Binocular vision disorders (BVD) are quite common in subjects with cerebellar dysfunctions. Also individuals with strabismus often suffer from many motor deficits, such as impaired body balance and walking. It is known that the cerebellum is necessary to maintain proper body posture but also to learn motor skills. It is conceivable that subjects with BVD would also have deficits in procedural (implicit) motor learning, one of the primary cerebellar functions. The primary aim of this study was to explore motor learning abilities in subjects with BVD (strabismic group, SG). Modified versions of a single reaction time task were used in the scheme proposed by Molinari et al. in 1997. A set of three different tasks (Experiment 1) were performed under dominant eye viewing to investigate (a) procedural (implicit) motor learning, (b) declarative (explicit) learning, and (c) simple stimulus–response associative learning. Because each task examined different aspects of motor learning abilities, it could be revealed which motor learning pathway is impaired in SG. Results showed that the SG had slower reaction times in all three tasks and demonstrated poor implicit motor learning ability compared to controls. To verify if these results were caused by reduced binocular vision or cerebellar deficits, per se, a nonstrabismic binocular anomalies group (NSG) was introduced, and all the same tests were performed (Experiment 2). These results revealed that there were no differences between the NSG and the control group with good binocularity. To conclude, the poor procedural learning ability and slower reaction times in strabismic subjects should not be explained as an effect of incomplete binocular vision that influences the maturity of the visual cortex and transformation of visual information into a motor program because binocular anomaly individuals without strabismus have motor learning abilities close to the controls. Some cerebellar deficits appear to be the origin of observed anomalies.

Introduction

In humans, binocular vision offers many benefits compared to monocular vision. Binocular vision includes more information about an object through the increments of visual acuity, contrast sensitivity, expansion of the visual field, and more efficient judgment of depth from the process of stereopsis and vergence effort/angle (Borish, 1970). Any obstacle to binocular vision (anisometropia, strabismus, or cataract occurring early
in life) interacts to decrease the overall development of the vision system and produce visual deficits (Alvarez & Kim, 2013; Bucci, Kapoula, Yang, Roussat, & Brémond-Gignac, 2002; Grant & Moseley, 2011; Kapoula, Bucci, Eggert, & Garraud, 1997; von Noorden & Campos, 2002). It is believed that the most important deficits related either to strabismus or uncorrected anisometropia are visual acuity impairment (amblyopia/lazy eye), lack of or impaired stereovision, and cosmetic aspects (Borish, 1970; von Noorden & Campos, 2002). Thus, therapies such as correction of refractive error combined with occlusion, penalization, and/or orthoptic/optometric vision training are introduced to improve visual acuity, and eye muscle surgery for the correction of angle of deviation in strabismus may be considered as well (Caloroso & Rouse, 1993). The effectiveness of any therapy is evaluated based on the level of visual acuity, angle of post-therapy eye alignment, level of binocularity (fusion, stereovision), and/or cosmesis (Barrett, 2009; Maruo, Kubota, Iwashige, & Kamiya, 1988; Mets, Beauchamp, & Haldi, 2003). If the results are not satisfactory, the therapy is considered ineffective. Recent studies on amblyopia and strabismus showed that not only visual, but also motor deficits are present in those individuals. The lack of or impairment in binocular vision could cause deficits in visuomotor coordination and motor control abilities, such as poor eye–hand coordination (Grant & Moseley, 2011; Suttle, Melmoth, Finlay, Sloper, & Grant, 2011; Webber, Wood, Gole, & Brown, 2008), eye movement deficits (Bucci, Kapoula, Yang, & Brémond-Gignac, 2006; Niechwiej-Szwed, Chandrakumar, Goltz, & Wong, 2012; Perdziai, Witkowska, Gryniewicz, Przekoracka-Krawczyk, & Ober, 2014), or greater body sways (Gentaz, 1991; Przekoracka-Krawczyk, Nawrot, Czajańska, & Michalak, 2014), or interact with walking strategies (differences in step width, power at the knee and at the ankle, depending on the value and direction of the strabismus) (Aprile et al., 2014; Odenrick, Sandsted, & Lennerstrand, 1984). These observations suggest that proper binocularity is necessary not only to a mature visual system, but also for some aspects of the motor system.

Despite the high influence of vision on the motor system, motor deficits related to binocular vision disorders are still poorly understood. Thus, it is necessary to investigate further which aspects of motor skills are impaired as an effect of poor or lack of binocularity during maturation.

The aim of the current study was to explore if adult subjects with strabismus exhibited motor learning (ML) deficits that rely on visual signals, and if so, what aspect of ML is impaired. ML is one of the fundamental functions of the cerebellum and basal ganglia. ML involves three different types of learning: procedural (implicit), declarative (explicit), and simple stimulus–response (S-R) associative learning. Procedural learning refers to the ability to acquire motor or cognitive skills gradually, through practice, without any knowledge about rules (implicit) (Cohen & Squire, 1980). This type of learning is responsible for the acquisition of skills such as walking, cycling, driving a car, and also reading and writing (Chambaron, Berberian, Delbecque, Ginhac, & Cleeremans, 2009; Dayan & Cohen, 2011). Declarative learning is the ability to remember factual knowledge about objects, places, or events that can be consciously recalled. It requires attention and awareness and can be used practically in manual therapy, helping patients to relearn functional skills (e.g., a disabled patient theoretically knows the motor sequence of how to stand from a sitting position and tries to perform the motor activity based on that knowledge) (Shumway-Cook & Woollacott, 2007). The third type, associative learning, is the process of learning by simple association between stimulus and response (S-R associative learning) and is based on the assumption that experiences reinforce one another (Laforce & Doyon, 2001; Passingham, Toni, & Rushworth, 2000). An example of this type of learning is acquiring the knowledge (a) which of the light switches turns on a specific lamp in the office or (b) about the causal consistent relationship between a specific light switch and the specific lamp in the office (Shanks, 1995).

What is more, studies have shown that the cerebellum and basal ganglia differ from each other with respect to their learning properties (Graybiel & Kimura, 1995; Hikosaka, Rand, Miyachi, & Miyashita, 1995; Ito, 1993; Pascual-Leone et al., 1993; Schultz et al., 1995). The cerebellum has been found to be crucial in maintaining procedural learning (Ferrucci et al., 2013; Gaytán-Tocavén & Olvera-Cortés, 2004; Hikosaka, Miyashita, Miyachi, Sakai, & Lu, 1998; Molinari et al., 1997). Other research performed with subjects who had suffered basal ganglia damage demonstrated their normal implicit ML but demonstrated a problem with simple associative learning (Knowlton, Mangels, & Squire, 1996; Laforce & Doyon, 2001; Singh et al., 1993).

To distinguish differences in ML abilities in participants with binocular vision disorders in the current study, three motor tasks were employed: implicit (procedural) sequential ML (Experiment 1A), explicit (declarative) sequential ML (Experiment 1B), and simple S-R (associative) ML (Experiment 1C). Modified versions of a single reaction time task (SRTT) (Nissen & Bullemer, 1987) were used as proposed by Molinari et al. (1997). This task is usually employed to examine ML abilities (Ferrucci et al., 2013; Molinari et al., 1997; Muslimović, Post, Speelman, & Schmand, 2007; Pascual-Leone et al., 1993). During SRTT, acquisition of a new skill is done by practicing a sequence of movements, and as the sequence becomes automatically performed, it results in better reaction times (RTs) (Hikosaka et al., 1998; Hikosaka et al., 1999; Molinari et al., 1997).
As was mentioned above, the impairment of binocularity affects visuomotor coordination in strabismic and amblyopic individuals, so it is possible that the process of acquisition of complex motor skills, as ML, may also be affected by improper binocularity. However, one can assume that poor motor control in strabismus may arise not from the impaired binocularity, but as an effect of improper motor control on the level of the striatum or cerebellum. To examine this hypothesis, two groups of subjects with impaired binocular vision (I = strabismus, II = nonstrabismic binocular anomalies) but with different levels of eye muscle motor control participated in the ML tests. Experiment 1 evaluated if subjects with eye misalignment (strabismus) suffered from a ML impairment. We attempted to ascertain the neural pathways that are most affected within the cortico-cerebellar or cortico-striatal circuit. The aim of Experiment 2 was to investigate if any potential ML deficits were purely related to individuals with incorrect eye alignment (strabismus) or were the deficits an effect of improper binocular and monocular signals during maturation. Thus, we performed the same three tasks on subjects with impaired binocularity but without strabismus.

### Material and methods

#### Apparatus and stimuli

In all experiments, subjects were seated in a totally dark and muted room in front of a 17-in. LCD screen set 80 cm from their eyes with their hands on the computer keyboard. Four green squares were horizontally arranged in the center of the dark screen (it was observable as dark gray because of the luminance of the backlight; brightness 0.3 cd/m²). The size of each square was 1.9° with 0.47° space between them. A black X (0.38°) appeared on one of the squares and was treated as a target.

Stimulus presentation and data collection were controlled by Presentation® Software (ver. 15.1, Neurobehavioral Systems, Inc.). The program stored time values for logging purposes with a precision of 0.1 ms (what is relevant to 10,000 Hz) and assessed the uncertainty of the notification of the event (the mean uncertainty was 2.4 ms [SD = 1.9] in experiments conducted in the study).

#### General procedure

The experimental paradigm was based on the study by Molinari et al. (1997). The variations of the SRTT (Nissen & Bullemer, 1987), that is, the most frequently employed paradigm in motor skill learning tests, were used. Subjects were required to put four fingers upon four keys (left hand: middle finger on C, index finger on V; right hand: index finger on N, middle finger on M). Each key corresponded to a particular square with target X. The first square was subordinate to the C key, the second to the V one, etc. Nevertheless, the last experiment required a different system of links between the keys and X that will be further specified. In all experiments, subjects were asked to press the key corresponding to the square in which the X appeared as quickly and accurately as possible. The X did not disappear until one of the four keys was pressed, and then the next stimulus was presented in a new position following a 300-ms delay. The results of each press in every block were automatically written in separate txt logfile by Presentation® software. RT was defined as the interval between the appearance of the target and the moment the subject pressed one of the keys. Next, the results were calculated by MATLAB® Software (ver. R2014b, The MathWorks, Inc.) using a specially prepared macro that provided the mean RT from the correct responses and mean error rate (ER, the percentage of incorrect responses; pressing the wrong key) from each block separately. The macro ignored the possible self-correction (second response to the same stimuli) and premature responses, i.e., trials in which a response was executed before the last picture was presented or when RT < 150 ms. Further, wrong responses (pressing the wrong key) and those given too late (RT > 2000 ms) were also excluded.

The subjects were tested in three different tasks:

- **Experiments 1A and 2A** – implicit sequential ML, giving information about the ability of procedural learning
- **Experiments 1B and 2B** – explicit sequential ML, giving information about the ability to use knowledge of previously learned sequences—declarative learning
- **Experiments 1C and 2C** – associative learning, giving information about the ability to learn simple associations between the appearance of the target and motor response

Each task was divided into blocks containing 12-stimulus sequences. There were no fully randomized stimulus sequences within any of the blocks because stimulus sequences for all experiments met the following limitations (Willingham & Goedert-Eschmann, 1999): stimulus position could not be repeated twice in a row (e.g., 1-2-2-4), each stimulus position appeared an equal number of times (three times for each block), and each sequence could not contain runs (e.g., 1-2-3-4) or trills (e.g., 1-3-1-3) of four keys. These limitations
were also applied to the beginning and the end of each adjacent sequence.

In all tasks, target position was determined by a special sequence or in pseudorandom order (described later).

Before starting each experiment, a practice block of a 12-stimulus sequence (different from the others in experiments) was administered to ensure that the subject understood the instructions. Short breaks (up to 20 s) were offered between blocks.

The mean duration of all experiments was ~1.5 hr conducted over 2 days, i.e., Experiment 1A was performed on the first day, Experiments 1B and 1C on the second one. Ten-minute breaks were obligatory between two experiments conducted on the same day.

We emphasize that all experiments were performed monocularly using either the dominant or the fellow eye to avoid problems with detection of the target (low visual acuity or possible double vision and confusion). The second eye was covered by a black patch attached with an elastic strip.

**Data analyses**

**Evaluation of rate of ML**

In order to assess the rate of ML, decreasing linear function was fitted to the results of Experiment 1A and 2A (blocks 1–11) and Experiments 1C and 2C. We used a linear decay function between blocks and RTs. We consider the slope of function as the rate of ML ($a$), summarized as a ML rate equation: $y = ax + b$, where $y$ is the RT, $a$ is the ML rate, $x$ is the number of the block, and $b$ is the initial value reached by the function. Precisely, parameter $a$ indicates how large an RT reduction occurred between successive blocks whereas parameter $b$ indicates the initial RT on the beginning of the task. Calculations were made in Mathematica® Software (ver. 8.0.1, Wolfram Research, Inc.).

**Statistical analyses**

Statistical analyses were performed in Statistica® Software (ver. 10, Stastoft, Inc.). The parameters with normal distribution were analyzed using parametric tests: Student’s $t$ test and ANOVA with repeated measurements. For parameters without normal distribution, a nonparametric test (Mann-Whitney $U$ test) was used. The differences were considered significant if the $p$ value was equal to or less than 0.05.

The investigation adhered to the tenets of the Declaration of Helsinki. All subjects gave written consent to participate in the study and were treated in accordance with the recommendation of the ethical committee that they could discontinue participation at any stage of the experiments.

**Experiment 1**

**Participants**

Thirty-five young adults were recruited from optometry students and strabismic patients of the Laboratory of the Vision Science and Optometry at Adam Mickiewicz University and the Optics and Optometry Center of the Adam Mickiewicz Foundation in Poznań. Each participant passed the three experiments on ML (Experiments 1A, 1B, and 1C).

Results were taken into analysis only when the subject did not report that he or she had detected the existence of the sequence in Experiment 1A (implicit ML). Thus, six participants were rejected from the analyses because they detected the sequence in Experiment 1A. Three other subjects discontinued participation immediately after Experiment 1 for personal reasons, and their results were also excluded from the study.

Based on a medical interview, all subjects were healthy with no neurological or musculoskeletal diseases. None were dyslexic or receiving medications known to affect attention or RT. A vision examination, with special emphasis on binocular vision functions, was performed on each individual. This included an extensive history interview, ocular dominance (fixating via hole task), refractive error, monocular and binocular visual acuity at far distance (Snellen’s letter chart) with and without optical correction, amplitude of accommodation (push-up test), and monocular and binocular accommodative facility (accommodative flipper ±2D). Binocular vision was evaluated by the following tests: alternating cover test with prism bar (angle of strabismus/phoria both near and far), fusional vergence ranges both near and far (prism bar base-in and base-out); pola mirror, cheiroscope, tranglyphs (Bernell®, series 500), Worth 4 dot, red lens (level of suppression and fusion), and a Titmus stereotest (Stereo Optical®) for stereopsis. A red lens test was performed in nine positions of gaze to detect any extraocular muscle paralysis. We also evaluated near point of convergence, ocular fixation by direct ophthalmoscopy (Heine®), and a retinal correspondence using both the Hering-Bielschowsky afterimage and Bagolini striated glass tests. Subjects with any ocular pathology (e.g., glaucoma, cataract, or macular degeneration) or vertical or paralytic deviation were rejected from the study.

After the evaluation of visual functions, participants were divided into two groups:

a) **Strabismic group (SG)** – A total of 13 subjects (11 females, two males) with a mean age of 29.2 ($SD = 10.0$) were placed in the SG. Four subjects demonstrated constant strabismus (two were eso-tropic and two were exotropic). Nine were occasionally strabismic, but most of the time they
had decompensated symptomatic phoria (exophoria > 10Δ at near and > 4Δ at far). Mean visual acuity of the nondominant/strabismic eye was logMAR +0.12 (SD = 0.26), and the mean visual acuity of the dominant/fellow eye was logMAR −0.05 (SD = 0.04) (all measurements of visual acuity were obtained by using decimal scale and then converted to logMAR units). One of subjects had congenital strabismus and underwent eye muscle surgery in the early childhood. Four subjects (with constant strabismus) were treated by patching in childhood. Table 1 presents the visual parameters of each subject.

### Table 1. Visual parameters of strabismic subjects (SG).

<table>
<thead>
<tr>
<th>ID</th>
<th>Age (y)</th>
<th>Sex</th>
<th>Snellen visual acuity (logMAR)</th>
<th>Angle of eye deviation (PD)</th>
<th>Eye deviation</th>
<th>Stereopsis (seconds of arc)</th>
<th>Interocular suppression</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>21</td>
<td>F</td>
<td>−0.07</td>
<td>EX18</td>
<td>Intermittent</td>
<td>40</td>
<td>No</td>
</tr>
<tr>
<td>2</td>
<td>23</td>
<td>F</td>
<td>0.00</td>
<td>EX14</td>
<td>Intermittent</td>
<td>40</td>
<td>No</td>
</tr>
<tr>
<td>3</td>
<td>25</td>
<td>F</td>
<td>−0.07</td>
<td>EX12</td>
<td>Intermittent</td>
<td>50</td>
<td>Intermittent</td>
</tr>
<tr>
<td>4</td>
<td>45</td>
<td>M</td>
<td>−0.07</td>
<td>ES25</td>
<td>Constant</td>
<td>Negative</td>
<td>Constant</td>
</tr>
<tr>
<td>5</td>
<td>18</td>
<td>F</td>
<td>+0.04</td>
<td>EX25</td>
<td>Intermittent</td>
<td>800</td>
<td>Intermittent</td>
</tr>
<tr>
<td>6</td>
<td>25</td>
<td>F</td>
<td>−0.07</td>
<td>EX30</td>
<td>Constant</td>
<td>Negative</td>
<td>Constant</td>
</tr>
<tr>
<td>7</td>
<td>25</td>
<td>F</td>
<td>−0.07</td>
<td>EX12</td>
<td>Intermittent</td>
<td>40</td>
<td>No</td>
</tr>
<tr>
<td>8</td>
<td>26</td>
<td>F</td>
<td>−0.07</td>
<td>ES25</td>
<td>Constant</td>
<td>Negative</td>
<td>Constant</td>
</tr>
<tr>
<td>9</td>
<td>39</td>
<td>F</td>
<td>−0.07</td>
<td>EX26</td>
<td>Intermittent</td>
<td>40</td>
<td>Intermittent</td>
</tr>
<tr>
<td>10</td>
<td>47</td>
<td>F</td>
<td>0.00</td>
<td>EX25</td>
<td>Intermittent</td>
<td>50</td>
<td>Intermittent</td>
</tr>
<tr>
<td>11</td>
<td>18</td>
<td>F</td>
<td>−0.07</td>
<td>EX14</td>
<td>Constant</td>
<td>200</td>
<td>Constant</td>
</tr>
<tr>
<td>12</td>
<td>28</td>
<td>M</td>
<td>−0.07</td>
<td>EX18</td>
<td>Intermittent</td>
<td>400</td>
<td>Intermittent</td>
</tr>
<tr>
<td>13</td>
<td>40</td>
<td>F</td>
<td>−0.07</td>
<td>EX25</td>
<td>Intermittent</td>
<td>50</td>
<td>Intermittent</td>
</tr>
</tbody>
</table>

Notes: F = female; M = male; EX = exotropia; ES = esotropia; PD = prism diopter. The pola mirror, tranaglyphs, and Worth 4 dot tests were used to assess the interocular suppression: No = no suppression on any test; intermittent = suppression on at least one test; constant = suppression on all tests.

### Procedure

The experiment consisted of 13 blocks of 12-stimulus sequences repeated eight times per block (96 stimuli per block). The first sequence of X positions (SEQ1: 42312431423) was presented in Blocks 1–11 and 13, and the second one (SEQ2: 42312431423) appeared only in Block 12 (Shanks & Channon, 2002; Shanks & Perruchet, 2002). Reed and Johnson (1994) provided sequences of three locations and named them second order conditionals, meaning that the next location of the target could be estimated from the last two locations, e.g., in SEQ1, 1-2 is always followed by 1; in turn, in SEQ2, it is always followed by 3. Because the sequences are identical in structure, any increase in RTs in the test block must reflect sequence knowledge rather than the frequency of reversals being the confounding of structural properties.

The subjects were not informed that a repeating sequence was being presented in the experiment. So, after the 13th block, we included a recall task to evaluate if the subjects acquired explicit knowledge of the sequence. They were asked whether the target had appeared in a random or repeating sequence. If they answered that they noticed a repeating sequence, they were asked to present the sequence by using the same keys that they had used to respond to stimuli. The responses were displayed as letters (C, V, N, M) in Notepad (Windows XP, Microsoft Corp.) on the screen. They were then assessed as to the number of positions correctly recalled in the sequence. We used a method similar to those proposed by Willingham and Goedert-Eschmann (1999). Our procedure included the

### Experiment 1A

**The aim**

The aim was to investigate the procedural (implicit) ML ability in strabismic subjects compared to controls with full binocularity.
following: If the subject correctly recalled at least two segments consisting of a minimum three consecutive positions of the target, he or she was excluded. These recalled segments did not need to be consecutive. For example, if a subject observed 121342314324 and recalled 134 432, he or she was excluded from further examination (Experiments 1B, 1C) because both 134 and 432 occurred in the sequence. Only subjects who did not recognize the sequence and went through all three experiments were considered in the analyses.

Results

Sequence ML

Results of RTs obtained in Experiment 1A are displayed in Figure 1.

Median RT obtained in Blocks 1–11 was higher in SG than in CG1 (476 ms, IQR = 19.6 vs. 423 ms, IQR = 127.65, Z = −2.71, p = 0.007). Poorer responses of SG were also observed in ER. SG performed 3% (IQR = 1.7) of ER and CG1 2% (IQR = 1.3) (Z = −2.06, p = 0.040).

Ability of sequence ML from Block 1 to Block 11 was assessed by fitting the data to a linear decay function. As can be observed in Figure 1, the rate of learning reflected in parameter a was of similar value for both groups (a = −6 for SG, SD = 5.4, and a = −8 for CG1, SD = 3.9). Student’s t test showed that a parameter for both groups were of similar values, t(24) = −1.04, p = 0.309, which indicated that both groups reached similar levels of sequence ML for SEQ1.

Implicit sequence ML

The effect of implicit sequence learning was assessed as a difference in RTs obtained from a block with a new sequence (SEQ2 in Block 12) and mean RTs from blocks with old sequences (SEQ1 in Blocks 11 and 13).

Mean RT was higher for SG than for CG1 (490 ms, SD = 87.6 vs. 409 ms, SD = 41 for SG and CG1, respectively), F(1, 24) = 9.86, p = 0.004, η² = 0.29, and responses were longer in general for SEQ2 than for SEQ1 (466 ms, SD = 74.5 vs. 433 ms, SD = 81.3, for SEQ2 and SEQ1, respectively), F(1, 24) = 30.68, p < 0.001, η² = 0.56. However, as can be observed in Figure 1, the groups differed in behavior when the new sequence (SEQ2) was displayed: RT in CG1 increased by 49 ms (SD = 34.7), and, at the same time, introducing a new sequence in the SG resulted in an increase in RT only by 17 ms (SD = 25.7). The difference in the effect of implicit learning between groups was confirmed by significant group and block interaction, F(1, 24) = 30.68, p < 0.001, η² = 0.56.

The effect of implicit learning was found only in RT but not in ER (Figure 2) as no main effect of group, F(1, 24) = 0.02, p = 0.882, η² < 0.01, and no main effect of block, F(1, 24) = 1.16, p = 0.292, η² = 0.05, or interaction between group and block, F(1, 24) = 1.38, p = 0.251, η² = 0.05, was observed.

Experiment 1B

The aim

The aim was to evaluate the use of declarative knowledge in performing a motor task and to check whether the potentially poor learning effect in Experiment 1A was due to a deficit in acquisition of a new sequence or extraction of the taught one.
learned sequence order (SEQ3), and the subjects were displayed. In Block 1, the target was presented in the that, four blocks with 12-stimulus sequences were sequence five times in a row without any error. After subjects were able to verbally and practically repeat the Procedure (info: no known sequence). CG 1

Figure 3. Mean RTs in Experiment 1B. Blocks: 1 = SEQ3 (info: known sequence); 2 = SEQ4, SEQ5 (info: known sequence may appear); 3 = SEQ6, SEQ7 (info: no known sequence); 4 = SEQ8 (info: no known sequence). CG1 = control group; SG = strabismic group. The vertical bars indicate the standard error.

Procedure

Only aspects of procedure different from those described in the general procedure and procedure of Experiment 1A are described in this section.

Experimental procedure was based on Pascual-Leone et al.’s (1993) and Molinari et al.’s (1997) studies. At the beginning of the experiment, subjects were asked to memorize the 12-digit sequence printed on a sheet of paper. For this purpose, the response keys (C-V-N-M) were numbered respectively (1–4), and the subjects were taught the numerical sequence of the target’s positions (SEQ3: 343124132142). The test did not begin until the subjects were able to verbally and practically repeat the sequence five times in a row without any error. After that, four blocks with 12-stimulus sequences were displayed. In Block 1, the target was presented in the learned sequence order (SEQ3), and the subjects were informed of this (sequence repeated 30 times = 360 stimuli with two short breaks after each 10 sequences); in Block 2, the presentation contained the two new sequences (SEQ4: 234131241243 and SEQ5: 413243123124), repeated 10 times each (240 stimuli with one short break after 10 sequences), and the subjects were informed that the target may appear randomly or in the already learned order. In Block 3, the presentation included another two new sequences (SEQ6: 14321432421 and SEQ7: 342142131432) repeated 10 times (240 stimuli with one short break after 10 sequences), and the subjects were informed that through the end of the experiment, the target would appear only in a random order; however, in Block 4, the target appeared again according to the learned sequence order (SEQ3 repeated 20 times = 240 stimuli with one short break after 10 sequences). Between the blocks, short breaks (30 s) were administered.

Results

Explicit sequence ML

As can be seen in Figure 3, SG reacted much more slowly than the control one.

Mean RT for SG was equal to 442 ms (SD = 84.6) and 372 ms (SD = 72.8) for CG1, F(1, 24) = 10.28, p = 0.004, \( \eta^2 = 0.30 \). RTs were also determined by the sequence in blocks. Blocks with the learned sequence (SEQ3) were related to shorter responses (346 ms, SD = 81.8 and 375 ms, SD = 75.2 in Blocks 1 and 4) than blocks with new sequences (460 ms, SD = 67.1 and 446 ms, SD = 65.0 in Blocks 2 and 3). This effect was confirmed by a significant main effect of block, \( F(3, 54) = 53.35, p < 0.001 \). \( \eta^2 < 0.69 \). Moreover, the type of information in Blocks 2 and 3 did not influence responses as post hoc tests showed that a significant difference in RT was observed between Blocks 1 and 2 ( \( p < 0.001 \)) and Blocks 3 and 4 ( \( p < 0.001 \)), but not between Blocks 2 and 3 ( \( p = 0.548 \)). Both groups of subjects showed the ability of explicit ML as they reacted to the known sequence in a similar way (Figure 3). This is an important aspect of this experiment, and this observation was shown by the lack of block x group interaction, \( F(2, 54) = 0.53, p = 0.610, \eta^2 = 0.02 \).

Sequence also affected ERs but in a different way. More errors were made in blocks with the known sequence (21%, SD = 17.0 and 12%, SD = 14.0 in Blocks 1 and 4) than in blocks with new sequences (6% in Block 2, SD = 4.0, and Block 3, SD = 4.4). This effect was confirmed by a significant main effect of block, \( F(2, 44) = 14.83, p < 0.001, \eta^2 = 0.38 \). As can be seen in Figure 4, the highest value of ER (27%, SD = 21) was made by CG1 in Block 1, in which the known sequence (SEQ3) was presented. However, in the next blocks, responses were much more accurate and of similar values for both groups of participants.

The difference between blocks was not found for the SG. The effect described above was confirmed by the significant block x group interaction, \( F(2, 44) = 3.39, p = 0.046, \eta^2 = 0.12 \).

Experiment 1C

The aim

The aim was to investigate essential S-R ML abilities, and a simple motor task was performed by the subjects.
Procedure

The SRTT in Experiment 1C was the same as before except the paradigm used consisted of 10 blocks each built of 10 different 12-stimulus sequences (1,200 stimuli per experiment), so there were no repeating sequences in any block.

As mentioned earlier, the last experiment required a different method of responding to the target position than Experiments 1A and 1B. We wanted to avoid a ceiling effect of ML, so an impediment to the response was introduced. A new response instruction was given: The first square was subordinate to the M key, the second square to the N key, the third square to the V key, and the fourth square to the C key. This change made the task harder to acquire the motor skill and gave the possibility of discovering small differences in S-R learning abilities between the groups.

Results

Results of the mean RTs obtained in Experiment 1C are presented in Figure 5.

In blocks in which the stimuli were presented without sequences and were changed from block to block, the SG were again much slower than CG1 (mean RT: 640 ms, SD = 93.4 vs. 527 ms, SD = 77.2 for EG and CG1, respectively), t(24) = –3.35, p = 0.003. However, SG was able to decrease RT with blocks in a similar way as CG1, which is shown in Figure 5. Rate of S-R ML (parameter a) was calculated by fitting RT data to the linear decay function. Results showed that parameter a reached a similar value for SG (a = –9, IQR = 3.0) as CG1 (a = –7, IQR = 8.6). This observation was proved by Mann-Whitney U test, Z = 0.82, p = 0.412.

Moreover, no significant differences between groups were found in ERs, as median ER for CG1 was 7% (IQR = 3) and 8% (IQR = 8) for SG, Z = –0.10, p = 0.918 (Figure 6).

Experiment 2

Earlier studies mentioned in the Introduction showed that not only strabismic subjects but also amblyopic individuals suffered from impaired visuomotor function. This may be an effect of inappropriate maturity of the visual system caused by improper visual
signal in the early period of life. To investigate whether a longer RT and impaired implicit ML in strabismic subjects was an effect of improper monocular and binocular visual signal during maturation, the series of ML tests used in Experiment 1 were performed by the subjects from a nonstrabismic binocular anomalies group, using the dominant/nonamblyopic eye.

However, it is important to stress that Experiment 2 was performed 6 months later, and a new computer and keyboard were used. The keys of the new keyboard had perceptibly more resistance, which required more power to press the key. In addition, the details of the new device hardware, connection hardware, and device drivers could affect the RT data. These factors could be a possible source of bias; thus, a new control group was introduced to compare reliably the results from the nonstrabismic binocular anomalies group with normals.

Participants

Participants came from the same population as described in Experiment 1. A total of 32 subjects were qualified for Experiment 2, but data from only 27 was taken for analyses (five participants recognized the sequence and were excluded from Experiment 2; none resigned from further attendance). Each participant had the same eye examination, met identical health criteria, and passed the same three experiments on ML (Experiments 2A, 2B, and 2C) as subjects in Experiment 1:

a) Nonstrabismic binocular anomalies group (NSG) – a total of 14 subjects (eight females, six males) with a mean age 25.3 (SD = 5.2) with nonstrabismic binocular anomalies joined the group. They did not have strabismus or microstrabismus, and all had orthophoria or heterophoria, which met the values within the normal range (<3 Δ exo, <1 Δ eso at far; <6 Δ exo, <2 Δ eso at near). Impairment in binocularity was caused by reduced visual acuity in one eye (amblyopia) in 13 subjects, and one of the participants was totally monocular. In most subjects (n = 12), the amblyopia was the result of anisometropia (mean difference in refractive error, spherical equivalent, between eyes was 3.31D, SD = 2.58). In addition, among them, one man had an eye injury in childhood, and one woman suffered from optic nerve hypoplasia and macular degeneration. In two other subjects, the lowered acuity was due to genetic, congenital eye malformation (n = 1) and postoperative complications (n = 1) after surgical treatment for persistent fetal vasculature syndrome. In all subjects, the binocular deficit developed before 3 years of age. Seven of 10 amblyopes were treated by patching in early childhood. Mean visual acuity of the nondominant/amblyopic eye was logMAR +0.34 (SD = 0.26), and the mean visual acuity of the dominant/fellow eye was logMAR −0.04 (SD = 0.08) (all measurements of visual acuity were obtained by using decimal scale and then converted to logMAR units). Table 2 presents the visual parameters of each subject.

b) Control group (CG2) – thirteen subjects (eight females, five males) with a mean age 25.1 (SD = 3.0) participated in experiment. All visual parameters were in the same range as in CG1 from Experiment 1.

Experiment 2A: Results

Sequence ML

Results of RTs obtained in Experiment 2A are presented in Figure 7.

Mean RT obtained in Blocks 1–11 was higher in NSG than in CG2: 483 ms (SD = 68.0) versus 476 ms (SD = 98.9), but this difference was not statistically significant, t(25) = −0.21, p = 0.834. Similarly, no significant difference was observed between groups in ER: 2% for both NSG (SD = 3.0) and CG2 (SD = 1.6), Z = 0.70, p = 0.482.

The ability of sequence ML from Block 1 to Block 11 was assessed by fitting the data to a linear decay function. As Figure 7 shows, both groups of participants improved their RTs between 1 and 11 blocks (a = −10 ms, SD = 5.3 for NSG and a = −8 ms, SD = 6.0 for CG2) in a similar way, t(25) = 0.80, p = 0.433.

Implicit sequence ML

Again, the effect of implicit sequence learning was assessed as a difference in RTs between blocks with the old sequence (SEQ1) in Blocks 11 and 13 and the block with a new sequence (SEQ2) in Block 12. ANOVA showed that responses in general were longer for SEQ2 than for SEQ1 (493 ms, SD = 68.0 vs. 443 ms, SD = 76.5 for SEQ2 and SEQ1, respectively), F(1, 25) = 22.46, p < 0.001, η² = 0.47, but mean RT was only marginally higher for NSG than for CG2 (471 ms, SD = 75.8 vs. 464 ms, SD = 81.2 for NSG and CG2, respectively), F(1, 25) = 0.07, p = 0.799, η² < 0.01. An increase in RT when the new sequence (SEQ2) appeared in Block 12 was observed in CG2 (RTseq2 − RTseq1 = 53 ms, SD = 64.3) as well as in NSG (RTseq2 − RTseq1 = 56 ms, SD = 45.7). Statistical analyses showed that there was no
significant difference in effect of learning between groups (sequence × group interaction), \( F(1, 25) = 0.25, p = 0.624, \eta^2 < 0.01 \).

No significant difference between groups was found also in ER (4% vs. 2.5 for CG2 and 3% vs. 1.7 for NSG), \( F(1, 25) = 1.46, p = 0.239, \eta^2 = 0.06 \), and no interaction between group and sequence was observed, \( F(1, 25) = 2.90, p = 0.101, \eta^2 = 0.10 \) (Figure 8).

### Table 2. Visual parameters of subjects from nonstrabismic binocular anomalies group (NSG).

<table>
<thead>
<tr>
<th>ID</th>
<th>Age (y)</th>
<th>Sex</th>
<th>Dominant eye (fellow)</th>
<th>Nondominant eye (amblyopic)</th>
<th>Angle of eye deviation (PD)</th>
<th>Stereopsis (seconds of arc)</th>
<th>Interocular suppression</th>
<th>Etiology of low visual acuity of nondominant eye</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>36</td>
<td>F</td>
<td>−0.07</td>
<td>(Negative)</td>
<td>0</td>
<td>0</td>
<td>Negative</td>
<td>Constant Severe eye malformation, nondominant eye totally blind</td>
</tr>
<tr>
<td>2</td>
<td>18</td>
<td>M</td>
<td>−0.07</td>
<td>+0.82</td>
<td>0</td>
<td>0</td>
<td>Negative</td>
<td>Constant Anisometropia (SEQ = 5.75D; sph ~ 8D)</td>
</tr>
<tr>
<td>3</td>
<td>22</td>
<td>F</td>
<td>+0.10</td>
<td>+0.22</td>
<td>0</td>
<td>140</td>
<td>No</td>
<td>Anisometropia (SEQ = 2.75D; cyl ~ 2D)</td>
</tr>
<tr>
<td>4</td>
<td>32</td>
<td>M</td>
<td>0.00</td>
<td>+0.19</td>
<td>EX2</td>
<td>80</td>
<td>No</td>
<td>Anisometropia (SEQ = 1.25D; sph ~ 1.5D)</td>
</tr>
<tr>
<td>5</td>
<td>22</td>
<td>M</td>
<td>−0.07</td>
<td>+0.30</td>
<td>EX5</td>
<td>600</td>
<td>No</td>
<td>Anisometropia (SEQ = 1D; sph &amp; cyl ~ 1.75D)</td>
</tr>
<tr>
<td>6</td>
<td>31</td>
<td>F</td>
<td>0.00</td>
<td>+0.22</td>
<td>0</td>
<td>40</td>
<td>No</td>
<td>Anisometropia (SEQ = 4.25D; sph ~ 4D)</td>
</tr>
<tr>
<td>7</td>
<td>21</td>
<td>M</td>
<td>−0.19</td>
<td>+0.10</td>
<td>0</td>
<td>40</td>
<td>No</td>
<td>Anisometropia (SEQ = 3D; sph ~ 3D)</td>
</tr>
<tr>
<td>8</td>
<td>27</td>
<td>F</td>
<td>0.00</td>
<td>+0.40</td>
<td>0</td>
<td>140</td>
<td>No</td>
<td>Anisometropia (SEQ = 5.5D; sph ~ 5.5D)</td>
</tr>
<tr>
<td>9</td>
<td>25</td>
<td>F</td>
<td>−0.19</td>
<td>+0.82</td>
<td>0</td>
<td>100</td>
<td>No</td>
<td>Complications after surgical treatment for PFVS of nondominant eye; pseudophakia</td>
</tr>
<tr>
<td>10</td>
<td>21</td>
<td>F</td>
<td>0.00</td>
<td>+0.10</td>
<td>EX4</td>
<td>100</td>
<td>No</td>
<td>Anisometropia (SEQ = 4.25D; sph ~ 4.5D)</td>
</tr>
<tr>
<td>11</td>
<td>23</td>
<td>F</td>
<td>0.00</td>
<td>+0.30</td>
<td>0</td>
<td>ES2</td>
<td>Intermittent</td>
<td>Anisometropia (SEQ = 1.5D; cyl ~ 2.5D)</td>
</tr>
<tr>
<td>12</td>
<td>23</td>
<td>M</td>
<td>0.00</td>
<td>+0.10</td>
<td>ES2</td>
<td>80</td>
<td>No</td>
<td>Eye injury in childhood &amp; anisometropia (SEQ = 0.5D; sph ~ 2D, cyl ~ 3D)</td>
</tr>
<tr>
<td>13</td>
<td>23</td>
<td>F</td>
<td>0.00</td>
<td>+0.70</td>
<td>EX4</td>
<td>100</td>
<td>No</td>
<td>Optic nerve hypoplasia, macular degeneration, &amp; anisometropia (SEQ = 9.5D; sph ~ 7.75, cyl ~ 1.75D)</td>
</tr>
<tr>
<td>14</td>
<td>30</td>
<td>M</td>
<td>−0.07</td>
<td>+0.19</td>
<td>EX5</td>
<td>EX2</td>
<td>No</td>
<td>Anisometropia (SEQ = 0.5D; cyl ~ 3D)</td>
</tr>
</tbody>
</table>

Notes: F = female; M = male; EX = exophoria; ES = esophoria; PD = prism diopter; SEQ = spherical equivalent refraction; PFVS = persistent fetal vasculature syndrome.

The pola mirror, tranaglyphs, and Worth 4 dot tests were used to assess the interocular suppression: No = no suppression on any test; intermittent - suppression on at least one test; constant = suppression on all tests.

### Experiment 2B: Results

#### Explicit sequence ML

Mean RT for NSG was similar as for CG2 (425 ms, SD = 93.6 vs. 411 ms, SD = 75.7 for NSG and CG2, respectively), \( F(1, 25) = 0.32, p = 0.576, \eta^2 = 0.01 \). As
can be seen in Figure 9, the block determined responses.

In blocks with known sequence (SEQ3 in Blocks 1 and 4), mean RT was faster (356 ms, $SD = 73.5$ and 396 ms, $SD = 87.1$ in Blocks 1 and 4, respectively) than in the blocks with new sequences (469 ms and 454 ms in Blocks 2 and 3, respectively), which was confirmed by the significant main effect of block, $F(3, 75) = 38.86, p < 0.001, \eta^2 < 0.61$. Both groups of subjects reacted on sequence presentation in a similar way, by increasing RTs with new sequences and decreasing RTs when the known sequence (SEQ3) was presented. This effect was proven by an insignificant interaction between blocks and group, $F(3, 75) = 0.67, p < 0.574, \eta^2 < 0.03$. Sequence also affected ERs (Figure 10).

Similar to Experiment 1B, in blocks with new sequences, mean ER was lower (5% in Block 2, $SD = 3.6$, and Block 3, $SD = 4.0$) than in blocks with the known sequence (14%, $SD = 13.6$, and 11%, $SD = 12.1$, in Blocks 1 and 4, respectively) mainly because of more concentration needed when new unknown stimuli order appeared. This effect was confirmed by the significant main effect of the block, $F(3, 75) = 7.92, p < 0.001, \eta^2 < 0.24$. However, mean ER differed between groups (7%, $SD = 10.0$ vs. 11%, $SD = 10.0$ for NSG and CG2, respectively), but this effect was not statistically significant, $F(1, 25) = 2.42, p < 0.132, \eta^2 < 0.09$. Both
groups also reacted in a similar way when new sequences were presented instead of the known sequence, which was proven by an insignificant block and group interaction, $F(3, 75) = 0.17, p < 0.914, \eta^2 = 0.01$.

**Experiment 2C: Results**

**Simple associative ML**

Results of the mean RTs in Experiment 2C are presented in Figure 11.

As can be seen, both groups of subjects reacted with similar mean RTs (629 ms, SD = 162.5 vs. 619 ms, SD = 117.8 for NSG and CG$_2$, respectively), $t(25) = -0.18, p = 0.862$. Both groups also decreased their RTs with blocks with almost the same speed. The learning rate reflected in parameter $a$ was of similar value for both groups ($-8$, IQR = 13.6 vs. $-14$, IQR = 6.9 for CG$_2$ and NSG, respectively; $Z = 0.56, p = 0.578$).

Again, no significant difference between groups was observed in median ER (7%, IQR = 5.3 vs. 6%, IQR = 6.2 for CG$_2$ and NSG, respectively; $Z = 1.09, p = 0.275$) (Figure 12).

**Discussion**

The current study attempted to investigate whether strabismus is limited mainly to the ocular motor control (eye alignment) or if it may be related to more general motor skills as the control of finger or hand movements and ML. The experimental paradigm used in the present study lets us explore if strabismic and amblyopic individuals show deficits in implicit, explicit, and simple S-R associative learning. Results obtained from the paradigm used in the current article could suggest which neural pathway, if any, might be impaired: cortico-cerebellar or cortico-striatal.

In the research, three types of tests were used (A–C) on adult subjects exhibiting strabismus (SG in Experiment 1) and binocular vision disorders without strabismus (NSG in Experiment 2). Results showed that only the SG, but not the NSG, demonstrated impairment in implicit (procedural) ML whereas other types of ML (explicit and S-R associative) were intact. The SG reacted more slowly (RTs) compared to controls when simple button pressing was required and a noncomplex motor plan, such as grasping or reaching, was required. This effect was so strong that it could also be detected when they used the better/fellow eye and no obstacles, such as diplopia or confusion, would interact to impact on the detection of the stimuli or the preparation of the motor plan because all tests were conducted monocularly.

**Sequence ML**

The results of Experiment 1A showed that strabismic subjects demonstrated poorer abilities in implicit (procedural) learning. The difference in RTs between blocks with the old sequence (SEQ$_1$) and the new one (SEQ$_2$) allowed us to assess how strongly the sequence had been learned implicitly. We found that strabismic subjects showed limited ML skills as indicated by a small reduction in RT with a new sequence compared to an old sequence (17 ms) when the sequence was learned outside the consciousness. It is important to note that a weak effect of implicit ML could be caused by (a) problems with implicit detection of sequence and
acquiring new motor skills—learning phase—or (b) inability to extract the information that was learned previously even when the learning phase was not intact. Experiment 1B indicated that SG had similar to control levels of explicit learning. This means that they could use the information that was learned previously, so the problem found in Experiment 1A might be in the learning phase but not in the phase of extraction of the information learned.

SG demonstrated also slower RTs in general that will be discussed later. Despite this fact, they demonstrated good ability of simple S-R associative learning. This suggests that despite binocular vision problems, neural function on the level of striatum and thalamus was not impaired. We base this on the assumption that the cortico-striato-thalamo-cortical loop is related to the ability of perceptual-motor programs necessary for learning the S-R association (Aosaki, Graybiel, & Kimura, 1995; Graybiel & Kimura, 1995; Knowlton et al., 1996; Laforce & Doyon, 2001; Marsden & Obeso, 1994; McDonald & White, 1993; Packard, Hirsh, & White, 1989; Packard & White, 1990; Singh et al., 1993; White, 1989, 1997).

Similar observations as ours were obtained in patients with focal cerebellar lesions who demonstrated severely impaired procedural learning of a visuomotor task while maintaining the ability of simple ML (Molinari et al., 1997). Pascual-Leone et al. (1993) showed also that patients with Parkinson’s disease (PD) performed long RTs but, in contrast, maintained the ability of implicit ML because the disease did not affect their cerebellum. Instead, PD patients have a problem with simple S-R associative ML due to reduced function of the cortico-striatal pathway (cortico-basal ganglia-thalamo-cortical loop) (Knowlton et al., 1996).

More evidence of the involvement of the cerebellum in implicit learning comes from studies on cortical cerebellar atrophy (Pascual-Leone et al., 1993) or with focal cerebellar lesions (Gómez-Beldarrain, García-Moncó, Rubio, & Pascual-Leone, 1998). Brain imaging studies revealed that the cerebellum, particularly the lateral parts, showed increased activity in the beginning of the acquisition stage (Doyon, Owen, Petrides, Sziklas, & Evans, 1996; Ellerman et al., 1994; Jenkins, Brooks, Nixon, & Frackowiak, 1994). Next, activation in the cerebellum generally decreases with practice, being almost unnoticeable when the sequence is learned (Doyon et al., 2009; Juettner, Frith, Brooks, Frackowiak, & Passingham, 1997; Rieckmann, Fischer, & Backman, 2010). Further proof of the essential role of the cerebellum in the procedural learning process comes from studies using transcranial magnetic stimulation (TMS) and transcranial electric stimulation (tDCS) methods. It was found that repeated TMS could impair (Torriero, Oliveri, Koch, Caltagirone, & Petrosini, 2004) and tDCS could improve (Ferrucci et al., 2013) the SRTT performance. Additionally, studies by Hikosaka et al. (1998; 1999) reported that an implicitly learned sequence must be properly extracted by the dentate nucleus of the cerebellum and was found to contribute to the performance of well-learned sequences (late learning stage). Interestingly, a dentate nucleus lesion causes deficits in executing learned sequences while the learning of a new sequence remains intact (Hikosaka et al., 1998; Hikosaka et al., 1999). Thus, we may expect that the dentate nucleus was not affected in our SG because they could learn the sequence explicitly and could use previously learned information in the same way as controls. This was demonstrated in Experiment 1B.

One can argue that poor implicit learning could be caused by general low visuomotor coordination, poor saccade ability, or immaturity of the visual cortex, which transfers the visual information necessary to improve motor skills. However, if this were the case, poor ability for all types of ML skills tested in the present study would be expected. Results showed that besides slower RTs in general in SG, they demonstrated a normal level of other aspects than implicit learning ability. Moreover, no deficits in any ML types were observed in NSG, which had similar levels of binocularity as SG. This aspect will be discussed later. We should, with this in mind, expect impaired implicit learning skills in both of our experimental groups, not only in SG.

Taken together, the results obtained in the present study suggest that subjects with eye misalignment (strabismus) may have a problem with motor control on the level of the cortico-cerebellar pathway, and this effect is not related to simple improper binocularity.

**Visuomotor coordination**

Results obtained showed also that subjects from SG, but not NSG, reacted more slowly (longer RTs) to visual stimuli than controls. Poorer responses, compared to the control group, were evident in all three tasks examined in the study and were not dependent on the complexity of the task. It is important to note that all experiments were conducted monocularly with the dominant/fellow eye that demonstrated good visual acuity, so neither the retinal image blur nor diplopia or confusion of the images would be responsible for this effect.

We wonder if the motor deficit observed in our study should be treated as a consequence of immaturity of the visuomotor neural pathways because of improper binocular signals during the maturation period.

It is known that amblyopia and most constant strabismus develop in early childhood and influence
binocular vision and central nervous system maturation (Grant & Moseley, 2011). It was shown that strabismic (von Noorden & Campos, 2002) and amblyopic (Schor & Levi, 1980; Van Hof-Van Duin & Mohn, 1986) as well as monocular subjects without strabismus (von Noorden & Campos, 2002) demonstrate asymmetric optokinetic nystagmus. It was concluded that poorly developed binocular vision inhibits maturation of the visual cortex. Studies on subjects with binocular vision disorders have demonstrated visuomotor dysfunctions. For example, strabismic and/or amblyopic subjects show slower saccadic eye movements (Bucci et al., 2006; Niechwiej-Szewdo, Goltz, Chandrakumar, & Wong, 2012; Perdziak et al., 2014), saccadic asymmetry between the left and right eyes (Bucci et al., 2002; Fu, Tusa, Mustari, & Das, 2007; Kapoula et al., 1997), and decreased convergence peak velocity during execution of vergence eye movements (Alvarez & Kim, 2013). Additionally, motor deficits, such as poor eye–hand coordination in reaching (Grant & Moseley, 2011; Niechwiej-Szewdo, Goltz, Chandrakumar, Hirji, Crawford et al., 2011; Niechwiej-Szewdo, Goltz, Chandrakumar, Hirji, & Wong, 2011; Niechwiej-Szewdo, Goltz et al., 2012; Suttle et al., 2011; Webber et al., 2008) and/or grasping skills (Grant & Moseley, 2011; Melmoth, Finlay, Morgan, & Grant, 2009; Suttle et al., 2011) were found. Suttle et al. (2011) showed that children with amblyopia performed slower and less accurate responses in a grasping task not only when using the amblyopic eye, but also when viewing with the better eye or even binocularly. They also found that the motor response was related to the level of binocularity, showing that grasping ERs were higher in subjects with poor binocularity when compared to amblyopes with moderate or normal binocular functions. It was suggested that the lack of stereovision impairs the initial learning phase of grasping (Mazyn, Lenoir, Montagne, Delaey, & Savelbergh, 2007). This interpretation sounds reasonable because binocular retinal disparity and stereovision contribute to reaching and grasping skills (Bhattacharyya, Musallam, & Richard, 2009; Grant & Moseley, 2011).

Our results add to the knowledge about visuomotor deficits in strabismic individuals by showing that they suffer from poor motor control even when they use their fellow eye and no complex motor plan, such as reaching or grasping, is necessary but only the transforming of the visual signals into motor commands is required. Looking at the examples described above, it seems reasonable to conclude that improper visual signals may affect the maturity of the visual cortex and/or the motor system, which is largely under the control of the visual system. However, the crucial point in the present study is that slower RTs were observed only in SG but not in NSG, which undermines this interpretation. The second experimental group (NSG) had similar levels of binocularity as SG: Three of 13 from SG and four of 14 from NSG had no stereopsis. The mean level of stereoaucity was of similar value in both groups: 171″ in SG and 142″ in NSG. Additionally, only four of 13 subjects from SG demonstrated amblyopia. The influence of amblyopia on motor skills seen in this article should not be the significant factor. Longer responses for SG may suggest that individuals with misaligned eyes suffer from more motor deficits than amblyopes or monocular individuals. This deficit may include problems with processing visual information (visual deficit), but it should imply that strabismus is more a sensory than a motor deficit, and eye misalignment can be the effect of improper processing of visual information. If this were true, we would expect deficits in whole visual functions and the impairment of all three types of learning. Our results do not confirm this idea.

Another reason for slower RTs could be the problem with eye movements, transforming visual information into motor commands (visuomotor deficit), or generation of movements (motor deficit). All these interpretations seem reasonable, but the results from the experiment performed in the current study cannot determine on which level of visuomotor control the problem appears. Future studies using the event-related potential (ERP) method may help to investigate whether longer RTs in strabismic subjects come from slower visual processing or transformation of visuomotor signals. Additionally, by using the electromyographic technique in combination with ERP and an eye-tracker device, it would be possible to detect whether slower RTs come from deficits in motor generation.

The results obtained in this study cannot explain the slower RTs, but this was not the main goal of the study; however, more aspects should be discussed here. First, impairment of sensory function with strabismic and/or amblyopic subjects was observed mainly when central stimuli were used (Ciuffreda, Kenyon, & Stark, 1978; Hamasaki & Flynn, 1981; Hess & Pointer, 1985; Levi, Klein, & Aitsebaomo, 1984), but detection of visual stimuli presented peripherally was comparable to normals (Hess & Pointer, 1985). Second, in amblyopia and/or strabismus, sensory deficits were primarily related to the worse/amblyopic eye only, not the fellow/nonamblyopic eye (Fronius & Sireteanu, 1989; Harrad, Sengpiel, & Blakemore, 1996; Sireteanu & Fronius, 1981). These observations could explain insignificant differences in RTs between NSG and controls but not longer responses of SG compared to controls. In our study, stimuli were presented peripherally, and all the tests were performed using the dominant/fellow eye, so no delay in RT in both experimental groups should be found. Based on the previous studies mentioned, it
seems that strabismic individuals suffer from stronger visuomotor deficits than others and poor binocularity should not be treated as a main cause of motor dysfunctions. More research on motor and visuomotor controls in that group of subjects is needed to understand the neuronal basis of strabisms.

Summing up, the level of binocularity for both experimental groups and the influence of improper binocular signals on the maturity of the visual and motor systems was almost the same in the experimental groups, but only strabismic subjects demonstrated impaired implicit ML and slow RTs. Thus, if poor binocularity and/or amblyopia in the early period of life were responsible for the motor dysfunction found in the present article, similar deficits in both groups would have been expected. However, this was not the case. Our results suggest that impairment in implicit ML and motor control in general, exist mainly in subjects who have problems with keeping their eyes aligned properly (strabismic subjects) and suggest more of a motor deficit than a sensory deficit in that group of individuals.

The role of the cerebellum in binocular vision

If our findings are not the consequence of generally poor binocularity, then what could be a cause of motor deficits and impairment of implicit (procedural) learning in SG?

The possible interpretation is that an implicit learning deficit could arise from a primary dysfunction of the cerebellum. Involvement of the cerebellum in eye alignment and binocular vision was demonstrated during the last decades. For example, Versino, Hurko, and Zee (1996) revealed that subjects with cerebellar dysfunctions demonstrated eye misalignment: esophoria (latent convergent deviation) and, many of them, esotropia (manifest convergent deviation) or some other various disturbances of ocular misalignment. Similar results were found in patients with progressive cerebellar tonsillar herniation (accompanying Chiari I malformation), which could produce divergence insufficiency esotropia (Pokharel & Siatkowski, 2004). Studies on monkeys (Takagi, Trillenberg, & Zee, 2001) showed that lesions of the dorsal part of the cerebellar vermis impaired vergence prism adaptation and induced esophoria. It is important to note that the oculomotor vermis and the posterior portion of the fastigial nucleus (fastigial oculomotor region) are believed to be also involved in vergence prism adaptation (Gamlin, 1999; Takagi et al., 2001). Further, studies in which muscimol was injected into the cerebellum vermis (VI/VII) of primates showed a decrease in convergence skills (Takagi, Tamargo, & Zee, 2003). The involvement of cerebellum in vergence eye movements was also demonstrated in a study by Nitta, Akao, Kurkin, and Fukushima (2008). They showed that dorsal vermal cerebellar outputs are sent to the midbrain via the caudal fastigial nucleus. Another reported reduced vergence dynamics in human subjects with lesions in the area of the cerebellum, mainly within the vermis (Sander et al., 2009). A recent fMRI study (Alvarez et al., 2010) on patients with binocular disorder (convergence insufficiency) showed that active vision training (vision therapy) decreased near dissociated phoria (latent strabismus) and was correlated to changes in not only functional activity within the frontal and prefrontal cortical areas, but also in the cerebellum.

It has additionally been revealed that the cerebellum might also be involved in vergence prism adaptation. Patients with various cerebellar diseases had impaired or absent prism adaptation not only to laterally displacing prisms (Martin, Keating, Goodkin, Bastian, & Thach, 1996) but also to prisms that change vergence effort—vergence prism adaptation (phoria adaptation) (Hain & Luebke, 1990; Kono, Hasebe, Obstuka, & Kashibara, 2002; Milder & Reinecke, 1983). A deficit in vergence prism adaptation is believed to be a factor in the occurrence of faulty binocular vision control and eye alignment (Schor & Ciuffreda, 1983). Based on the studies mentioned above, one can suggest that cerebellar dysfunction might be involved in both eye misalignment and impaired implicit learning skills.

We need to answer the question of whether motor deficits in strabismic subjects have a primary or secondary origin; however, what is sure is that strabismic individuals, even in adulthood, suffer not only from poor binocularity but also from poor motor skills that can influence their everyday life. Strabismic individuals are usually less coordinated than age-matched normals and have poorer body balance (Aprile et al., 2014; Gaertner et al., 2013; Legrand et al., 2011; Matsu, Narita, Senda, Hasebe, & Ohtsuki, 2006; Przekoracka-Krawczyk et al., 2014). So far, it has been treated as a consequence of improper binocular vision. However, studies on motor control in strabismus, together with the results obtained in the current article, suggest that some motor deficit may indicate not only immaturity of the visuomotor system, but a primary motor deficit at the level of the cortico-cerebellar pathway as well.

Returning to the problem of the treatment effect of strabismus indicated in our Introduction, important questions appear: (a) Should effectiveness of any therapy (extraocular muscle surgery, occlusion, orthoptic or optometric vision therapy) be based only on the level of visual acuity, stereoacuity, and the angle of post-therapy eye alignment? (b) Can we be sure that after some type of therapy that possibly improves the strabismic angle and binocularity, motor functions will
also be enhanced? Moreover, (c) should it be claimed that, in adults, when improvement in visual acuity is usually not possible and stereovision is very hard to obtain (Griffin & Grisham, 2002), there are no other functions to enhance except that of cosmesis achieved by eye-muscle surgery? The results of our experiments presented in the current article, together with other studies mentioned above, suggest that effective treatment in strabismus should consider both motor and visuomotor skill enhancement. In a previous article (Przekoracka-Krawczyk et al., 2014), it was shown that adult strabismic subjects also demonstrated poor body balance even when viewing with the dominant eye and with their eyes closed. This was interpreted as a result of improper oculomotor signals and cerebellar functions. Recently, Aprile et al. (2014) found that strabismic individuals show deficits in walking skills. All this indicates that many strabismic subjects, because of expanded motor deficits, may have many benefits from treatment therapy to increase visual functions and also motor skills. That kind of therapy is known as an optometric vision therapy (Allison, Gabriel, Schlange, & Fredrickson, 2007; Ciuffreda, 2002; Press, 2008), which might improve not only visual acuity and stereovision, but also enhance extraocular muscle tonicity, eye–hand coordination, body balance, and muscle coordination during walking—all activities that could also enhance cerebellar functions and could improve motor control in general.

In order to get more insight into the mechanism responsible for longer RTs in strabismic subjects when viewing the dominant/fellow eye, it seems necessary to perform more examinations with the use of devices controlling eye movements. It would give information about whether that group of subjects is able to execute the same level of saccade velocity, accuracy, and fixation, which could influence RTs executed by the hand or finger. It suggests also that in all future research on sequential ML, eye movements should be controlled—also in studies on cerebellar deficits and PD because motor control is, to a large extent, under the control of vision. General motor deficits in strabismic subjects should be studied more thoroughly to be sure whether motor deficits found in the present article are of primary or secondary origin. It is important to explore this area because if motor deficits are of primary origin, intensive motor therapy should be considered in the cases of nonpathological and nonrefractive strabismus within the first years of life. Improvement of cerebellar functions and eye–hand coordination should be reflected in better eye alignment and/or ocular control. As shown in the above literature, the cerebellum is apparently involved in muscle coordination, including oculomotor muscles and binocular vision.

Conclusions

Our results showed that strabismic individuals have poor ability for implicit (procedural) ML and poorer eye–hand coordination (slower RTs). It indicates that strabismus is not only a visual disorder, but some motor skills are also affected. We found that deficits at the level of cortico-cerebellar connections may occur in subjects with eye misalignment.

The findings could not be explained as an effect of poor visual function or improper binocularity in childhood alone because the nonstrabismic patients with binocular vision disorders demonstrated normal ability of implicit, explicit, and associative ML.

Keywords: amblyopia, cerebellum, motor learning, procedural learning, strabismus, vision therapy

Acknowledgments

The authors thank Dr. Willis Clem Maples from Southern College of Optometry, USA, for his assistance, valuable suggestions, and proofreading of the final English version of the manuscript, and Agata Gryc (MA in english philology and translation studies at Adam Mickiewicz University in Poznań) for proofreading of the revised version of the manuscript.

Commercial relationships: none.

Corresponding author: Anna Przekoracka-Krawczyk. Email: ania_pk@amu.edu.pl.

Address: Laboratory of Vision Science and Optometry, Faculty of Physics, Adam Mickiewicz University, Poznań, Poland.

References


Ciuffreda, K. J. (2002). The scientific basis for and efficacy of optometric vision therapy in nonstrabismic accommodative and vergence disorders. *Optometry*, 73, 735–762.


cerebellar lesions on procedural learning in the serial reaction time task. Experimental Brain Research, 120, 25–30.


Melmoth, D. R., Finlay, A. L., Morgan, M. J., &


