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Cerebellar signals drive motor adjustments and visual perceptual changes during forward and backward adaptation of reactive saccades

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ABSTRACT

Saccadic adaptation (*SA*) is a cerebellar-dependent learning of motor commands (*MC*) which aims at preserving saccade accuracy. Since *SA* alters visual localization during fixation and even more so across saccades, it could also involve changes of target and/or saccade visuospatial representations, the latter (*CD_v*) resulting from a motor-to-visual transformation (forward internal model) of the corollary discharge of the *MC*. In the present study, we investigated if, in addition to its established role in adaptive adjustment of *MC*, the cerebellum could contribute to the adaptation-associated perceptual changes. Transfer of backward and forward adaptation to spatial perceptual performance (during ocular fixation and trans-saccadically) was assessed in eight cerebellar patients and eight healthy volunteers. In healthy participants, both types of *SA* altered *MC* as well as internal representations of the saccade target and of the saccadic eye displacement. In patients, adaptation-related adjustments of *MC* and adaptation transfer to localization were strongly reduced relative to healthy participants, unraveling abnormal adaptation-related changes of target and *CD_v*. Importantly, the estimated changes of *CD_v* were totally abolished following forward session but mainly preserved in backward session, suggesting that an internal model ensuring trans-saccadic localization could be located in the adaptation-related cerebellar networks or in downstream networks, respectively.

Keywords: Saccadic adaptation; Cerebellum; Trans-saccadic perception; Corollary discharge; Visuo-spatial representation

List of abbreviations

| | |
|------------------------|---|
| ΔCDv | Change after saccadic adaptation of the CDv (internal representation of the saccade displacement in visual coordinates) |
| $\Delta LOC_{FIX/SAC}$ | Change after saccadic adaptation of localization errors under fixation condition (FIX) or trans-saccadically (SAC) |
| ΔSAC | Change after saccadic adaptation of saccadic amplitude during trans-saccadic localization trials |
| CD | Oculomotor corollary discharge |
| CDv | Internal representation of the saccade displacement in visual coordinates |
| CDN | Cerebellar dentate nucleus |
| FA | Friedreich ataxia |
| FEF | Frontal eye fields |
| FP | Fixation point |
| $fMRI$ | Functional magnetic resonance imaging |
| $hMT/v5$ | Middle temporal visual area |
| SAR | Saccadic adaptation rate |
| $LOC\ FIX$ | Localization task performed under fixation |
| $LOC\ SAC$ | Localization task performed trans-saccadically |
| MC | Motor command |
| PEF | Parietal eye fields |
| PV | Peak velocity |
| $S_{BACK/FOR}$ | 'Similarity' value computed as $\Delta CDv - \Delta SAC$ (forward adaptation) or $\Delta SAC - \Delta CDv$ (backward adaptation) |
| SA | Saccadic adaptation |
| $SAC-T_{OFF}$ | Saccade trials where the target disappears during the movement. |
| $SAC-T_{ON}$ | Saccade trials where the target remains visible post-saccadically at the same location (control session) or at another position (forward/backward adaptation) |
| $tDCS$ | Transcranial direct current stimulation |
| TMS | Transcranial magnetic stimulation |
| VL | Ventrolateral part of the thalamus |
| $X\text{-eye}\ ref$ | Mean horizontal eye position during fixation, used as a reference for stimuli presentation in localization trials |

INTRODUCTION

From as early as the 19th century with the seminal works of James (1890) and Lotze (1852), a long questioning in neuroscience has been to understand how our actions and perceptions interact with each other. Especially relevant to this problem are active vision mechanisms which rely on a close and continuous interplay between motor and perceptual systems. For instance, despite the fact that you are constantly shifting your gaze in a rapid and ballistic manner through saccadic eye movements while you are reading this sentence, you succeed in maintaining a stable visual representation of the whole text. This percept of “stability” suggests that some information about our impending oculomotor actions are sent to the neural structures which contribute to our visual perception. An internal representation of the saccade displacement in visual coordinates (CDv) resulting from a motor-to-visual transformation (forward dynamic model) of the oculomotor corollary discharge (CD) has been suggested to play such role (Masselink & Lappe, 2016). This assumption has at least two implications: (1) a modification in the metric of saccades could lead to a distortion of the internal representation of visual space and (2) the cerebral and cerebellar motor structures traditionally associated with saccade generation could play a role in non-motor perceptual functions.

Modifying the metric of a saccade can be easily done by taking advantage of oculomotor plasticity, one of the most important properties of the oculomotor system thanks to which the saccade amplitude can progressively adjust when systematic targeting errors are detected (Robinson, 1973). In laboratory, saccadic adaptation can be triggered non-invasively by the double-step target paradigm (McLaughlin, 1967). Subjects are instructed to perform a saccade to a target which is surreptitiously displaced during the movement to a nearby position, thus mimicking a saccade targeting error. When this procedure is repeated several times, this systematic error leads to a readjustment of the saccade metric so that the eyes land progressively closer to the shifted target. Many studies have pointed out that different mechanisms are invoked depending on the direction of the target displacement relative to the saccade (‘forward’ or ‘backward’), namely ‘forward adaptation’ increasing saccade amplitude versus ‘backward adaptation’ decreasing saccade amplitude (e.g., Golla et al., 2008; Nicolas, Bidet-Caulet & Pélisson, 2020; see Pélisson et al., 2010 for a review). For instance, forward adaptation needs more trials to reach a steady state which, moreover, is lower and more variable as compared to the backward adaptation steady state (Ethier et al., 2008; Straube & Deubel, 1995). Differences in terms of saccade dynamics (duration, peak velocity) have also been observed in some studies (Golla et al., 2008; Schnier & Lappe, 2011).

Therefore, [Ethier et al. \(2008\)](#) postulated that forward adaptation could involve a target remapping process while backward adaptation could be based on a modification of the internal feedback that controls saccades trajectory (see also [Semmlow et al 1989](#)).

It is now well established that the cerebellum plays a key role in saccadic adaptation mechanisms. A major contribution of the oculomotor vermis and of the fastigial nucleus has initially been observed in lesion studies in monkeys ([Barash et al., 1999](#); [Takagi et al., 1998](#)). In humans, several clinical studies showed that patients with cerebellar lesions have impaired saccade adaptation capabilities, particularly when the lesion encompasses the oculomotor vermis ([Golla et al., 2008](#); [Xu-Wilson et al., 2009](#)) but also the cerebellar hemispheres ([Alahyane et al., 2008](#); [Choi et al., 2008](#); [Straube et al., 2001](#)). Some studies have also supported a partial distinction between the cerebellar substrates of forward and backward adaptation. For instance, in the sample of patients with a vermal lesion studied by [Golla et al. \(2008\)](#), forward adaptation was totally abolished while backward adaptation was partially altered. Moreover, numerous neurophysiological studies in healthy volunteers are consistent with this distinction. First, transcranial direct current or magnetic stimulation applied over the cerebellum during an adaptation exposure differently disrupts forward and backward adaptation (tDCS: [Panouillères et al. 2015](#); [Avila et al., 2015](#); TMS: [Panouillères et al., 2011](#); see also [Jenkinson & Miall, 2010](#)). Second, neuroimaging studies have consistently disclosed a contribution of the cerebellum during saccadic adaptation (fMRI: [Guillaume et al., 2018](#); [Gerardin et al., 2012](#); PET: [Desmurget et al., 1998, 2000](#)) but different cerebellar loci are involved in the processing of backward versus forward targeting errors ([Liem et al., 2013](#)). fMRI studies have additionally brought the very new finding that saccadic adaptation mechanisms are also associated with activation of several cortical areas such as temporo-parietal junction and hMT+/V5 ([Gerardin et al., 2012](#)), pre-cuneus ([Guillaume et al., 2018](#)), supplementary eye field ([Blurton et al., 2012](#)) and frontal areas ([Gerardin et al., 2012](#); [Guillaume et al., 2018](#)). This last set of findings suggests a strong link between motor and perceptual systems.

Saccadic adaptation could affect our spatial visual perception either by (1) introducing a mismatch between the amplitude of the CDv signal and of the actual (adapted) eye movement and/or (2) modulating the target position internal maps. The first possibility can be addressed in laboratory by testing trans-saccadic localization performance before and after an adaptation procedure. In practice, a stimulus is briefly flashed just before a saccade and its position must be reported after the gaze shift by adjusting the position of a mouse pointer

(Schnier et al., 2010) or pointing with the hand at the estimated position (Bruno & Morrone, 2007), or by providing a keypress force-choice response of whether the saccade target has been shifted to the right or to the left during the movement (Deubel et al., 1996). Bahcall & Kowler (1999) postulated that an adaptation-induced mislocalization could occur if the internal saccade representation derived from a copy of the motor command ('efference copy': Von Holst & Mittelstaedt, 1950 or 'corollary discharge CD ': Sperry, 1950) does not match the actual (adapted) eye saccade amplitude. Given that no visual reference is available post-saccadically in these tasks, CD signal indeed constitutes the most reliable information to remap the pre-saccadic position of the stimulus, as supported by behavioral studies (Deubel et al., 1996; Paeye et al., 2017), computational models (Ziesche et al., 2014) and clinical studies (Ostendorf et al., 2010, 2012; Cheviet, Pisella & Pélisson, 2021). Consistent with this hypothesis in the case of forward adaptation, a distortion of visual space in the direction of the target shift (overestimation of the actual stimulus position, as compared to the baseline, pre-adaptation, performance) has been observed in such tasks (Schnier, Zimmermann & Lappe, 2010; Schnier & Lappe, 2012; Hernandez et al., 2008; Bruno & Morrone, 2007; Bahcall & Kowler, 1999). For backward adaptation in contrast, while some studies reported a significant underestimation of the to-be-localized stimulus following adaptation (Schnier & Lappe, 2012; Zimmermann & Lappe, 2009; Collins et al., 2007; Bahcall & Kowler, 1999; Klingenhoefer & Bremmer 2011; Collins, Heed & Röder 2010; Collins, Rolfs, Deubel & Cavanagh, 2009), others researchers found no (or only a minor) transfer of backward adaptation (Awater et al., 2005; Cotti et al., 2007; McLaughlin et al., 1968) or found that this transfer depends on specific conditions such as stimuli contrast (Souto, Gegenfurtner & Schütz, 2016). These differences between forward and backward adaptation are not surprising given the former is potentially based on a more complex (remapping) process underpinned by a wider network of structures (Liem et al., 2013; Ethier et al., 2008). Moreover, the lower steady state of forward adaptation implies a longer-lasting persistence of visual error during exposure, as compared to backward adaptation (Chen-Harris et al., 2008), and hypothetically the emergence of stronger perceptual mislocalization (Zimmermann & Lappe, 2010).

In parallel, a second part of literature addressed whether saccadic adaptation could directly affect the target position internal maps (i.e., brain structures involved in both visual localization and saccade targeting) with the assumption that the CDv signal could change to accurately reflect the true (adapted) saccadic eye movement (Collins et al., 2007, 2009). This hypothesis has been supported by at least three findings. First, in trans-saccadic

localization tasks, the spatial pattern of mislocalization errors resembles the adaptation field (Collins et al., 2007; Schnier et al., 2010), contrasting with the uniform pattern predicted by the hypothesis of a CDv immune to adaptation processes. Second, consistent with this framework's prediction that the execution of a saccade is no longer a pre-requisite to reveal adaptation-induced mislocalization errors, a small but significant perceptual shift has been reported under gaze fixation after a forward adaptation session (Zimmermann & Lappe, 2010; Awater et al., 2005; Moidell & Bedell, 1986; Schnier et al., 2010; Schnier & Lappe, 2012) but again, not following a backward adaptation exposure (Collins et al., 2007; Georg & Lappe, 2009; Schnier & Lappe, 2012 but see Garaas & Pomplun, 2011). Third, Masselink & Lappe (2021) designed a new model of collective sensorimotor learning allowing them to quantify the changes of internal representations of the visual target, saccade size and CDv . They showed that the representations of visual target and of CDv both change in the direction of learning in forward and backward adaptation. However, CDv changes underestimated the changes of actual saccade size, reconciling both hypotheses.

Hence, since these two theoretical frameworks attach some importance to motor information in localization mechanisms, the cerebellum could constitute an ideal candidate to drive adaptation-induced mislocalization for the following main reasons. First, several CD -related pathways have been anatomically identified (see Thakkar et al., 2017 and Wurtz et al., 2011 for a review) and some of them could transfer the adaptation-related state to the cerebral cortex (Zimmermann & Lappe, 2016). Although the most studied pathway (Sommer & Wurtz 2002, 2008) is the one originating in the superior colliculus, passing through the medio-dorsal thalamus, and targeting the frontal eye fields (FEF), another pathway emerging directly from the cerebellum and targeting the FEF via the ventro-lateral (VL) portion of the thalamus has also been highlighted (Gaymard et al., 2001; Zimmermann et al., 2015). Second, a deficit of visual space updating in trans-saccadic perceptual tasks has been observed in different populations of patients suffering from a lesion of the cerebellum (Synofzik, Linder & Thier, 2008, see also Peterburs et al., 2012), the VL thalamus (Ostendorf et al., 2012; see also Bellebaum et al., 2005 in a motor context), as well as in healthy volunteers when applying TMS over the right FEF (Ostendorf et al., 2013). Third, a growing body of evidence suggests a significant role of the cerebellum in non-motor functions (see Strick, Dum & Fiez, 2009 and Baumann et al., 2015 for a review). For instance, recent works demonstrated that visual attention and visual working memory functions are supported by the dorsomedial lobule VIIb/VIIIa of the cerebellum (Brissenden & Somers, 2019; Brissenden et al., 2016,

2018). Also, shifts of attention elicit robust activation within Crus I and within a midline portion of lobule VII (Le, Pardo & Hu, 1998) and lesion of Crus I as well as of mid-cerebellar regions lead to covert attention deficits (Baier et al., 2010; Striemer et al., 2015). Finally, van Es, van der Zwaag & Knapen (2019) revealed the presence of five distinct cerebellar visuospatial maps, notably within the oculomotor vermis and the lobules VIIb and VIIIb. Taken together, these data suggest that the cerebellum could drive adaptation-induced mislocalizations, either by providing a *CDv* signal when localization is coupled with a saccade or by modulating visuospatial information when localization is performed under gaze fixation.

Here, we addressed this question in a sample of eight patients suffering from a neurodegenerative cerebellar disease compared to a healthy control group. Visual localization performance was tested under both gaze fixation and saccade conditions, before and after an exposure to forward / backward adaptation of reactive saccades and a control exposure (i.e., without any target shift). We predicted that in healthy subjects, a perceptual shift in both localization conditions (fixation/saccade) should be mostly evidenced after the forward adaptation exposure as compared to the two other sessions (backward/control). In cerebellar patients, we expected at the group level a partial or total deficit of both forward/backward saccade adaptation and, therefore, a reduced or absent change of perceptual responses after adaptation under both localization conditions (saccade/fixation). Finally, as different cerebellar loci could underpin each type of adaptation and each localization signal (i.e., *CDv* /target representation), we will also assess the presence of potential dissociations in cerebellar patients at the individual level.

1. METHODS

1.1. PARTICIPANTS

Eight patients with neurodegenerative cerebellar disease (mean age: 55.5 ± 9.61 years; characteristics in *Table 1*) and eight healthy participants (mean age: 49.25 ± 7.67 years; four male and four female) took part in the study.

| Patient | Sex | Age | Disease | Disease duration (years) |
|---------|-----|-----|-------------------------------|--------------------------|
| P1 | M | 57 | Spinocerebellar ataxia type 1 | 21 |
| P2 | F | 59 | Friedreich ataxia | 7 |

| | | | | |
|----|---|----|--|----|
| P3 | F | 48 | Spino-cerebellar ataxia – type 3 | 13 |
| P4 | M | 44 | Unknown autosomic dominant inherited cerebellar ataxia | 15 |
| P5 | M | 43 | Spino-cerebellar ataxia – type 28 | 9 |
| P6 | M | 70 | Fragile X–Associated Tremor/Ataxia Syndrome | 8 |
| P7 | F | 63 | Late onset sporadic ataxia | 2 |
| P8 | F | 60 | Friedreich ataxia | 20 |

Table 1. Characteristics of the cerebellar patients

Before the experiment, each patient passed a clinical examination at the Neurological Hospital Pierre Wertheimer (Bron, France) to assess inclusion and exclusion criterion and their ability to perform the experiment. Inclusion criteria were the following: (1) chronic progressive cerebellar ataxia (2) normal or corrected-to-normal visual acuity, (3) ability to concentrate and to remain seated for extended periods (at least 30 min). Note that the heterogeneity of duration and semiology of the disease (Table 1) resulting from our deliberate choice of these recruitment criterion may constitute a limitation of the present study. Exclusion criteria included: (1) other neurological disease (2) unstable medical condition, (3) psychotropic medication intake, (4) pronounced nystagmus or ocular instability and (5) inability to maintain a stable position of the hand during 30 seconds due to important tremor. All participants gave their informed consent, and the protocol was conducted in accordance with the ethical standards prescribed in the 1964 Helsinki Declaration and received approval from the Ethics Committee (CPP Est-III; ID-RCB: 2017-00942-51; n° 17.05.09).

1.2. GENERAL DESIGN

1.2.1. Apparatus

The participants were comfortably seated in a totally dark room in front of a 19 inches CRT monitor (resolution: 1280 x 1024 pixels; vertical frequency: 85 Hz) at a viewing distance of 57 cm. The monitor was covered with a neutral density filter (ND4; transmittance = 25%) to avoid the contribution of visual landmarks or references (e.g., screen border) in perceptual judgements. The Experiment Builder software (SR research, Canada) was used for stimuli presentation and data collection in all tasks. Eye movements were recorded at a frequency of 1000 Hz using the *remote* configuration of the EyeLink 1000 and the 940 nm illuminator ensuring a fully dark

environment. Each experimental session began after a 10 min dark adaptation period (note that during each break of the experiment, the room was dimly illuminated for 30 seconds to maintain subjects' level of dark adaptation as similar as possible than at the beginning of the experiment).

1.2.2. Time-course of a typical session

Every subject participated in three experimental sessions ('forward adaptation', 'backward adaptation' and 'control session') in a randomized way. The minimum delay between each assessment was fixed to 1 week to preclude any adaptation retention effect (Alhayane & Pélisson, 2005). A typical session is presented in Figure 1A. In the 'pre-exposure phase', after an initial training phase, four blocks of localization task under gaze fixation ('LOC-FIX') alternated with 4 blocks of localization coupled with a saccade ('LOC-SAC'). This alternation occurred every 5 trials to make the experiment less monotonous. This was followed by a classical saccade task with disappearance of the target post-saccadically ('SAC-T_{OFF}'; 20 trials) aimed to establish a saccade amplitude baseline. In the 'exposure phase', all trials were identical, and participants were instructed to perform a saccade toward a target that could shift during the movement (adaptation sessions) or remain at the same position (control session), and persisted post-saccadically ('SAC-T_{ON}'). A total of 100 trials was performed during the exposure phase with a break after the 50th trial. The 'post exposure phase' consisted of 4 repetitions of the following sequence of 3 trials blocks: a block of 20 'SAC-T_{ON}' trials with shift (adaptation session) or without shift (control session) to maintain the adaptation state, a block of 5 LOC-FIX trials and a block of 5 LOC-SAC trials. To further reduce any de-adaptation in the LOC tasks, the fixation condition was always performed before the saccade condition. Finally, each LOC-SAC task was followed by a 30 seconds break under dim illumination, allowing reducing dark adaptation and giving the participants the possibility to rest with the instruction to move their gaze as little as possible to preclude de-adaptation. Before each experimental session, we calibrated the eye tracker by asking the participant to fixate a set of 5 fixed points distributed across the screen. Also, after each break and before each new condition, the subject had to look at a target located at the center of the screen for a 1-point calibration drift check.

A.

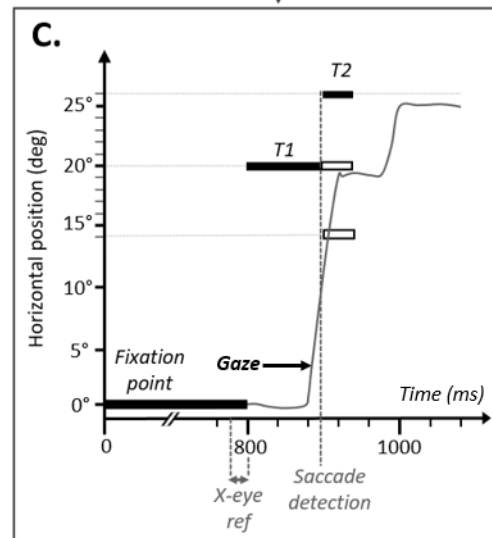
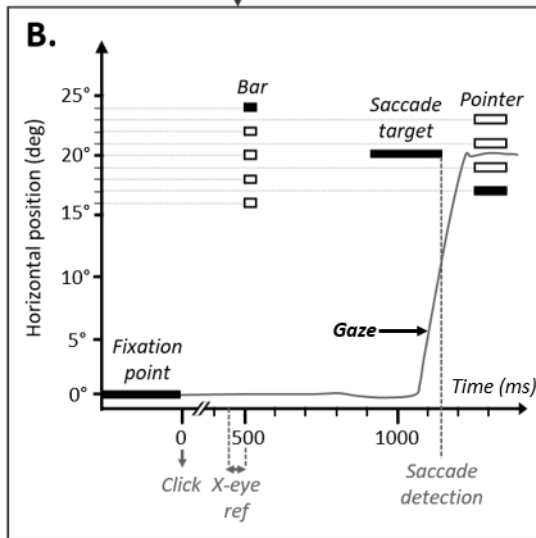
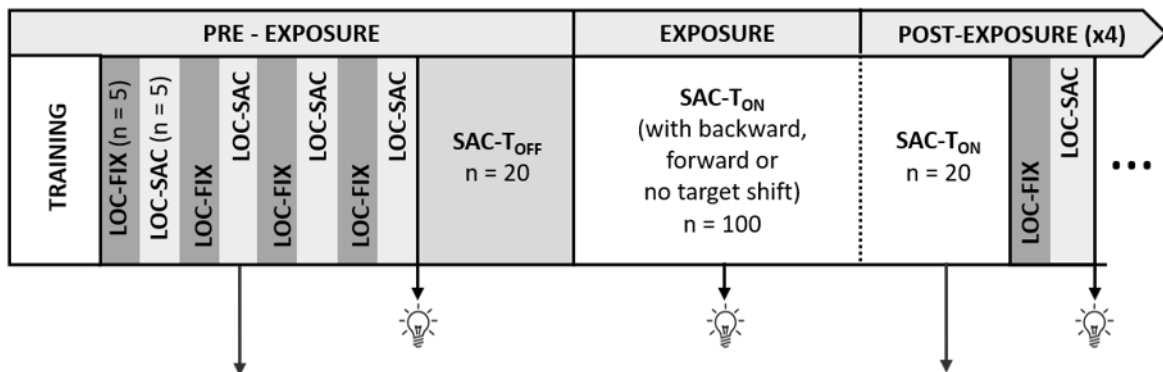


Figure 1. **A:** structure of a typical session. **B:** time-course of a LOC-SAC trial. **C:** time-course of a SAC-T_{ON} trial. Each bulb in **A** denotes the 30 seconds breaks under dim illumination.

1.2.3. Behavioral tasks

VISUAL LOCALIZATION TASKS

The time course of the LOC-SAC task is presented in figure 1B. The trial began with a fixation point FP (red circle, \varnothing 1°) appearing along the horizontal meridian at 5° to the right of the left border of the screen. The participant had to focus his/her gaze on this point and to click on the mouse as soon as he /she was ready to begin the trial. When the mouse button was pressed, the fixation point disappeared, and the participant was required to not move its line of sight. A control of gaze fixation in the (extinguished) FP zone ('FP invisible box': 10° wide, 29° high) was initiated 450 ms later for a period of 50 ms. This was done to prevent early trial failures due to intrusive saccades or potential nystagmus which could potentially occur in patients given this long fixation period. In addition, the eye position along the X axis was averaged during this 50 ms validated period ('X-eye ref') and all subsequent stimuli were presented with respect to this gaze X-position. When this

reference was computed, the window ensuring a continuous control of gaze position was restricted to 5° wide and 5° high centered around the X-eye ref. The to-be-localized stimulus (a blue vertical line, 0.2° wide and 29° high) appeared on the screen during 1 frame (~10 ms) at five possible eccentricities to the right (+16; +18; +20; +22 or +24° from X-eye ref) followed by a black screen during 400 ms. After this delay, the saccadic target (red point, \emptyset 1°) was presented at an eccentricity of +20° to the right relative to X-eye ref. The 400 msec lead time between the localization stimulus and the appearance of the saccade target has been chosen to help participants to clearly distinguish both stimuli. This also ensured that the ocular movement was driven accurately to the saccade target and not to the bar or to an averaged position between the two stimuli given their close spatial proximity ('global effect': [Van der Stigchel & Nijboer, 2013](#)). As soon as the saccadic eye movement fulfilled the predefined criteria (eye position outside the FP box, velocity threshold: 22°/sec and acceleration threshold: 4000°/s²), the target switched off and the resulting black screen lasted 100 ms. The disappearance of the saccadic target during the movement was a fundamental prerequisite since it ensured that localization is performed in the absence of allocentric visual cues and thus relies on egocentric, internal monitoring signals ([Collins et al., 2007](#); [Schnier et al., 2010](#)). Finally, a pointer (blue line, 10° height, 0.2° width) appeared on the right bottom of the screen. It appeared 10° below the horizontal meridian of the screen, at a horizontal position varying randomly between four possible locations (+17; +19; +21 or +23° from X-eye ref) that never matched the position of the previous stimuli. Participants were instructed to displace with the mouse the pointer to the spatial position where they had perceived the previous bar and to click to validate their response. As soon as a movement with the mouse was detected, the vertical position of the pointer jumped and was blocked to the horizontal meridian of the screen so that participants exclusively focused on horizontal position adjustments to make their judgement. After the perceptive response, a black screen (lasting 800 ms) ended the trial.

The time course of the LOC-FIX task was exactly the same as that of the LOC-SAC task except that: (1) the fixation point was not a red circle but a "prohibited direction" sign (\emptyset 1°) to better distinguish the two tasks, (2) the participant was instructed to continuously fixate the FP location from the first click of the mouse (that triggered the trial) until the second mouse click (that provided the perceptive judgement), using a 'FP invisible box' of 10° height and 10° width, (3) the saccade target was not presented and (4) the duration of the black screen between the disappearance of the to-be-localized stimulus and the appearance of the pointer was

extended to 750 ms in order to match the localization stimulus to pointer interval of the LOC-SAC condition (i.e. first black screen of 400 ms + saccade latency of ~250 ms + second black screen of 100 ms).

Note that for these two tasks, if a participant failed to complete a trial (e.g., due to a break of required fixation), the trial was replayed at the end of the sequence.

TRAINING

Before each experimental session, the participants first executed 5 training trials in the LOC-FIX condition. If they encountered difficulties during this phase, they were presented with three 'gradual training blocks' of a minimum of 5 trials each. In the first block, the second 'FP invisible box' of this task (10° wide, 10° high) and the actual gaze position were both made continuously visible to the subjects (a blue square around the fixation point and an 'eye picture' contingent to eye position, respectively). Thus, this block allowed a self-directed learning of the task and the identification of the inappropriate behavior(s) that led to a failure. In the second block, the procedure was similar except that the actual gaze position was no longer displayed, allowing the subject to practice with the help of the visible FP box acting as a visual reference. In the third block, the FP box was removed and the procedure was the same as in the experimental session. After succeeding in the LOC-FIX condition, participants were trained in the LOC-SAC task (5 trials). If a participant failed to execute this task, the experimenter asked the subject not to make any saccade or to delay it in order to prevent the execution of anticipatory saccade which could interfere with proper presentation of the saccade target. When this familiarization was done, the participant was instructed to perform again a saccade as soon as he/she saw the target.

SACCADIC TASKS

The two main saccadic tasks differed by the absence ('SAC-T_{OFF}') or the presence ('SAC-T_{ON}'); Figure 1C) of the target post-saccadically. In each task, a trial began with the appearance of a fixation point (red circle, \emptyset 1°) 5° to the right of the left border of the screen; its vertical position varied in a randomized way between three locations (-1.5; 0 or +1.5° with respect to the horizontal meridian); its duration varied between 800 and 1400 ms. As in the localization trials, gaze position was monitored relative to an invisible FP box (10° wide, 29° high) during the last 50 ms of the fixation period and the 'X-eye ref' was calculated. Then, a saccade target (red circle, \emptyset 1°) appeared 20° to the right of X-eye ref. The participant was instructed to shift its line of sight toward this stimulus. As soon as the movement was detected (with the same criteria as described above for

localization trials), the target could either: switch off ('SAC-T_{OFF}' task), jump by 6° in the saccade direction ('SAC-T_{ON}' task; forward condition) or against the saccade direction ('SAC-T_{ON}' task; backward condition) or stay at the same location ('SAC-T_{ON}' task; control condition). In the 'SAC-T_{ON}' task, the target was visible during a short period of 100 ms and the trial ended with a black screen lasting 800 ms (a similar intertrial interval was implemented as soon as the saccade was detected in the 'SAC-T_{OFF}' task). Participants were advised to blink during this period or while they looked back to the fixation point position.

1.3. DATA ANALYSIS

1.3.1. Saccadic tasks

OFFLINE ANALYSIS

Saccadic eye movements recorded in all tasks were analyzed offline using a custom-made Matlab routine. We accepted only trials in which: (1) the amplitude ranged between 12 and 28° (exceeding by +/-2° the 14 to 26° range of final target locations in the backward and the forward saccade adaptation procedures, respectively) and (2) the latency exceeded 100 ms. After applying these criteria, we excluded 7.15% (± 7.67) of the saccades in the control group and 16.6% (± 8.51) in the patient group (all sessions pooled).

SACCADIC ADAPTATION RATE

The modification of the saccade metric induced by the sensorimotor learning procedure (referred as '*saccadic adaptation rate*' or '*SAr*') was calculated, for each participant and each session, by the following formula:

$$SAr = Amplitude_{POST\ SAC\ T_{ON}} - Amplitude_{PRE\ SAC\ T_{OFF}}$$

in which the '*Amplitude_{PRE SAC T_{OFF}}*' parameter is the mean saccadic amplitude in the SAC-T_{OFF} task and the '*Amplitude_{POST SAC T_{ON}}*' parameter is the saccadic amplitude inferred from linear regression across the four SAC-T_{ON} blocks performed during the 'post-exposure' phase (see Figure 2).

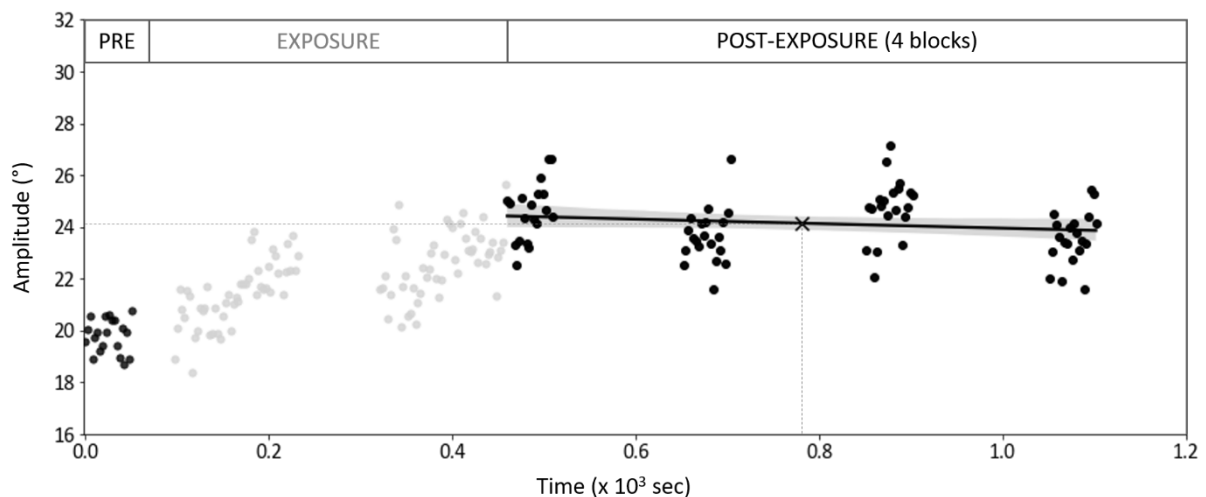


Figure 2. Illustration of saccade amplitude changes during the forward session in a typical healthy subject. Each dot represents the saccade amplitude in a particular trial during the pre-exposure phase (SAC-T_{OFF} task; left black dots), the exposure phase (SAC-T_{ON} task; grey dots) and in the post-exposure phase (SAC-T_{ON} task; right black dots). For each participant and each session, the linear regression across the 4 post-blocks allowed us to infer the mean post-saccadic amplitude (taken at the median point in time between the first and the last trial, see 'x' symbol).

STATISTICS

In a first step, we tested whether the baseline oculomotor behavior, assessed before any saccadic adaptation, was similar in our samples of patients and healthy participants. To do this, we pooled the SAC-T_{OFF} pre-exposure data across the three experimental sessions. We considered the following saccade parameters: gain (ratio between the mean saccade amplitude and the eccentricity of the target), duration, latency, peak velocity. We used two-sample *t*-tests to assess potential statistical differences between the two groups of subjects. If homoscedasticity and normality could not be verified (Levene's *F*-tests and Shapiro-Wilk tests, respectively), we used instead Mann-Whitney U tests. In a second step, we focused on the *SAr* parameter. As the assumption of normality was violated in cerebellar patients during the backward session (Shapiro-Wilk test: $W = .82$; $p < .05$), we chose to use a one-sample *Wilcoxon* signed-rank test to compare the *SAr* value to zero in each group and each session.

1.3.2. Localization tasks analysis

OFFLINE ANALYSIS

In a first step, we calculated for each participant the number of additional localization trials, i.e. trials replayed due to an initial failure. Regarding the pre-exposure phase of all sessions pooled, the median number of additional trials in the LOC-FIX task for healthy (1.5) and cerebellar (4.83) groups did not differ significantly (Mann-Whitney U = 15; $p = .08$). However, in the pre- LOC-SAC task, cerebellar patients exhibited significantly more replayed trials (13) than healthy participants (1.5) (Mann-Whitney U = 9; $p < .05$). In the post-exposure phase, a similar pattern was observed: in the LOC-FIX task, healthy volunteers (1.8) and patients (6) did not differ significantly (Mann-Whitney U = 18; $p = .16$) whereas in the LOC-SAC task, patients again performed significantly more replayed trials (7.5) than healthy participants (2.67) (Mann-Whitney U = 10.5; $p < .05$). Note that the higher number of trials in the patient group is not likely to disrupt the effect of saccadic adaptation on

visual perception since the replayed trials were homogeneously distributed over the 4 post-blocks of LOC-SAC task, each of these blocks being intermixed with refresh blocks of saccadic adaptation.

In a second step, we extracted for each localization task the X coordinate of the pointer at the time of response in each participant. These raw data were analyzed offline using a custom-made Matlab routine. Since we did not have *a priori* hypotheses regarding the behavior of patients in such tasks (particularly after the saccade adaptation procedure), we chose to exclude from the statistical analyses all trials in which the mislocalization error exceeded $\pm 7^\circ$ (that is, a range slightly superior to the 6° size of saccade target jump in the exposure phase). Moreover, for the LOC-SAC task, trials were also rejected if the saccadic amplitude did not fall in the 12 to 28° range. Based on these criteria, the proportion of excluded trials (all sessions pooled) was less than 4% in the LOC-FIX task (patient group: $3.54\% \pm 4.69$; control group: $0.83\% \pm 1.41$) and $\sim 6\%$ in the LOC-SAC task (patient group: $5.73\% \pm 4.62$; control group: $5.83\% \pm 4.01$).

LOCALIZATION AFTER-EFFECT

The modification of the perceptive responses after the sensorimotor learning procedure, referred as ' ΔLOC ' was evaluated separately for each condition (i.e., fixation or trans-saccadic), each session (i.e., backward, control or forward) and each participant by the following formula:

$$\Delta LOC_{FIX(or SAC)} = (Localization\ error_{FIX(or SAC)})_{POST} - (Localization\ error_{FIX(or SAC)})_{PRE}$$

in which 'Localization error' is the mean perceptive judgement in the 'PRE' and 'POST' phases either for the fixation ('FIX') or the trans-saccadic ('SAC') condition.

To check whether saccadic adaptation transferred to oculomotor response in the trans-saccadic localization task, we computed the saccade amplitude change (ΔSAC) in this task as follows:

$$\Delta SAC = Amplitude_{POST\ SAC} - Amplitude_{PRE\ SAC}$$

STATISTICS

We performed the same analyses as those detailed above for SAr , mostly using non-parametric tests when homoscedasticity and normality were not verified, to assess: (1) the baseline perceptual performance before the induction of the sensorimotor adaptation procedure, considering separately the pre-exposure raw data from the LOC-FIX and the LOC-SAC conditions, and (2) the effect of saccadic adaptation on perceptual performance (ΔLOC). Finally, we looked for the presence of dissociation between SAr and ΔLOC in individual

patients by comparing their performance to those of the healthy group using Crawford *t*-tests for single cases (Crawford & Garthwaite, 2002).

RESULTS

1. Baseline responses in the pre-exposure phase

The behavior of the cerebellar and healthy groups before the induction of any saccade adaptation procedure is reported in *Table 2*. In terms of saccade kinematics (SAC T_{OFF} task), cerebellar patients behaved like healthy participants regarding the duration, the gain and the ratio between the peak velocity and the amplitude of saccadic eye movements. The sole exception was the saccade latency. Patients took a significantly longer time to initiate their saccade (median: 330.95 ms) than healthy subjects (256.47 ms ; Mann Whitney U = 5.00; p <.01). Repeated-measures ANOVAs were applied for each session to assess how latency evolved in healthy and patient's group (between factor) during the PRE- and the four POST- blocks of the SAC-T_{ON} task (within factor). Results showed that for each session, a group effect approached or reached significance (backward: F (1,14) = 3.90, p = .07; control: F (1,14) = 3.65, p = .08; forward: F (1,14) = 9.52, p<.01), an inconsistent effect of the blocks emerged (backward : F (4,56) = 2.34, p = .07; control: F (4,56) = 3.08, p <.05; forward: F (4,56) = .33, p = .86) but no group*block interaction was found (backward : F (4,56) = 1.14, p = .35; control: F (4,56) = 1.22, p = .31; forward: F (4,56) = 0.76, p = .56) suggesting that the difference of latency between patients and healthy subjects was rather stable across the whole experiment. Note that for each of these parameters, patients were somewhat more variable than healthy participants, although the homoscedasticity assumption was validated for all tests. Considering next the perceptive performance in the LOC-SAC task, the mean localization error was near 0 for both healthy (-0.73° ± 0.40) and patients' groups (-0.04° ± 0.53), revealing a quite accurate perceptual report of the position of the stimulus, although a statistical difference between the two groups emerged such that patients underestimated the stimulus less than healthy subjects (t = 2.98; p = .01). Localization errors were more variable in the patients than in the healthy group, but this difference did not reach significance. Finally, in the LOC-FIX task, both groups accurately localized the position of the bar (patients: 0.62° ± 0.87; healthy participants: -0.11° ± 0.69) with a higher variance in patients (6.40 ± 3.02 versus 4.58 ± 1.92) but neither the mean nor the variable error differed statistically between the groups. Overall, these results indicate that the oculomotor and the perceptual behaviors were quite similar in the patient group

and in the healthy subjects' group. These results also attest of the feasibility of the perception task in the patient group.

| | PATIENTS | HEALTHY | Statistical difference (t or [U]) |
|--|----------------|----------------|--|
| <i>Oculomotor behaviour (SAC T_{OFF})</i> | | | |
| <i>Gain</i> | 0.98 (±0.09) | 0.99 (±0.05) | -0.47 |
| <i>PV/ amplitude ratio</i> | 23.60 (±5.93) | 22.53 (±2.54) | 0.47 |
| <i>Latency (ms)</i> | [330.95] | [256.47] | [5.00**] |
| <i>Duration (ms)</i> | 64.34 (±10.49) | 64.21 (±6.62) | 0.03 |
| <i>Perceptive behaviour (LOC-SAC)</i> | | | |
| <i>Localization errors (°)</i> | -0.04 (± 0.53) | -0.73 (± 0.40) | 2.98 ** |
| <i>Localization errors variance</i> | 6.47 (± 2.02) | 4.99 (± 2.55) | 1.29 |
| <i>Perceptive behaviour (LOC FIX)</i> | | | |
| <i>Localization errors (°)</i> | 0.62 (± 0.87) | -0.11 (± 0.69) | 1.87 |
| <i>Localization errors variance</i> | 6.40 (± 3.02) | 4.58 (± 1.92) | 1.44 |

Table 2. Oculomotor and perceptive behavior of participants in the pre-exposure phase. Statistical differences between patients and healthy subjects were assessed using Student independent t-tests, except for latency as the assumption of normality and the equality of variance was not verified (in this case, a Mann-Whitney U test was used and we reported the median rather than the mean: see brackets). Note: for the latency and duration analyses, we rejected saccade exceeding an upper limit of 1000 ms for the latency and 100 ms for the duration. ** (bold values) = $p < .01$.

2. Saccadic adaptation

2.1 Healthy subjects

The SAr values obtained for the healthy group in each session are summarized in Figure 3 (light plots). A clear modification of the saccade metric is observed in the backward and forward sessions and the direction of such change (shortening or lengthening) is consistent with the direction of the target shift. Thus, the mean SAr averaged over all subjects was negative in the backward session ($-3.87^\circ \pm 1.23$) and positive in the forward

session ($3.17^\circ \pm 1.43$), differing significantly from zero in both conditions (Wilcoxon signed-rank one-sample test: $V = 0.00$; $p < .01$ and $V = 36.00$; $p < .01$, respectively). Note that no statistical difference of absolute SAr values was reported between the backward and forward sessions (Wilcoxon signed-rank two-sample test on absolute values: $W = 24.00$, $p = .46$), indicating that saccadic adaptation in our conditions was similarly effective in both directions. Importantly, in both cases, saccadic adaptation was not complete as only about half of the target jump size was compensated (saccade amplitude dropped to 16.37° or increased to 22.86° , respectively), leaving an uncorrected visual error in the post SAC-T_{ON} tasks of 2.37° in the backward session, and of 3.15° in the forward session. Regarding the control session, a minor and statistically non-significant SAr was observed ($.17 \pm 1.12^\circ$; Wilcoxon test: $V = 25.00$; $p = .38$) that differed significantly from the above-mentioned SAr (Wilcoxon signed-rank test comparison with backward session: $W = 0.00$, $p < .01$ and forward session: $W = 35.00$, $p < .05$). In this control session, the amplitude was thus stable (change from 19.71° to 19.88°) and almost normometric, yielding a very small visual error in the post exposure phase (0.12°).

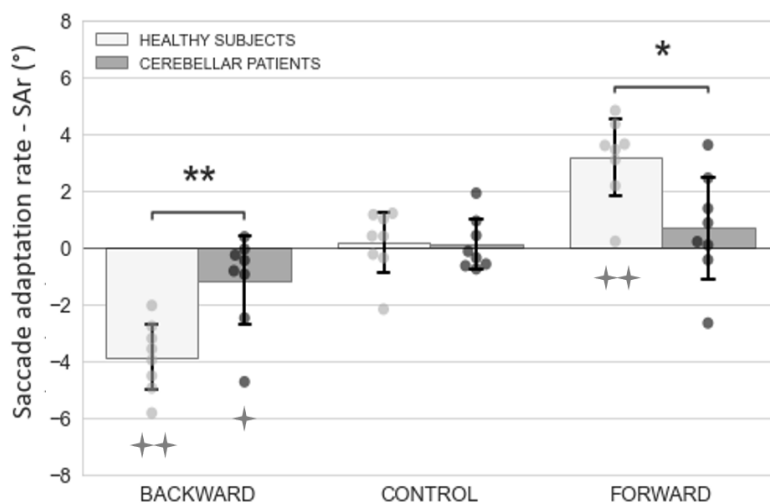


Figure 3. Saccadic amplitude rate in the different experimental sessions and groups of subjects. Bar plots denote the mean values in each group for a given session (whiskers show SD) while dots represent data of individual participants. Significant differences of SAr with 0 (one plus sign: $p < .05$; two plus signs: $p < .01$) or between patient and healthy groups (*: $p < .05$; **: $p < .01$).

2.2 Cerebellar patients

For the cerebellar patient group (Figure 3, grey bars), the sign of SAr value in each session was identical to that in the healthy group but the size of such saccade metric changes was much lower (backward: $-1.18^\circ \pm 1.67$; forward: 0.68 ± 1.9). Regarding the backward adaptation, the mean saccade amplitude evolved from 19.32° in

the pre-exposure phase to 18.14° in the post SAC-T_{ON} task, leaving a mean final visual error of 4.14°. Interestingly, the *SAr* value was significantly different both from zero (Wilcoxon test: $V = 3.00$; $p < .05$) and from the corresponding *SAr* value in the healthy group (Mann Whitney $U = 7.00$; $p < .01$), revealing a partial deficit of oculomotor command adjustments. In contrast, during the forward session, the saccade amplitude increased from 20.01° to only 20.69°, leaving a large final visual error of 5.31°. Hence, the resulting *SAr* value did not differ significantly from zero (Wilcoxon test: $V = 26$; $p = .31$) and was statistically lower than the corresponding *SAr* value observed in the healthy group (Mann Whitney U ; $W = 55.00$; $p < .05$). These results suggest a more pronounced deficit of forward adaptation than of backward adaptation, although this difference of *SAr* value did not reach statistical significance (Wilcoxon signed-rank test with absolute values: $W = 13.00$, $p = .55$). Regarding the control session, no major saccade amplitude change occurred between the pre- and the post- exposure phases (19.46° to 19.56°), as evidenced by a low and non-significant *SAr* value ($0.09^\circ \pm 0.94$; Wilcoxon test: $V = 18$; $p = 1.00$). Hence, the mean visual error in the post-exposure phase of the control session was only 0.44°. Note that *SAr* in the control condition did not differ significantly from the *SAr* values reported above for the backward and forward sessions (Wilcoxon signed-rank tests: $W = 9.00$, $p = .25$ and: $W = 25.00$, $p = .38$, respectively). To ensure that the lack of saccadic adaptation was not linked to the fatigue engendered by the additional trials in the localization tasks and/or to the multiple breaks during each session, we further analyzed the slope of the regression used to define the mean amplitude value in the post-exposure phase (see Figure 2). Results showed that for each session, the mean slope of the regression in the cerebellar patients' group did not differ significantly from that reported in the control group (Mann-Whitney U tests; W values within 29 to 31; p values $> .05$) nor with zero (Wilcoxon tests: V values between 12 and 18; p values $> .05$). Thus, saccadic amplitude in cerebellar patients was stable during the whole post-exposure phase. Altogether, results from our sample of cerebellar patients reveal a clear deficit of saccadic adaptation during both backward and forward sessions which is not linked to fatigability.

3. Localization tasks

3.1 Healthy subjects

Change of localization performance in the gaze fixation condition

The ΔLOC_{FIX} measured in healthy participants (Figure 4A, light plots) are consistent with the SAr in terms of direction. Thus, the mean ΔLOC_{FIX} was negative in the backward session ($-0.75^\circ \pm 0.91$), indicating an underestimation of the position of the bar in the post-exposure ($-0.63^\circ \pm 0.79$) as compared to the pre-exposure ($0.12^\circ \pm 1.07$) phase. In the forward session, the ΔLOC_{FIX} ($0.62^\circ \pm 1.32$) revealed an overestimation of the bar in post-exposure phase ($0.29^\circ \pm 0.92$) relative to pre-exposure ($-0.33^\circ \pm 0.80$). In the control session, the ΔLOC_{FIX} was null ($0.01^\circ \pm 0.26$) with equivalently small mislocalization in both phases (pre: -0.11 ± 0.68 ; post: $-0.11^\circ \pm 0.62$). Statistical comparisons of ΔLOC_{FIX} with zero approached significance in the backward session (Wilcoxon test: $V = 4$, $p = .055$), while no other statistical effect emerged (forward session: $V = 28$, $p = 0.20$; control session: $V = 18$, $p = 1.00$).

Change of localization performance in the trans-saccadic condition

The ΔLOC_{SAC} measured in healthy participants was again consistent with the direction of SAr (Figure 4B). Thus, the localization change in the backward session (ΔLOC_{SAC} : $-0.31^\circ \pm 0.93$) resulted from an increase of underestimation error from -0.62° in the pre-exposure phase to -0.93° in the post-exposure phase. In the forward session, the localization change ($\Delta LOC_{SAC} = 1.20^\circ \pm 0.48$) resulted from an overestimation in post-exposure (0.37°) as compared to an underestimation in pre-exposure (-0.83°). In contrast, the perceptive judgements in the control session remained similar in the pre- (-0.73°) and the post- (-0.54°) exposure phases so that the ΔLOC_{SAC} value was close to zero ($0.19^\circ \pm 0.35$). Statistical comparisons of ΔLOC_{SAC} with zero indicated a significant difference for the forward session (Wilcoxon test: $V = 36$, $p < .01$) but not for the two other sessions (backward: $V = 20$, $p = 0.84$; control: $V = 27$, $p = .25$). Importantly, the lack of a significant ΔLOC_{SAC} in the backward session cannot be attributed to a lack of saccadic adaptation transfer since the ΔSAC value (-2.24°) was significant in the backward session (pre: $18.99^\circ \pm 1.92$; post: $16.75^\circ \pm 0.80$; Student paired-sample t-test: $t = 4.80$; $p < 0.01$). Note that the ΔSAC value in the forward session (1.67°) was also significant (pre: $19.17^\circ \pm 1.09$; post: $20.85^\circ \pm 1.82$; Student paired sample t-test: $t = -3.53$; $p = .01$).

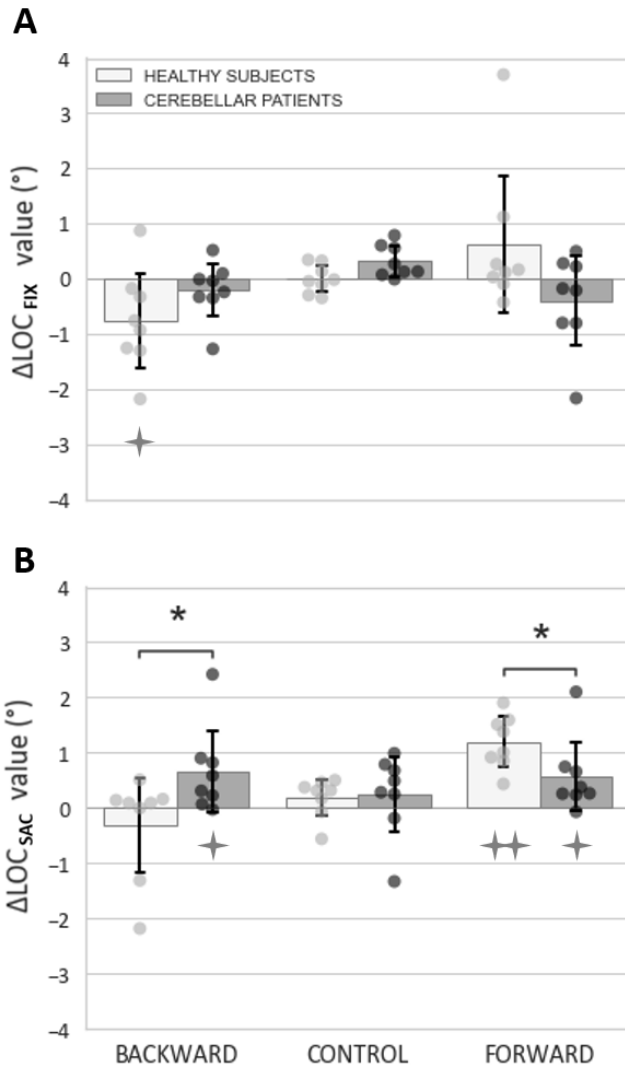


Figure 4. Change of localization performance following sensorimotor training in the different experimental sessions, groups of subjects and gaze conditions (panel A: gaze fixation; panel B: saccade). Bar plots denote the mean ΔLOC in each group (whiskers show SD) while dots represent data of individual participants. Statistical differences between groups are shown by the black stars (*: $p < .05$) while gray plus signs denote the statistical ΔLOC difference with zero (one plus sign: $p \leq .05$; two plus signs: $p < .01$).

3.2 Cerebellar patients

Change of localization performance in the gaze fixation condition

Considering all three sessions, the exposure phase did not affect the perceptive judgements of the patients (Figure 4A, grey plots). Indeed, the ΔLOC_{FIX} were very small (backward session: $-0.19^{\circ} \pm 0.51$; control: $0.32^{\circ} \pm 0.29$; forward: $-0.39^{\circ} \pm 0.86$) and did not differ significantly from zero (Wilcoxon test: V values restricted to between 11 and 19, p values $>.05$). Localization errors actually denoted a slight overestimation both in the pre-exposure phase (backward session: $0.6^{\circ} \pm 0.73$; control: $0.42^{\circ} \pm 1.05$; forward: $0.88^{\circ} \pm 1.23$) and in the post

exposure phase ($0.40^\circ \pm 0.65$; $0.75^\circ \pm 0.97$ and $0.49^\circ \pm 0.89$ respectively). Note that for the backward adaptation session, despite ΔLOC_{FIX} differed significantly from zero in the healthy group, the ΔLOC_{FIX} values did not differ significantly between the two groups (Mann Whitney U test: $W = 18$; $p = .16$).

Change of localization performance in the trans-saccadic condition

In the LOC-SAC tasks, cerebellar patients were on average very accurate during the pre-exposure phase of all three sessions (backward: $-0.13^\circ \pm 0.49$; control: $0.05^\circ \pm 0.69$; forward: $-0.04^\circ \pm 0.81$) but in the post-exposure phase their judgments tended to be biased in the direction of the saccade (i.e., overestimation), regardless of the session (backward: $0.54^\circ \pm 0.71$; control: $0.30^\circ \pm 0.76$ and forward session: $0.53^\circ \pm 1.30$). This resulted in positive mean ΔLOC_{SAC} values ($0.66^\circ \pm 0.79$; $0.25^\circ \pm 0.73$; $0.57^\circ \pm 0.67$, respectively). This increased overestimation tendency was also seen at the individual level as the ΔLOC_{SAC} was positive for most subjects (see Figure 4B, black dots). This overestimation differed significantly from zero in the forward session (Wilcoxon test: $V = 35$, $p < .05$) and also, unexpectedly, in the backward session (Wilcoxon test: $V = 35$, $p < .05$). No significant effect was found in the control session ($V = 27$; $p = .25$). Then, we tested whether these significant ΔLOC_{SAC} values (from zero) in the backward and forward sessions in patients also differed from ΔLOC_{SAC} in healthy subjects. Results confirmed that patients statistically differed from healthy subjects in the backward session (Mann Whitney U test: $W = 13$, $p = .05$) as well as in the forward session ($W = 54$; $p < .05$). As a last step, we checked the changes of saccade amplitude in the LOC-SAC task (ΔSAC). Results showed that the sign of ΔSAC was consistent with the target shift displacement for both forward (pre: $19.37^\circ \pm 1.34$; post: $20.25^\circ \pm 2.07$; $\Delta SAC = .88^\circ$) and backward (pre: $18.92^\circ \pm 1.99$; post: $18.74^\circ \pm 1.59$; $\Delta SAC = -.18^\circ$) but the ΔSAC values did not reach significance (Student paired t-test between pre and post phases, forward : $t = -1.68$; $p = .14$, backward: $t = 0.34$, $p = .75$).

4. Association/dissociation between saccadic adaptation and perceptual localization

4.1 Correlation analyses

Since in the healthy group, in both the LOC-FIX and LOC-SAC tasks, the sign of SAr and ΔLOC was consistent with the direction of target shift induced in the saccade exposure phase, we performed correlation analyses between the SAr and the ΔLOC parameters to assess whether saccade adaptation could induce subtle changes of perceptive responses. We pooled the data of the three sessions to perform such correlations. Results are depicted in Figure 5 separately for the LOC-FIX and the LOC-SAC tasks and for the two subjects' groups.

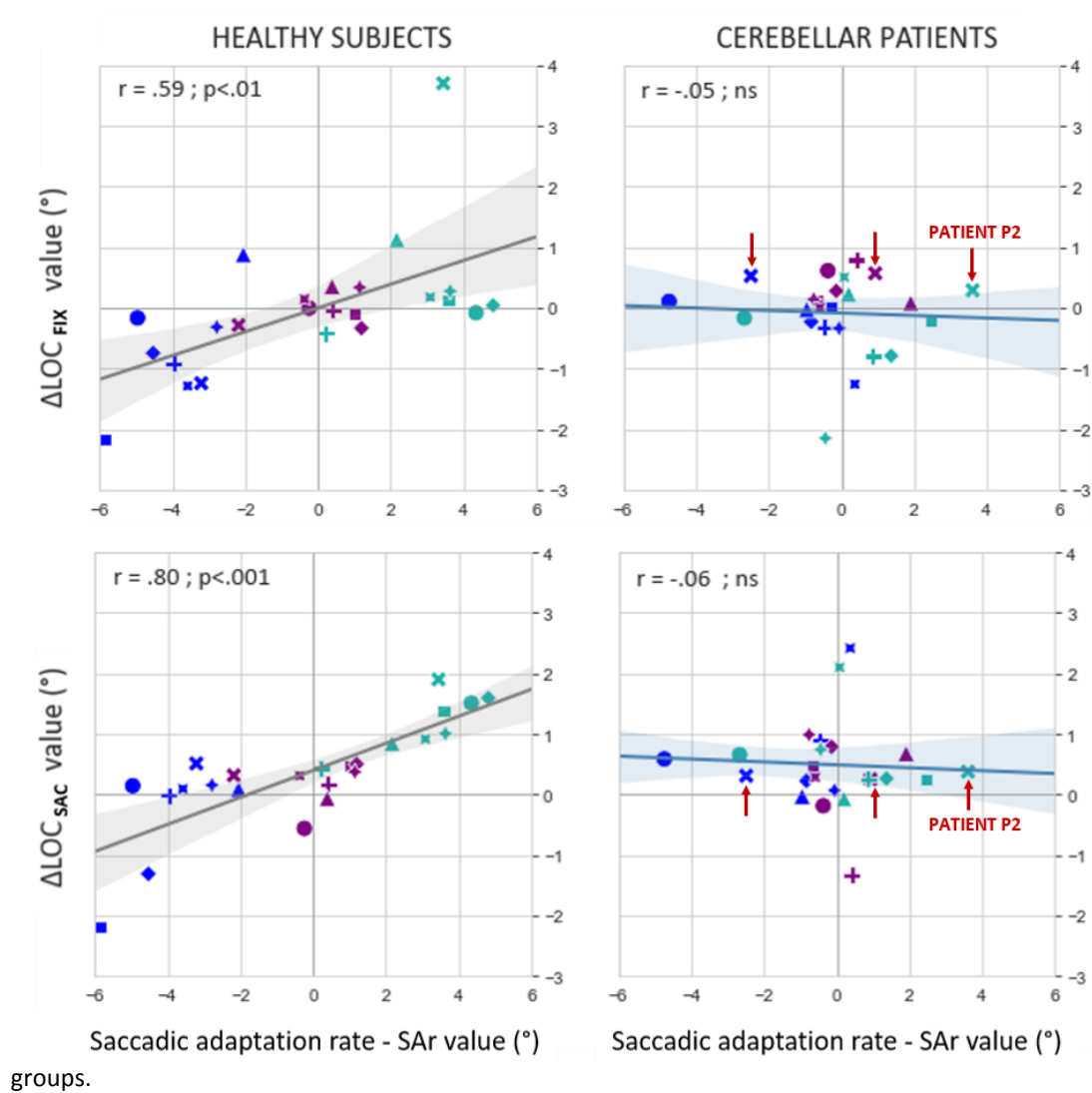


Figure 5. Correlation analyses between the saccadic adaptation rate and the change of localization performance in healthy subjects (left) and cerebellar patients (right). Each individual is represented by a different symbol (e.g., cross symbol represents patient P2). Upper plots: LOC-FIX task; lower plots: LOC-SAC task. Linear regression slopes and 95% confidence interval (shaded area) and correlation parameters were computed on the backward (blue symbols), control (violet) and forward (cyan) sessions pooled together.

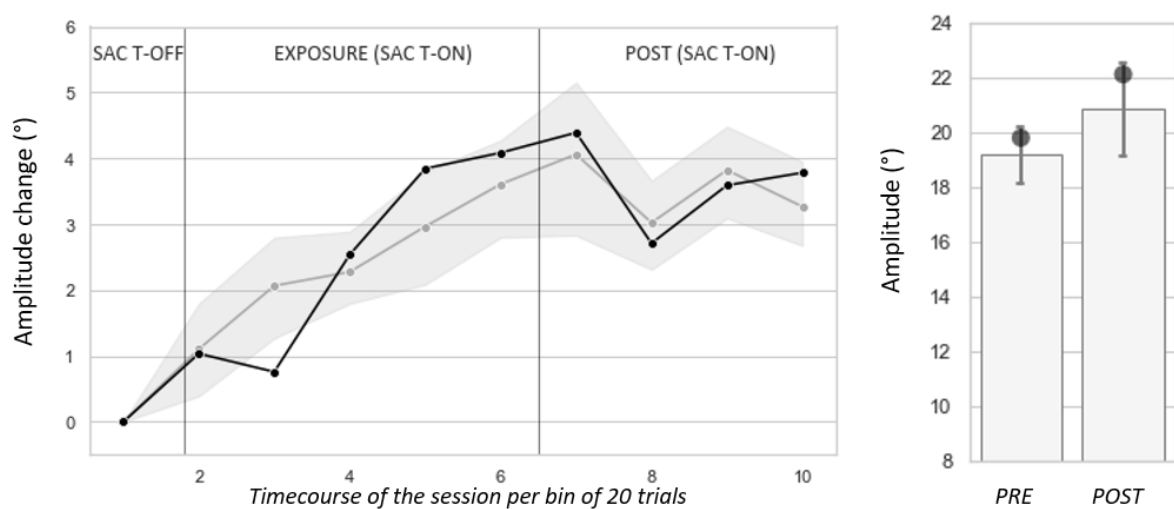
In healthy participants, correlation analyses disclosed in both LOC-FIX and LOC-SAC tasks a strong association between the ΔLOC and the SAr . The strongest association was obtained in the LOC-SAC task ($r = .80$; $p < .001$), which could be primarily due to the highly consistent pattern that can be observed in the forward session. Considering separately each session of the LOC-SAC task, a positive correlation nonetheless emerged both in the backward ($r = 0.72$, $p < .05$) and the forward ($r = 0.80$, $p < .05$) sessions while no such association was found in the control session ($r = 0.22$, $p = .60$). We also found a link between SAr and ΔLOC in the LOC-FIX task ($r = 0.59$, $p < .01$), suggesting that the effect of saccade adaptation on visual perception under fixation of gaze is present but too subtle to be disclosed by the statistical methods used above (see section 3). Note however that no correlation emerged when considering separately each session of the LOC-FIX task (backward session: $r = 0.66$, $p = .08$; control: $r = 0.29$, $p = .49$; forward: $r = 0.10$, $p = .82$). In cerebellar patients, this pattern was totally absent. No association between the SAr and the ΔLOC parameters was reported neither in the LOC-SAC task ($r = -.06$, $p = .80$) nor in the LOC-FIX task ($r = -.05$, $p = .81$).

4.2 Clinical dissociation in cerebellar patients

In a last step, we tested individual performance in patients to reveal potential dissociations between the SAr and ΔLOC_{SAC} values. We focused on the effect of forward adaptation on localization judgements in the LOC-SAC task given that in our healthy subjects group, only the forward adaptation exposure led to a significant shift of perceptual responses (see Figure 4B). Interestingly, one patient (P2) presented a preserved saccadic adaptation ability, which additionally transferred to saccades in the LOC-SAC task, but without any modification concerning space perception (see cross symbol in Figure 5). Thus, as seen in Figure 6A (left panel), the time-course of saccade amplitude change during the forward adaptation exposure in this patient closely resembled the average time-course in healthy subjects. In addition, the final amplitude change reached was also similar, as the SAr value of this patient (3.61°) did not differ significantly from the mean SAr value of 3.17° reported in the healthy group (Crawford t-test for single cases, $t = 0.29$, $p > .39$). Also, saccade amplitude recorded in the LOC-SAC task increased from $19.79^\circ \pm 1.34$ in the pre-exposure phase to $22.11^\circ \pm 3.31$ in the post phase (Figure 6A right panel, Student paired t-test: $t = -3.26$; $p < .01$), attesting that in P2, forward adaptation was maintained during localization trials. In contrast, her perceptive judgements measured in the LOC-SAC tasks disclosed a slight underestimation in the pre-exposure phase ($-0.38^\circ \pm 2.08$) that was nullified in the post-exposure phase ($0.00^\circ \pm 1.86$). The resulting ΔLOC_{SAC} value in P2 (Figure 6B right panel) did not differ significantly from zero

(one-sample Student test: $t = 0.65$; $p = .53$) and showed a tendency approaching significance to be lower than in the healthy group (Crawford t-test: $t = -1.61$; $p = .07$). Since the lack of perceptive judgement change in this patient cannot be attributed to a lack of saccadic adaptation transfer, these results suggest that the cerebellar dysfunction in this patient P2 could have preserved the modification of the saccade metric induced by the adaptation procedure but disrupted specifically the mechanisms that lead to the adaptation-related perceptual modification when a saccade is performed.

A. Oculomotor behaviour of patient P2 during the forward session



B. Perceptive behaviour of patient P2 during the forward session

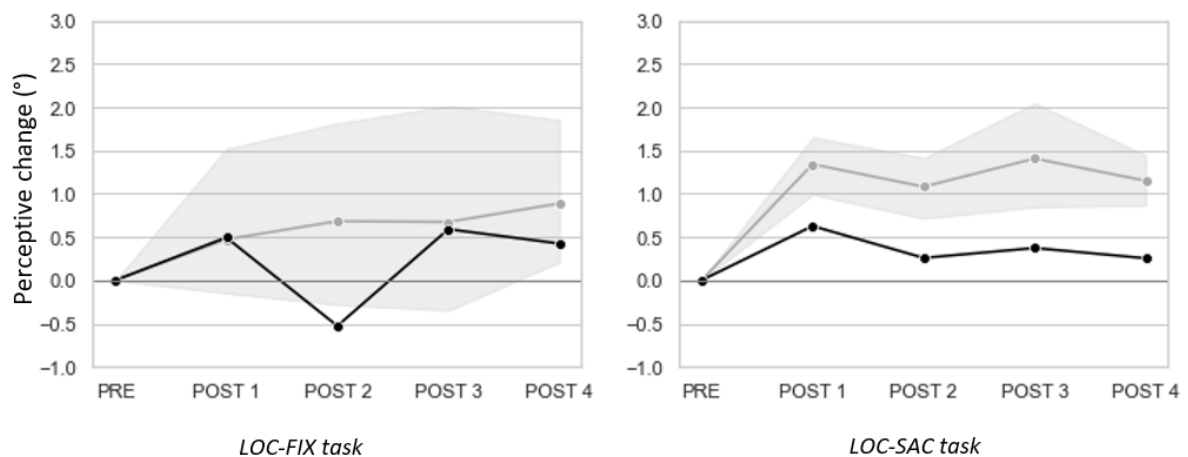


Figure 6. Behavior of patient P2 (black) compared to those of the healthy subjects (grey) in the forward session. **A.** Left panel: time course of saccadic adaptation in the SAC T_{ON} task ('EXPOSURE' and 'POST' phases). Each point represents the mean amplitude increase (as compared to the SAC T_{OFF} task of the 'PRE' phase) averaged per bin of 20 trials. Right panel: Mean saccadic amplitude in the LOC-SAC task in P2 and healthy subjects. **B.** Time-course of the ΔLOC values across the different post exposure blocks of the LOC-FIX task (left panel) and

the LOC-SAC task (right panel). Grey areas: 95% confidence interval of the healthy subjects' responses. Note: for a better illustration of the data of P2 as compared to the healthy group, we exclude in these plots one healthy subject that did not show any adaptation effect.

In a last step, we checked the behavior of patient P2 in the two other sessions. During the backward adaptation exposure, the SAr value of P2 was slightly lower (-2.49) than the mean SAr in the control group (-3.87) but again this difference did not reach significance ($t = 1.06$; $p = .16$). Similarly, no statistical difference of ΔLOC_{SAC} was found between P2 and the healthy group (P2: $.31^\circ$; healthy group: -0.31° ; $t = .63$; $p = .27$). Thus, saccadic adaptation ability in P2 seems to be preserved for both directions while for the localization judgements, only the forward session led to a different pattern than in healthy subjects (a conclusion to be momentarily taken with caution given the high variability exhibited by healthy participants in the LOC-SAC task following the backward exposure; see Figure 4B). Finally, during the control session, the behavior of P2 was similar to that of the healthy group both in terms of SAr (P2: $.93$; healthy group: $.17 \pm 1.12$; $t = .64$; $p = .54$) and of ΔLOC_{SAC} (P2: $.25$; healthy group: $.19 \pm .35$; $t = .16$; $p = .88$). Noteworthy, the ΔLOC_{SAC} in P2 was positive and very homogenous across the three sessions (backward session: $.31^\circ$; control session: $.25^\circ$; forward session: $.38^\circ$). This observation suggests that the slight overestimation observed in P2 during the forward session could not be the consequence of the sensorimotor learning procedure. To summarize, when compared to healthy subjects, patient P2 showed a clear dissociation between saccadic adaptation rate and trans-saccadic localization judgements in the forward session but not in the backward session.

Discussion

In the present study, we examined the oculomotor and perceptual effects of inducing adaptation of 20° rightward reactive saccades in healthy subjects and cerebellar patients. In healthy subjects, irrespective of the direction of the target shift that successfully induced saccadic adaptation ('backward' or 'forward'), a modification in the subjective localization of the flashed visual bar was disclosed in both the trans-saccadic task and in the gaze fixation task (although more strongly in the former). In cerebellar patients, results at the group level showed a lack of saccade adaptation ability and of its associated-perceptual effects. Finally, one patient exhibited a dissociation between motor and perceptual changes in the forward adaptation session: patient P2 could adapt the amplitude of its ocular movements but no significant perceptual change emerged thereafter.

1. Healthy subjects: comparison with previous studies

1.1. Localization under fixation of gaze

Several studies have suggested that localization perceptive judgements during fixation are based on target registration or planning stages that could be modulated by saccadic adaptation (Schnier & Lappe, 2011; Awater et al., 2005; Collins et al., 2007). Note however that inconsistent results have been reported and only minor effects emerged, the largest appearing particularly after a forward adaptation session (Moidell & Bedell, 1988; Georg & Lappe, 2009; Zimmermann & Lappe, 2010; Schnier & Lappe, 2012; Awater et al., 2005). Our statistical comparisons of the ΔLOC_{FIX} values against zero seemed to contradict these previous studies. Although the absolute size of the ΔLOC_{FIX} was grossly similar in both adaptation sessions ($\sim 70^\circ$), it did not reach significance after forward adaptation while only a trend was reported after the backward session. However, across these two conditions and the control condition, this parameter correlated significantly with the SAr . We propose that this nearly equal perceptive bias (in terms of absolute size) following the two adaptation sessions could be linked to the persistence of the visual error during saccadic adaptation (see Zimmermann & Lappe, 2009 for a similar interpretation). Indeed, while several previous studies have reported a higher saccade metric change in the backward rather than the forward learning procedure (Straube & Deubel, 1995; Ethier et al., 2008), the SAr in the present study was similar in both sessions and not complete (forward: 3.17° ; backward: 3.87°), leaving uncorrected a significant amount of saccade-target error. One may argue that the development of a stronger forward adaptation than in previous studies could result from some methodological choices in our study, such as presenting all stimuli in a gaze-contingent way, i.e. with respect to the eye position rather than to the fixation point. In addition, in the localization task, the combination of this gaze-contingent method with a simplified perceptual response (cursor motion restricted to the X-axis) could have helped to diminish the inherent variability of individual behavior. Finally, our correlation analysis of localization errors revealed itself more sensitive to highlight subtle changes after adaptation. Thus, we conclude that saccadic adaptation affects visuo-spatial representation of the target itself and that some contradictory results in literature could be due to different experimental procedures and statistical methods.

1.2. Localization coupled with a saccade

Statistical comparisons of ΔLOC_{SAC} with zero revealed that the effect of saccadic adaptation on visual perception was mostly present in the forward rather than the backward session, pointing apparently toward different adaptation mechanisms. In addition, we find again a strong correlation between the shift of perceptive judgment reports and the saccadic adaptation rate, either when data were pooled across the 3 sessions or analyzed separately for the backward and forward sessions. These results replicate previous findings (Schnier et al., 2010; Schnier & Lappe, 2012). An interesting point to report here is the fact that in our LOC-SAC task, the to-be-localized stimulus appeared 400 ms before the presentation of the saccade target. To our knowledge, only two previous studies used a similar procedure (Awater et al., 2005 and Georg & Lappe, 2009). The authors emphasized that the observed adaptation-induced mislocalization could not result from changes of transient signals related to saccade execution or planning. Rather, this effect was disclosed whenever a stimulus is presented before the saccade preparation but the response is expressed several hundred of msec later, after the gaze shift. However, the presence of visual references during perceptive judgements in these two experiments could constitute a confounding factor limiting this interpretation. For instance, in Georg & Lappe (2008), the LOC-SAC judgement was performed just after performing a saccade under the same conditions as in the motor learning stage (that is, with a target shift during its execution). It has been shown that such displaced target providing a changing reference necessarily biases the perceptual judgement (Collins et al., 2007; Schnier et al., 2010). In our study in contrast, we ensured that localization performance relied on egocentric, internal signals, since no visual reference such as the screen boundary or the saccade target itself could contribute to an ‘allocentric’ encoding process. Therefore, our study confirms and extends these previous findings by showing that the adaptation-induced mislocalization is stable and directly linked to the processing of egocentric signals.

1.3. Saccadic adaptation as a multiple component process

A still unclarified issue in healthy subjects is whether the internal representation of the saccade for trans-saccadic perception (CDv) is uninformed, fully informed or partially informed about the adaptation state. Keeping in mind that a perceptive bias is present in the fixation condition, our data in the saccade condition led us to reject the two first hypotheses. First, if the CDv was not subject to adaptation processes (the internal forward model not taking into account the oculomotor adjustment), then the difference between the ‘trans-saccadic’ and ‘eye fixed’ localization errors ($\Delta LOC_{SAC} - \Delta LOC_{FIX}$) should be equal to the saccade amplitude

change (ΔSAC). This is not what we found, neither in the forward session ($\Delta SAC = 1.67^\circ$, $\Delta LOC_{SAC} - \Delta LOC_{FIX} = 0.58^\circ$) nor in the backward session ($\Delta SAC = -2.24^\circ$, $\Delta LOC_{SAC} - \Delta LOC_{FIX} = 0.44^\circ$). Second, if on the contrary, the CDv change (ΔCDv) reflected faithfully the ΔSAC (i.e., the internal forward model estimate perfectly matching the actual, adapted saccade), then the above difference between ΔLOC_{SAC} and ΔLOC_{FIX} should be equal to zero which, again, contradicts what we found in both adaptation sessions. Thus, we propose that for both sensorimotor learning procedures, the CDv is partially informed about the adapted state. In other words, saccadic adaptation led to modifications of the CDv and SAC parameters in the direction of the target shift but with a mismatch between their respective size. We illustrate in Figure 7 how we assessed such changes of the CDv signal. Congruently with [Masselink & Lappe \(2021\)](#), we can express the change of localization error in saccade condition (ΔLOC_{SAC}) as the sum of the localization error change under gaze fixation (ΔLOC_{FIX}) and of the mismatch between changes of actual saccade (ΔSAC) and represented (predicted) saccade (ΔCDv):

$$\Delta LOC_{SAC} = \Delta LOC_{FIX} + (\Delta SAC - \Delta CDv)$$

From the above equation, we can derive ΔCDv :

$$\Delta CDv = \Delta LOC_{FIX} - \Delta LOC_{SAC} + \Delta SAC$$

Then, to appreciate how faithfully the ΔCDv reflects the ΔSAC in each subjects' group and in patient P2, we calculated a "similarity" value (S) by subtracting these two parameters. For the sake of clarity, the subtraction order depended on the direction of the target shift displacement, that is:

$$S_{BACK} = \Delta SAC - \Delta CDv \quad \text{and} \quad S_{FOR} = \Delta CDv - \Delta SAC$$

Thus, for both backward and forward sessions, a positive S signals a stronger ΔCDv than ΔSAC while a negative S denotes a weaker ΔCDv than ΔSAC . Whatever its sign, a S value different from zero thus reveals a mismatch between changes of the motor command and of the CDv signal.

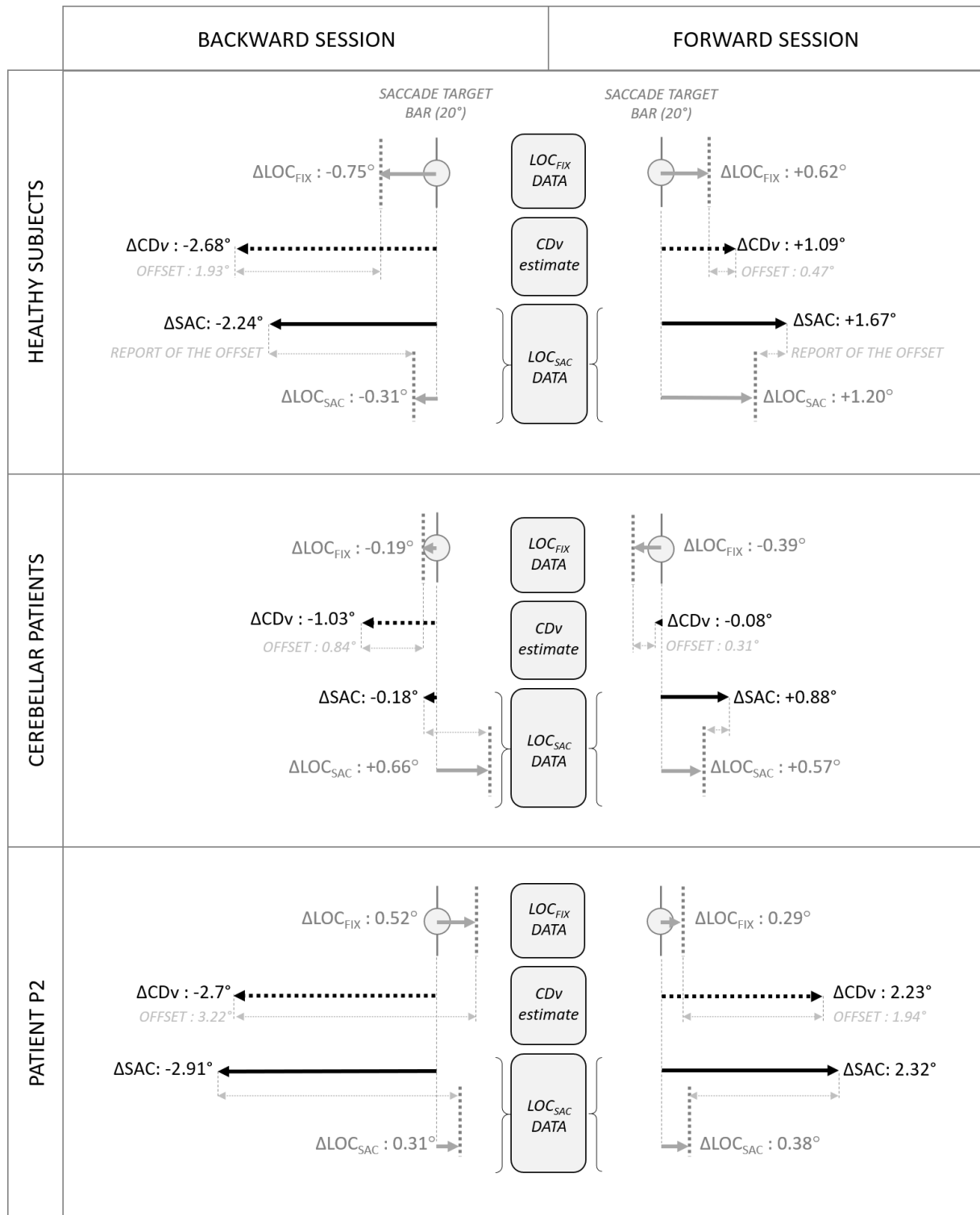


Figure 7. Data summary and interpretation. The measured parameters (ΔLOC_{FIX} , ΔLOC_{SAC} , ΔSAC) and the estimated ΔCDv parameter are shown for the healthy group (top panel), cerebellar group (middle panel) and patient P2 (bottom panel) for both backward (left column) and forward (right column) adaptation sessions. For the sake of clarity all values were normalized to 20° (thus, the saccade target and the bar position are at 20° and arrows indicating saccade and localization changes and ΔCDv all start at 20°). First, healthy participants data in the LOC-FIX condition revealed a change of internal representation of the bar by about 0.7° in the

direction of adaptation (first row). Second, healthy subjects estimate during the saccade planning phase of the LOC-SAC condition the difference between the bar internal representation and the predicted eye landing position ('offset' in second row); then after saccade execution, reporting this predicted offset to the actual eye landing position yields the bar localization error (last row). Therefore, the localization error in LOC-SAC (ΔLOC_{SAC}) is a combination of the localization error in LOC-FIX (ΔLOC_{FIX}) and of the mismatch between ΔSAC and ΔCDv (the latter being inferred from ΔLOC_{FIX} , ΔLOC_{SAC} and ΔSAC measured values according to equation in text). The same reasoning applies to the cerebellar patients' group and P2 (second and third panels).

Inferred changes of CDv in healthy subjects are presented in the upper panel of Figure 7. As shown in the second and the third row, ΔCDv and ΔSAC vectors slightly differ in size in both backward and forward sessions. This mismatch is consistent with S different from zero (backward session: 0.44° ; forward session: -0.58°). Note that S absolute values are much smaller than the ΔCDv itself (backward session: 2.68° ; forward session: 1.09°) suggesting that the mismatch is due to a CDv which follows to some extent the oculomotor command after adaptation rather than to a CDv completely immune to adaptation processes. These results are not consistent with the Bahcall & Kowler (1999) hypothesis and rather support the hypothesis of saccadic adaptation as a multiple component process developed in Introduction section (Collins et al., 2007, 2009; Masselink & Lappe, 2021), in particular of a CDv partially informed about adaptation state for both types of adaptation. Beyond this common feature, subtle differences between backward and forward adaptation emerged. First, the absolute size of both ΔCDv and ΔSAC were greater in backward session than in forward session, revealing that the temporal dynamics of plasticity mechanisms is faster in the former case than the latter. Second, the opposite signs of S between backward and forward adaptation point to different plasticity mechanisms with a stronger modulation of the CDv or of the motor command, respectively. Thus, in addition to a global slower temporal dynamic in the forward session, the changes of CDv itself develops also more slowly than the saccade motor changes ΔSAC . Third, the mismatch between changes of CDv and SAC interestingly lead to the dissimilarities of perceptual responses emerging in the LOC-SAC task despite equivalent performance in the LOC-FIX task. Such differences add to a large set of arguments in favor of partly distinct mechanisms of backward and forward adaptation (Pélisson et al., 2010).

2. Cerebellar patients

2.1. Behavioral results at the level of the group

Our group of cerebellar patients showed a strongly impaired saccadic adaptation ability during both the backward and the forward exposure, as already largely documented in the literature (Straube et al., 2001; Golla et al., 2008; Xu-Wilson et al., 2009; Alahyane et al., 2008). Other factors than a saccadic adaptation defect itself seem insufficient to explain this finding, for the following reasons. First, we have recruited our sample of patients with strict criteria so that at the level of the group, the oculomotor behavior of the patients was similar to that of healthy subjects in terms of gain, peak velocity / amplitude ratio and duration. Thus, there was no pronounced dysmetria or increased variability which could have prevented the development of sensorimotor learning in our patients. Second, fatigue can impact the oculomotor performance as suggested by Golla et al., 2008, but we deemed this possibility quite unlikely for our participants since (1) several breaks were implemented during the whole experiment, (2) the performance of the patient group in the control session was as accurate as in the healthy group (see Figure 2) and (3) the slope of the regression computed over the saccade amplitude of adaptation trials in the post-exposure phase did not differ significantly from zero for each session. Therefore, we interpret the overall lack of saccade amplitude changes in our group of patients as a marked saccadic adaptation deficit and secondarily suggest that the perceptive behavior in the localization tasks can be directly linked to this deficit of oculomotor plasticity. Also, this pattern cannot be attributed to a general failure to localize a stimulus in space (due to tremor or other factor) since the localization performance of the patients in the pre-exposure phase was as accurate as in healthy subjects (Table 2).

In the LOC-FIX condition, saccadic adaptation (backward / forward) led to small changes in the performance of cerebellar patients. Several non-exclusive factors could contribute to this pattern, but it is hard to dissociate them. First, despite lacking statistical significance, saccade amplitudes of patients are inherently more variable than those of healthy subjects. Thus, the post-saccadic visual error was more 'unstable' trial by trial during the course of adaptation procedure in our cerebellar as compared to our control group. Since the size and consistency of this error could be key factors to induce a modification of the representation of the visual target position (Zimmermann & Lappe., 2010), this increased variability in patients could have potentially disrupted the (expected) perceptual changes. Second, another possibility is that due to this saccade amplitude variability, saccadic adaptation and its effect on visual perception could develop slower in patients than in healthy subjects and could have been disclosed with a longer exposure. Indeed, some studies in healthy subjects implement up to 1000 adaptation trials (Zimmermann & Lappe., 2010) to disclose a strong change in visual

target representation. Thus, both saccadic adaptation and resulting effects on visual perception may have been missed as, in order to reduce patients' fatigue, we had to limit the number of SAC-T_{ON} trials to 180. Third, an interesting explanation of the cerebellar patients' pattern could be that a cerebello-cortical pathway dedicated to visual information processing has been disrupted by the pathological condition.

In the LOC-SAC condition, our patient group tended to overestimate the position of the stimuli regardless of the adaptation type. This aspect remains quite mysterious, but it is interesting to note that even at baseline, patients localized stimuli more forward than healthy participants, suggesting that their internal representation of the saccade vector could be slightly hypometric as compared to healthy subjects. Despite much lower changes of CDv and SAC than in healthy subjects (Figure 7, middle panel), two aspects in cerebellar patients kept the pattern of healthy subjects: S values (1) differed from zero for both backward (0.85°) and forward adaptation (-0.96°), suggesting a mismatch between the changes of the CDv signal and of the oculomotor command and (2) were opposite in sign for the two adaptation types. However, drastic differences between the two sessions emerged regarding the respective size of ΔCDv and ΔSAC . In backward adaptation, despite a lack of transfer of adaptation to saccades generated in the LOC-SAC task ($\Delta SAC = -.18$), the CDv seemed to change after adaptation (-1.03°). Recall that in this session, the SAr value of cerebellar patients reached -1.18° and was statistically different from zero. Such observations suggest that the CDv signal could emerge either in preserved neurons population at the level of the cerebellum or in a downstream structure and/or that the transfer of backward adaptation to saccades in the LOC-SAC task (that is, without a target shift) could be disrupted. In contrast, the reverse pattern was observed in the forward session, with a ΔCDv very close to zero ($-.08$) and a larger change of saccade amplitude (0.88°) following the sensorimotor learning procedure. Thus, the ability to adapt the CDv signal in the forward session seems totally disrupted by the pathological condition, suggesting that the CDv signal emerges at the level of the cerebellum itself. Another possibility could be that the cerebellum lesion has led to a disrupted CD signal itself (in motor coordinates) resulting in a faulty error between the intended and actual saccadic eye movement that is sent to cerebral cortex (Cont & Zimmermann, 2021; 'recalibration hypothesis'). Following this assumption, this altered cerebellar CD signal would result in a disrupted cortical CDv signal. Whatever the explanation, both hypotheses converge toward an involvement in visual perception of a cerebellar CD signal, that is disrupted in our context.

Taken together, compared to healthy subject's data, our results in the group of patients reveal: (1) a partly distinct mechanisms for backward and forward adaptation and (2) different neural substrates at the level of the cerebellum or in a downstream structure subtending the adaptation of the CDv signal for each adaptation type. Finally, note that while explaining in healthy subjects the observed dissimilarity of perceptual transfer between backward and forward adaptation, the mismatch between ΔCDv and ΔSAC in cerebellar patients can interestingly explain the counter-intuitive overestimation performance in the LOC-SAC task following backward adaptation.

2.2. Clinical dissociation

One interesting finding of this study comes from patient P2 which shows a preservation of saccadic forward adaptation ability while her perceptive judgements remained largely unaffected by this exposure phase. To better understand this behavior, we reported in Figure 7 (bottom panel) the measured saccadic and perceptual changes and the estimated ΔCDv .

We first discuss the results of patient P2 in the forward session as they differ from the healthy as well as the cerebellar group. First, this patient showed the greatest modification of several "saccade-related" parameters as compared to the two groups: SAr (P2: 3.61° ; healthy group: 3.17° ; cerebellar patients: $.68^\circ$), ΔSAC (2.32° ; 1.67° and 0.88° , respectively) and ΔCDv (2.23° ; 1.09° and $-.08^\circ$, respectively), suggesting that the adaptation-related circuitry is not only functional but leads to larger oculomotor effects. Second, the S value of P2 in this session was very close to zero (-0.09°). This shows that in addition to a faster dynamic change of the oculomotor command, the changes of the CDv signal in P2 are also faster than in healthy subjects. Thus, in this patient, changes of CDv fitted almost perfectly the changes of motor command. We propose that this even faster adaptation of the CDv could reflect a modified motor-to-visual transformation of the CD by a forward internal model or a modified transmission of the resulting CDv to the cerebral cortex. This implies that each node of the adaptation-related circuitry could be (to some extent) preserved but that an independent structure involving the computation and / or the transmission of the CDv to the cerebral cortex would be dis-inhibited. One possibility is that this structure is the cerebellar dentate nucleus (CDN) since CDN (1) is commonly affected in Friedreich Ataxia (FA), (2) has been suggested to play a key role in forward dynamic model (Cabaraux et al., 2020) and in providing ascending CD - signals to the cerebral cortex by projections to the SC (May et al., 1990) and to the FEF and the PEF via the ventro-lateral thalamus (Lynch et al., 1994; Prevosto et al., 2010; Clower et

al., 2001), 3) contains neurons that exhibit saccade-related activity before the initiation of the ocular movement (Mackay, 1988; Gruart & Delgado-Garcia, 1994) and 4) is functionally connected with several subcortical areas devoted to saccadic adaptation and/or post-saccadic visual error processing such as NRTP (Shinoda, Sugiuchi & Futami, 1993) and lobules VI, VIIb, VIIIb, X and Crus I of the cerebellum (Bernard et al., 2014). Note however that although neuroimaging studies have reported an association between CDN activity and oculomotor control processes (Kunimatsu, Suzuki & Tanaka, 2016; Dieterich et al., 2000), its role has been preferentially identified in voluntary rather than reactive saccades (Rosini et al., 2017), leaving open the possibility that another cerebellar node could play a similar role for reactive saccades.

In the backward adaptation session, the 'saccade-related' parameters in P2 did not show a systematically stronger change than the healthy group: SAr (P2: -2.49° ; healthy group: -3.87°), ΔSAC (-2.91° ; -2.24° respectively) and ΔCDv (-2.7° and -2.68° , respectively). In contrast with the forward adaptation, these results show that the backward adaptation-related circuitry kept a broadly normal function in this patient, reinforcing the assumption of partially distinct mechanisms for backward and forward adaptation. Also, it is interesting to point that the S value of P2 in this session was negative (-0.21) comparatively to the healthy group (0.44°). This could reflect a slowing of the adaptive modification of the CDv relative to the motor command. Alternatively, the CDv change could be preserved, reflecting the true programmed saccadic eye movement, but due to a potential disruption of the efferent cerebellar pathways, the saccadic command would become more hypometric than initially planned. Hence, our assumption of different CDv -related neural substrates for backward and forward adaptation are also relevant at the individual level.

Obviously, the fact that P2 showed a ΔCDv reflecting partially (or almost faithfully -for the forward session-) the ΔSAC parameter as in healthy subjects, cannot explain why her performance in the LOC-SAC task deviated from those of the healthy subjects (backward session: 0.31° in P2 and -0.75° in healthy subjects; forward session: 0.38° and 0.62° respectively). This difference can be attributed to another deficit concerning the visuo-spatial representation of the stimulus, as evidenced by her positive localization error in the LOC-FIX task in the backward (0.52°) and forward (0.29°) sessions. The nature of this deficit is quite uncertain but we would like to speculate that a cerebello-thalamo-cortical pathway dedicated to visual processing was also disrupted in this patient.

Conclusion

The present study provides the first evidence that the cerebellum plays a joint role in the adaptation of reactive saccade and in the effect of adaptation on visual perception. We show in healthy subjects that the two types of adaptation exposure (forward and backward) invoke both a visual remapping and an internal representation of the saccade vector that broadly keeps encoding the (adapted) motor command. In our cerebellar patients group we observe both a global failure to adapt and a lack of associated changes of localization responses, but a dissociation between saccade adaptation ability and perceptive changes was disclosed in one Friedreich ataxia patient (P2). Finally, in all cerebellar patients, we find difference between the size of the CDv signal changes depending on the adaptation session, supporting the hypothesis that different neural substrates could encode the CDv and convey it to the cerebral cortex, namely the cerebellum itself for forward adaptation, and possibly an additional downstream structure for backward adaptation.

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