial cognition deficits, although to a lesser extent, are also present in pre-clinical AD stages (Lithfous et al., 2013). Moreover, adults at genetic AD risk were shown to express a reduced grid-like BOLD signal in the entorhinal cortex and a higher tendency to navigate near environmental boundaries, well before AD could be diagnosed (et al. Kunz, 2015). These data suggest that spatial navigation tests might provide behavioral markers of future pathology. The data gathered through the cognitive screening of our study population did not show any evidence for a higher cognitive decline (in terms of memory, attention, and executive functions) in subjects using geometry, as compared to subjects using landmarks. Yet, the hypothesis of an inverted-U shape profile of landmark vs. geometry processing across lifespan might suggest that the ability to use geometric cues is the last bastion of healthy spatial cognitive aging (as opposed to, e.g., AD). A previous desktop VR reorientation study found that AD patients, as well as participants with a mild-cognitive impairment, expressed reorientation deficits related to both landmark and geometry processing (Caffò et al., 2017). New longitudinal experiments are needed to test whether this result can be reproduced in ecological environments, and, ultimately, to what extent geometric spatial processing deficits could serve as biomarkers of pre-clinical AD.

How do the complexity and size of the environment influence cue preference? In our experiments, navigation was performed in *vista spaces*, in which environmental information, including the goal location, could be seen from a single viewpoint (Montello, 1993). One limitation of experimental studies involving vista spaces is that it is not clear whether it is necessary for the navigator to self-localize in order to compute the trajectory to the goal (Wolbers and Wiener, 2014). As discussed earlier (Sec. 6.2.4), our motion tracking data combined with the analysis of oculomotor behavior can be instrumental to the study of the nature of the spatial processes implicated in navigation in vista spaces. For example, approaching the choice point in the Y-maze and fixating a salient cue (e.g., the landmark that was directly in front of the participant during the learning trials) before choosing to turn right on the probe trial of the Y-maze would be indicative of a rather egocentric-kind of behavior. In contrast, an active visual scanning of the surrounding landmark configuration from the start position may suggest an allocentric self-localization process. Therefore, it is interesting to consider whether specific oculomotor and body motion patterns can indirectly reveal specific cue processing and, subsequently, navigation strategies. This approach may lead to a unified behavioral characterization of the cognitive processes underpinning spatial behavior, independently from the type of environmental space used in the experiments. Following the path of studying of natural behavior, it would be interesting to test the impact of geometric cue preference in older adults in larger and even more ecological environments, where egocen-

tric, viewpoint dependent coding is less plausible. We would predict, based on our results, that wayfinding, shortcut taking, and route planning would be facilitated in aging when geometric cues are provided (not-grided layouts), relatively to when only environmental landmarks are available on a grided layout with right-angled intersections.

8.2 Discussion on aging & eye movement control

8.2.1 Achievements

The objective of our study of eye movement control was twofold: *i*) to characterize the impact of aging on fixation stability, fixational (micro)saccades and regular saccades, including saccade generation and inhibition; *ii*) to provide a novel characterization of age-related consequences on oculomotor control in optic flow conditions.

Our results showed that fixation stability is as efficient in older adults as in young, despite more frequent fixational saccades. We have developed a new method, based on an unsupervised clustering algorithm, to accurately detect fixational saccadic movements. We have shown that this method is resilient to high-frequency noise, frequently observed in eye-tracking data in older subjects. Application of this method to microsaccade detection in our data allowed us to characterize, more precisely than previous studies, a global increase with aging in all fixational saccade parameters. In particular, we observed that when trying to fixate a visual target, older adults produce more frequent, larger and faster fixational saccades. Concerning regular saccades, we showed in older subjects a decrease in their latency and accuracy as well as an increased number of failures to inhibit unwanted saccades voluntarily.

Optic flow is always affecting the way we see in natural conditions, especially during navigation. Therefore, in the second part of our studies focusing on eye movements, we addressed the novel question of how optic flow affects oculomotor control. We found that, when optic flow was present, the fixation stability improved and the frequency of fixational saccades decreased. To our surprise, these effects were not specific to the optic flow motion pattern. On the other hand, optic flow patterns influenced angular properties of saccades by increasing the number of saccades made in the direction opposite to visual motion direction.

8.2.2 Implications

An important conclusion from this doctoral work is that the study of oculomotor control in older adults requires careful examination of pre-processing and analysis methods applied to eye tracking data. Indeed, technical issues such as noise cleaning, saccade detection, and stability estimation criteria critically influence the results. Unified quantitative definitions of various events observed in eye-tracking data can help to avoid incoherent results. Concerning microsaccades classification, research teams used different upper size threshold. We reported the threshold

used by two leading teams in the field (0.5° by Rucci and colleagues; 1° by Martinez-Conde and colleagues). However, many other thresholds were used in the literature (e.g., 15 min arc in Collewijn and Kowler, 2008 or 2° in Martinez-Conde et al., 2006). The global increase in fixational saccade properties in older adults, observed in our study, suggests that a large portion of these saccades passed over the threshold generally used by researchers to classify microsaccades, leading to a relative "decrease" in the number of microsaccades in aging.

From a technological point of view, we developed a new algorithm that is capable of detecting small eye movements even in a high noise regime. Application of this method for saccade detection significantly reduces the time and it increases the accuracy of detection as compared to both other existing methods and manual labelling. Moreover, it avoids massive data loss that results in the application of more conservative detection methods in a high noise regime.

One long-term objective of our study is to provide normative data for aging with respect to fixational eye movements. For this purpose, we conducted multiple screening tests with our participants, including cognitive screening, ophthalmological screening, optical coherence tomography, and fundus photography to ensure that participants were not suffering from any ophthalmological condition. These data can potentially be useful for the research related to the study of microsaccades dysfunctions as biomarkers of age-related pathological conditions (Alexander et al., 2018). For instance, microsaccades were found to be more oblique in Alzheimer's disease (Kapoula et al., 2014) and larger, but not more frequent, in macular diseases (Kumar and Chung, 2014). Recently, Smith and Zhu (2014) used machine learning methods to classify patients diagnosed for glaucoma based on their eye movements scanpaths. With the breakthrough advances in modern machine learning tools, it may be possible to detect small deviations from normal fixation behavior, which are characteristic of early onset of an ocular or neurological pathology. This approach is being framed within the a collaborative project involving the host laboratory and the Quinze-Vingts National Ophthalmology Hospital, and experimental data collected in our experiments will contribute to this clinical research.

8.2.3 Raised questions & future studies

Are age-related changes in fixational saccades detrimental to vision? We reported age-related changes in several properties of the oculomotor system, but it is not clear whether these changes are detrimental to visual processes or they reflect compensatory adaptation mechanisms at stake in the aging visual system. The comparison of results on fixation area (Sec. 7.1) and those on fixational saccades (Sec. 7.3) leads to the following conclusions. When considering the fixation area including saccadic-like movements, the area in young is of 1.38° whereas it is of 1.62° in older adults. On the other, the median fixational saccade size in young adults is of 0.26° and 0.38° in older adults. The increase in fixational saccade size (ratio young/old: 1.46) does not lead to an equal increase in the fixation area (ratio young/old: 1.17). Moreover, the fixation area in each age group, even when comprising saccades, is well within the size of fovea (i.e., the 2° central part of

the retina), where visual acuity is highest (Jacobs, 1979; Leigh and Zee, 2015), suggesting that the increase in fixational saccade properties in aging might not have a gross effect on acuity, in terms of eccentricity from the fovea. Advanced age leads to multiple structural and functional changes in the visual system, including: a decrease in the number of ganglion cells (Curcio and Drucker, 1993; Gao and Hollyfield, 1992); a lower absorption rate of photons by photoreceptors, and a higher cortical noise in visual areas (Silvestre et al., 2018); a higher size of population receptive fields within the foveal region in the visual cortex (Brewer and Barton, 2014); finally, a lower contrast sensitivity, especially for high spatial frequencies (Nomura et al., 2003; Owsley, 2011). How the oculomotor changes that we found do relate to these changes in the visual system across lifespan needs to be understood. A first step in this direction could be to run high-acuity or contrast-sensitivity tasks while recording fixational eye movements, and to correlate visual performance with the dynamics of fixational saccades in young and older adults.

8.3 Discussion on eye movements & spatial navigation

8.3.1 Achievements

One of the objectives of our work was to investigate the role of eye movements for navigation in the context of aging. First, we wanted to understand how spatial information, and more specifically geometric cues, are extracted through spatio-temporal gaze dynamics in ecological environments. Second, we wanted to characterize individual age-related navigation differences by analyzing eye movement statistics. Our results provide novel experimental evidence addressing these questions.

Past experiments (e.g., Hamid et al., 2010) suggested that the extraction of landmark information can be associated with fixations targeting individual landmarks. However, the gaze-related strategies associated with extraction of room geometry were never studied. We reasoned that perceiving distances between geometric elements of the environment would be instrumental to that purpose. It appears that the ground plane is of particular importance for participants who spontaneously use this spatial cue to reorient, since most of fixations were distributed on the floor and near the environmental corners, reflecting the room's symmetry. It is possible that gazing at the floor corners is an efficient way of perceiving the relative length of walls and distances between them. A support for that interpretation comes from results showing that distances between objects are computed in reference to the ground surface, rather than in reference to other environmental surfaces (Bian and Braunstein, 2005; Bian et al., 2006).

Overall, gaze seems to target critical information at a critical task-related time. In the reorientation paradigm, participants were disoriented, suggesting that the first putative action is to find the bearings and re-establish the heading, so as to know in which direction the movement should be initiated. On the basis of this reasoning, we separated each trial into two periods, during which we expected the visual exploration policies to be different: an orientation period (bearing

finding and navigation choice about the direction to take), and the navigation period (where the navigation decision is observable). In the orientation period, we observed that participants directed their gaze at the spatial information which had a higher weight on the representation of space, since it was spontaneously preferred on the probe trial. Thus, participants in the landmark group engaged in active scanning behavior, as supported by a higher proportion of explorative fixations on panels. This behavior is instrumental to find, before movement initiation, the individual landmarks that were associated to the goal position (e.g., those located near the goal corner). Visual exploration policies in this case could resemble those in a visual search task, where exploratory behaviors are rewarded and exploitation rates are low (Hills et al., 2015; Peterson et al., 2001). Importantly, the higher exploration rate was observed just before navigation decision making and locomotion initiation. The exploration policy of participants in the geometry group is more complex. Contrary to landmark information, the room's geometry is ambiguous in indicating the bearings and the goal position. Accordingly, gaze distributions in this group of subject reflected this ambiguity at the very beginning of a trial. The observation of subsequent navigation decision suggests that the landmarks were also taken into account, since rotational errors happened less than 50% of the time, and the number of rotational errors decreased during the learning phase. Therefore, bearings maybe established early in the trial and early in the learning process in geometry-preferring participants, but the movement direction was disambiguated later, with the help of landmark-related information, resulting in a reduction of rotational errors.

During the navigation period, i.e., once locomotion was initiated, gaze continued to be used to inform the subject about the goal position. This goal-related activity appears to be computed relative to the participant's preferred cue. While walking, participants using geometric cues gazed at the floor, in particular they fixated the position that coincided with the spatial position of the invisible goal. On the other hand, participants using landmarks gazed at the panels near the goal location. Moreover, during the navigation period, in both groups the gaze was oriented towards three nearest spatial elements. However, in landmark-group participants these elements corresponded to three landmarks nearest to the goal, while in the geometry group the gaze patterns followed the walls nearest to the goal. These results suggest a gaze-informed triangulation of the goal position relative to the preferred spatial cues.

Finally, by analyzing eye movements in a navigation framework, we identified suboptimal gaze behaviors in older adults, partially explaining age differences in navigation efficiency. First, we replicated previous evidence showing that older adults have suboptimal navigation capacity in a real environment, as opposed to a virtual one (e.g., Rodgers et al., 2012; Head and Isom, 2010). Indeed, aged subjects expressed less precise navigation trajectories, and they were delayed in reaching the goal. This was not influenced by spatial cue preference, and it therefore reflected a general effect of aging on navigation performance. Despite the fact that older adults walked slower than young ones, most of the escape latency increase was explained by a delayed navigation

decision making, quantified by the duration of the orientation period. During that period, older participants produced more fixations than young ones, and those fixations were exploitative, especially at the very beginning of the trial. This analysis suggests that older adults needed more time before movement initiation, potentially related to the decision as to which direction to take.

8.3.2 Implications

Scientific impact. How geometric cues influence spatial representations is under the research spotlight since the seminal work of Cheng (1986). Subsequent research addressed how geometric cues influence search behavior in different species including humans (e.g., Cheng et al., 2013), how geometric information is implemented in the brain, and how it exerts control over spatially sensitive cells (e.g., Weiss et al., 2017). More recent evidence addressed how visual processing, mediated by eye movements in foveated species, is involved in the construction of spatial representations (e.g., Nau et al., 2018b). It is surprising that active visual exploration during spatial navigation received so little attention in the research community, given the fact that human spatial navigation depends crucially on visual processing. To fill this gap, our work provides one of the first evidences showing that analysis of gaze patterns can be a useful approach to study spatial navigation. We hope that our results will trigger more interest and encourage researchers to continue this line of research.

Technological implications. Technology-wise, our results demonstrate the utility of the experimental platform combining eye-tracking and motion capture systems. This avoids time consuming frame-by-frame analysis of scene camera of mobile eye-trackers available on the market. Further, it allows natural navigation and spontaneous exploration strategies to be studied with virtually no limitations on the subjects' field of view and in realistic environments (with experimentally controlled auditory and visual cues). Finally, our results suggest that caution must be taken when analyzing spatial behavior using desktop VR. Indeed, in our studies gazing at the ground was instrumental to extracting geometric information. Such a ground reference might be limited in standard desktop VR setups, in which the participant cannot naturally control the virtual head pitch, precluding this type of spatial strategy.

Societal payoff. As we have shown, older adults prefer using geometric cues when navigating and the geometric information useful for navigation is probably extracted during ground fixations. One of the issues that we have identified in our experiments is related to the fact that progressive lenses, which are almost universally used by older adults, distort information coming from the lower part of the visual field, just where relevant geometric information originates from. To overcome this issue, we, in a collaboration with Essilor International, proposed a practical solution to reduce distortion in the lower part of the visual field, for facilitating older adults' navigation in the real world (see patent in Appendix A).

8.3.3 Raised questions & future studies

What can immersive VR and eye-tracking tell us about spatial navigation? There is an increased interest in immersive mobile VR to study natural behaviors (e.g., Diaz et al., 2013b), and technical guidelines emerge to help the detection of eye movements with a mobile HMD (Diaz et al., 2013a). Our results suggest that by analyzing eye movements, we can get a deeper insight into the nature of brain processes involved during navigation in street-like environments that we encounter on an everyday basis. This constitutes an additional step on the path of studying ecological spatial navigation in humans.

Do age-related changes in the oculomotor system contribute to gaze pattern differences in ecological conditions? In other terms, do age-induced differences in oculomotor control (Chapter 7) contribute to suboptimal gaze behaviors observed in ecological setups? It is difficult to directly link these results for two reasons. First, eye movements were assessed at different frequencies, making the comparison of the two datasets inconclusive. The frequency of the mobile eye-tracker we used in the Streetlab (i.e., 60 Hz) was not high enough to capture the dynamics of fast saccadic eye movements, and even less so for the dynamics of small-sized saccades. Second, the two datasets were acquired in behaviorally different situations: in the controlled setup, saccades were triggered exogenously by an appearing target, whereas eye movements in the ecological conditions were driven endogenously by the participant and determined by task demands. Similarly, fixations were produced under head restraint in controlled conditions, while they were performed in combination with head movements in the ecological conditions. Experimental data obtained in our Streetlab study are currently used by other members of the laboratory to analyze, on a finer scale, how young and older participants coordinate body, head, and eye movements to maintain gaze stability in natural conditions.

CONCLUSION

Healthy aging induces a complex pattern of perceptual, cognitive, and executive functional changes. This study investigates the behavioural consequences of aging within a spatial cognition framework, which offers a representative case of high-level brain function prominently mediated by active vision. Probing age-related effects on visual-spatial behaviour has the potential to uncover autonomy loss markers pertinent to older people's mobility and to their interaction with the world (e.g., through visual sensing and contextual learning).

A first key novelty of this doctoral work is the use of an ecological paradigm, which allowed us to test spatial navigation in real-world, and yet controlled, experimental conditions. We assessed behaviour of young and older participants as they explored and navigated a real street-like setup, made of ecological relief sceneries providing a natural interaction between the navigator and the environment. We recorded eye movements, as well as head and full body kinematics. These biometrical variables informed us about correlations between overt spatial navigation and visual exploration strategies, to understand how aging shapes the visual focus of attention during natural way-finding behaviour. This ecological approach is in contrast with most of previous studies on aging and spatial navigation, which used computer-based virtual tasks that might bias older adults' behaviour. Indeed, joystick-operated motion prevents the use proprioceptive and vestibular cues, while it has been consistently shown that multisensory integration is crucial to older subjects' reorientation and navigation. Also, screen-based setups limit the visual field extent, potentially perturbing active visual exploration as compared to natural conditions.

A second methodological asset of this work lies in the manifold clinical and functional screening of participants. Both young and older subjects were taken from our cohort study population SilverSight (Vision Institute – Quinze-Vingts Hospital). Upon inclusion, we conducted high-resolution retina imaging (e.g., OCT, adaptive optics), visual evaluation (e.g., binocular acuity,

contrast sensitivity, useful field of view), audio-vestibular as well as balance evaluation (e.g., postural/stability measures), and psycho-cognitive assessments (e.g., visuo-spatial memory, mental rotation, perspective taking, working & long-term memory, fear of fall, anxiety). This multivariate profiling allowed us to control whether the main sensorimotor and cognitive functions at stake during spatial contributed to differences we observed. To the best of our knowledge, this approach is uncommon as compared to all previous studies of aging and spatial navigation, and it entails an unbiased interpretation of behavioural data (by controlling for multiple co-factors with reference to inter-individual variability).

Third, the scientific questioning set forth by this study takes place in a context of a vivid interest in how geometric cues contribute to neuro-behavioural spatial responses. Whereas traditional views focused on relations between landmarks, the importance of geometric information was demonstrated in various species (e.g., primates including humans, rodents, birds). However, very few studies addressed so far the impact of aging on the interplay between landmark and geometric spatial information in human navigation. Moreover, these studies were based on computer-based virtual tasks and produced diverging results that do not draw a clear picture. Our findings shed light on how aging modifies the anchoring of mental representations by altering the preferential encoding of task-relevant information when young and older adults naturally navigate in real environments. We showed that older adults reoriented and navigated preferentially according to the geometric shape of the environment. On the other hand, and in accordance with previous studies, young adults preferentially used landmarks. Strikingly, recording of gaze and body dynamics allowed us to identify oculomotor and behavioural signatures that were predictive of the upcoming landmark or geometric high-level spatial coding preference.

Brought closer to previously demonstrated geometric preference in children, this is the first time, to the best of our knowledge, that spatial cue preference is shown to undergo a life-span development in an inverted-U shape. This can be of importance for other researchers in the field because it feeds the evolutionary approach by showing that cross-species variability is also associated with intra-species, aged-related variability. It also challenges the current debate on egocentric versus allocentric navigation strategies in aging. Indeed, older adults have traditionally been shown to prefer egocentric (self-centred) rather than allocentric (environment-centred) strategies. We show in doctoral work that this preference for egocentric strategies was found in a particular case, i.e., when only landmark information was useful for navigation. On the other hand, older adults, similarly to children, were as efficient as young adults at using allocentric strategies, given that their preferred cue (i.e. geometry) was available at the time of navigation decision. Age-related changes in cue processing may thus explain age-related differences in spatial strategies employed, such that the presence of the spatial cues (geometry vs. landmark) critically frames how allocentric and egocentric strategies are employed. In our opinion, this novel view will make an important contribution to the aging and navigation debate.

Finally, we think that this view can be useful to healthcare practitioners developing innovative

solutions to prevent/counteract the autonomy loss induced by visuo-spatial cognitive aging. This larger scope is in line with public policy priorities supporting gerontechnology and sustainable wellbeing program.

APPENDIX



LIST OF CONTRIBUTIONS

Journal papers

Bécu M, Tatur G, Sheynikhovich D, Agathos C, Bologna LL, Arleo A. Age-related preference for geometric spatial cues during real-world navigation. (Under review by Nature Human Behaviour, 2nd round)

Bécu M, Tatur G, Sheynikhovich D, Ozier-Lafontaine, A, Arleo A. Modulation of spatial cue preference across lifespan: geometric cues enable children and older adults to successfully use allocentric strategies (in preparation).

Bécu M, Tatur G, Arleo A. Impact of healthy aging on ocular fixation stability. (submitted to Investigative Ophthalmology and Vision Science).

Bécu M, Sheynikhovich D, Tatur G, Arleo A. Age-related modulation of micro-saccadic eye movements during optic flow stimulation (in preparation).

Sheynikhovich D, Bécu M, Wu C, Arleo A (2018) Unsupervised detection of microsaccades in a high-noise regime. *Journal of Vision*, 18(6):19. doi: 10.1167/18.6.19.

Ramanoel S, Bécu M, Tatur G, Lagrené K, Habas C, Arleo A. Age-related changes in spatial learning correlate with gray-matter integrity (in preparation).

Patents

Bécu M, Arleo A et al. Method for determining an optical system an ophthalmic lens and ophthalmic filter determined by said method. In the name of Essilor International. File N. 17306047.6 (EPO, Aug 2017).

Oral presentations at international conferences

Bécu M et al. (2018) Age-related preference for geometric cues during real-world navigation: behavioral and neuroimaging correlates. Oral presentation at the Interdisciplinary Navigation Symposium (iNav), Mont-Tremblant, Canada.

Bécu M et al. (2018) Age-related preference for geometric cues during real-world navigation: behavioral and neuroimaging correlates. Oral presentation at Spatial Cognition, Tübingen, Germany.

Poster presentations at international conferences

Bécu M et al. (2018) Age-related preference for geometric cues during real-world navigation: behavioral and neuroimaging correlates. Poster at Spatial Cognition, Tübingen, Germany. Honorable mention

Bécu M et al. (2018) Age-related changes in gaze dynamics during real-world navigation. Poster at Forum of Neuroscience (FENS), Berlin, Germany.

Bécu M et al. (2017) Age-related changes in gaze dynamics during real-world navigation. Poster session presented at the Vision Science Society, Florida, USA, abs in *Journal of Vision* 2017;17(10):540.

Arleo A, Bécu M et al. (2017) Effect of aging on ocular fixation and microsaccades during optic flow. Poster session presented at the Vision Science Society, Florida, USA, abs published in *Journal of Vision* 2017;17(10):890.

Bécu M et al. (2017) Age-related changes in gaze dynamics during real-world navigation. Poster session presented at the European Conference on Eye Movements, Wuppertal, Germany.

Bécu M et al. (2017) Effect of aging on ocular fixation and microsaccades during optic flow. Poster session presented at the European Conference on Eye Movements, Wuppertal, Germany.

Bécu M et al. (2017) Age-related changes in spatial learning of a real environment and gray-matter integrity. Poster session presented at the Neuroscience Workshop Saclay: Neural Circuits and Behavior, Saclay, France. Best poster award.

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