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When assistive eye tracking fails: communicating with a brainstem-stroke patient through the pupillary accommodative response – a case study

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ABBREVIATIONS

AAC	Augmentative and alternative communication
ALS	Amyotrophic lateral sclerosis
BCI	Brain-computer interface
CLIS	Complete locked-in state
EEG	Electroencephalography
LIS	Locked-in state
PAR	Pupillary accommodation response
PLR	Pupil light reflex

Abstract

Purpose Poor control of eye movement and coordination may impair the use of eye-trackers for communication in patients affected by severe motor diseases. Recently, the “voluntary” pupil accommodative response (PAR) was suggested as a possible alternative to traditional assistive technology. Aim of this study is to provide a proof of concept of this methodology in a clinical setting.

Materials and Methods A low-cost communication system was implemented, which detects the accommodative pupillary constrictions in real time and generates trigger events to drive a commercial scanning-selection interface. As a first implementation, a simple binary yes/no selection interface was designed to be tested with a brainstem stroke patient, unable to use standard communicators based on eye tracking. The patient was instructed to operate the intended selection by switching the focus of attention from a far to a near target, and was then presented with 10 questions with obvious answer.

Results The patient easily understood how to perform the accommodative task. The pupillary constrictions were marked and clearly detectable in spite of the disturbing action of persistent nystagmus. On the first presentation of the device, the patient managed to correctly answer 8 out of 10 questions.

Conclusions The present results provide a proof-of-concept for PAR-based communication in a clinical setting and support its usefulness with patients who, due to impaired control of eye movements, may be unable to use tracking-based devices.

Keywords: Brain computer interface; locked-in syndrome; augmentative alternative communication; assistive device

Highlights:

- Communication without movement remains an open research and clinical challenge.
- Voluntary control of pupil size is a novel approach to serve this purpose
- A low-cost communication system, based on the pupil accommodative response, is presented
- For the first time this approach is successfully tested in a clinical condition

1. Introduction

Patients suffering from stroke, spinal traumas, brain lesions, and progressive motor diseases such as multiple sclerosis and amyotrophic lateral sclerosis (ALS) may eventually develop a condition of complete muscular paralysis, in which consciousness and awareness are retained, known as locked-in state (LIS) [1–4]. For many of these patients, the ability to control eye movements is spared, and, therefore, they often rely on augmentative and alternative communication (AAC) devices, based on gaze tracking as the main aid for communicating [5,6].

However, the use of gaze tracking devices is hindered when oculomotor control deteriorates, as eventually happens in the progression of ALS, or if brain lesions affect ocular mobility. In the condition known as completely locked-in state (CLIS) [7], eye movements can be completely lost. For these patients, the only chance to maintain communication is to rely on other systems, for example based on EEG signals to control AAC devices. These methods are commonly referred to as brain computer interfaces (BCIs) [8]. Partial success in communicating with CLIS patients has been achieved with some BCIs, especially those based on event-related potentials [9,10]. However, these systems require a relatively long preparation, as well as the presence of specialized AAC facilitators, and have difficult learning curves because the patient must learn the proper control of specific physiological signals [11]. Moreover, they are often quite expensive. Thus, simpler and more patient-friendly methods are desirable.

We have recently described a method to establish reliable and rather fast binary communication in healthy individuals based on a very simple and natural act, namely, shifting the gaze from a far to a near target. Such gaze shift in depth is associated to pupillary constriction, the pupillary accommodation response (PAR), which is controlled by the autonomic nervous system and which is normally easily measurable, even with an ordinary webcam [12–15]. Therefore, responding “yes” to a question may be achieved by simply shifting visuospatial attention from a far to a near target. We suggested that this approach could be exploited to communicate with patients in whom the skeletomotor and oculomotor systems are impaired, but with spared autonomic control.

We here present a simple implementation of this approach designed to integrate a widely used commercial AAC interface. This software interface can be easily configured to offer different possibilities ranging from text writing, to surfing the internet to control other devices (domotics) and is normally driven with eye-movements detected by eye-tracking devices. As a proof-of-concept, this interface is here configured to implement a simple binary YES/NO communication and integrated in a pupil-driven communication prototype. The effectiveness of the system is tested in a brainstem-stroke patient, unable to control AAC devices by means of eye movements.

2. Materials and Methods

2.1 The communication prototype

A system was devised to implement a pupil-controlled scanning-selection interface, as illustrated in **Fig. 1a**. Pupil size and eye movements are binocularly and continuously detected by a low-cost eye-tracking device (EyeTribe, Denmark) and transmitted to a personal computer via USB. A custom program (Matlab, Natick MA, USA) manages the data acquisition (sampling frequency: 30 Hz) and recording of all signals and the real-time processing of pupil size (monocular). In particular, signal processing included artifact removal, low-pass filtering (cut-off frequency: 5 Hz), and PAR detection (see below). Upon PAR detection the PC emits an audio signal (“beep”) which is collected from the headphones output, and converted to a digital TTL (0-5 V) by amplification, rectification and low-pass filtering. This signal is then fed into a keyboard simulator connected to the tablet (actually, a PC all-in-one, ASUS, screen size 15.6”) where the Grid 3 (Smartbox Assistive Technology, Malvern, UK) software is running. Upon receiving this trigger signal, the keyboard simulator conveys to the tablet the equivalent of a “F7” key stroke on the keyboard, thus operating a selection command on the graphical interface. The Grid 3 software was in this case configured to implement a binary YES/NO scanning-selection, with a vertical line continuously scanning the screen, left to right, employing 12 s per cycle. If the trigger arrives when the scanning line is over the left side of the screen (green smiling face) the “yes” answer is selected and loudly vocalized by the tablet. Conversely, if the selection is made on the right side of the screen (red glowering face) a “NO” is selected and vocalized. This visual interface implements a sort of a two-interval forced-choice response which is commonly used in psychophysical experiments [16] : users have to opt for one of two possible alternatives, either the first time interval (before the scanning line reaches the midline) or the second time interval (after the scanning line has reached the midline). At variance with psychophysical experiments, here the response is not given a-posteriori but in real time, i.e., it is vocalized *during* the selected time interval. **Fig. 1b** shows how the relevant items need to be arranged: the eye tracker is positioned at 50-60 cm from the subject's eyes, a *near* target is positioned at about 40 cm and the tablet, which constitutes the *far* target is positioned at about 2 m. This arrangement has been used in the second visit to the patient (see below).

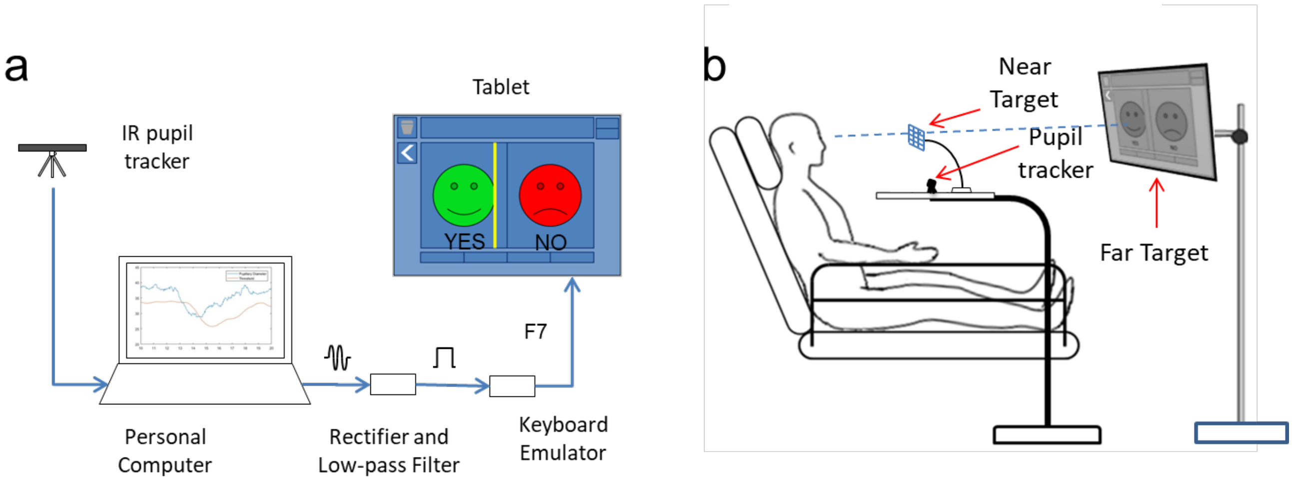

Figure 1. a) Functional scheme of the communication prototype: the personal computer, fed by the eye-tracker, detects the pupil constriction and generates a «beep» on the headphones output; this signal is transformed into a trigger signal for the scanning selection operated on the tablet. b) Experimental set-up: note the alignment of the semi-transparent near target and the far target (tablet), with the subject's gaze

2.2 The patient

The patient was a 50 year old male in LIS state, due to an hemorrhagic stroke caused by a burst basilar artery aneurysm occurred on 2008, . Since then, he has been hospitalized at the "Mons. Luigi Novarese" Recovery and Functional Re-education Center (CRRF, Moncrivello (VC), Italy). Cognitive functioning was normal, except for a mild deterioration of attentive capabilities, as clinically assessed.

An expert examination visit concluded that the patient did not need eyeglasses, but had limited lateral eye movement capacity and left eye ptosis. Moreover, he presented persistent spontaneous nystagmus binocularly. Due to these limitations, the use of eye tracking devices was impossible, and AAC was ensured by no-tech and low-tech devices.

We evaluated the patient a first time to test pupillary functionality and a second time to test the performance of pupil-based communication with the described prototype.

Three months after our second visit, the patient suddenly worsened because of a large ischemic middle cerebral artery stroke, entering vegetative state.

All procedures were in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. An informed consent was obtained from the patient.

2.3 First Visit: assessment of pupillary function

Pupillary function was tested by means of the pupillary light reflex (PLR) and PAR. The patient was staying on a bed in a semi recumbent position, with 45-deg reclined trunk. In order to assess the PLR, the patient was exposed to four 4-s lasting bright stimuli alternated with 30-s lasting dark condition, starting after a 60-s interval in the dark condition (Fig. 2a). To this aim, the room was darkened and stimuli were delivered by alternating complete white and black screens on a monitor (17 inch, 75 Hz. Belinea 1705 S1 LCD monitor), located at 50 centimeters from the patient's face. During this task the patients was asked to focus on a visual cue (a gray square, 20 by 20 pixels) displayed at the center of the screen.

In order to assess the PAR, the patient was presented with a transparent acrylic slab with a visible grid pattern, located at an approximate distance of 40 centimeters from the face (referred to as the "near target", as in Fig. 1b). A poster with a recognizable pattern was placed on the wall, located at an approximate distance of 3 meters from the face (referred to as the "far target"). Both the near and far targets were approximatively aligned with the patient's gaze of the dominant eye, so that the poster could be seen through the transparent slab.

The patient was instructed to shift the focus from the far to the near target (i.e., to the grid on the slab) upon a verbal command. This task was repeated 5 times.

In both tests, pupil size and eye movements were recorded from the dominant eye at a sampling frequency of 30 Hz with a low-cost eye tracker (the Eye Tribe) [17], located at an approximate distance of 60 centimeters from the patient's face. Scripts for signal recordings were written in Matlab (the MathWorks Inc.) and were run on a notebook (Asus P2530U).

2.4 Second Visit: Communication trial

In this occasion, PAR-communication was tested, based on the prototype previously described (**Fig. 1a**).

The patient was staying in a semi-recumbent position, with the acrylic slab as the near target and the Tablet presenting the scanning-selection interface as the far target (**Fig. 1b**). Both the near and far targets were approximatively aligned with the patient's gaze **(Fig. 1b**).

The patient was instructed to simply look at the tablet, follow the movement of the vertical line, cyclically scanning the screen from left to right, and to transiently shift the focus on the near target at the right time to perform the intended YES/NO selection. The patient was invited to test this functionality for a few times, for him to get accustomed with the latency of response of the system.

After this brief training period, the patient was presented with a sequence of ten questions with obvious answers. The scanning line was cycling continuously and the time at which questions were posed was not synchronized with the scanning cycle (i.e., position of the selection bar was not reset after each question). The signals from the eye tracker were continuously processed and recorded on the PC after each question was posed, and until an answer was given.

The patient's answer was noted by the operator and a data file containing pupil size and eye movement recordings as well as the instant of PAR detection was generated, for each of the posed questions.

The list of the 10 questions sequentially posed (in Italian) to the patient is reported in **Table 1**.

2.5 Data analysis

Data analysis was performed with a Matlab script. Horizontal and vertical components of eye position as well as pupil size signals were firstly interpolated upon blinking or other signal loss and then low-pass filtered (15 Hz for eye movements and 5Hz for the pupil).

2.5.1 Pupillary light reflex

The pupillary light reflex was characterized in terms of latency, pupillary constriction rate and magnitude of constriction, as indicated in **Fig. 2b**.

The latency of response was calculated from the time distance between onset of the bright stimulus and onset of the pupil constrictory response, the latter was calculated as the intersection of the two lines corresponding to the linear interpolation of the pupil size signal in the 5 s interval preceding the stimulus (baseline) and in the 0.3 s interval starting when the pupil size decreased below 95% of baseline. The pupillary constriction rate was calculated as the slope of this latter linear interpolation. The magnitude of constriction was calculated as the difference between basal pupil size and the average size reached during the last 0.3s of the bright stimulus

2.5.2 Pupillary accommodative response

In order to detect in real-time the PAR, a MATLAB script implemented a simple threshold-crossing algorithm. Even in a luminance-controlled environment, the pupil size may fluctuate considerably as a result of spontaneous changes of cognitive and emotional state [18,19] and a fixed threshold would have been inadequate to detect PAR events. therefore, a dynamic threshold was computed using a time-delayed (delay = 0.8 s) moving average (averaging interval= 0.8 s) of pupil size, attenuated by a factor of 0.9, i.e., the threshold value at time *t* was equal to 90% of the average pupil size in the interval [t-1.2 s; t-0.4 s]. A PAR was detected whenever pupil size crossed the threshold and remained below that value for at least 500 ms.

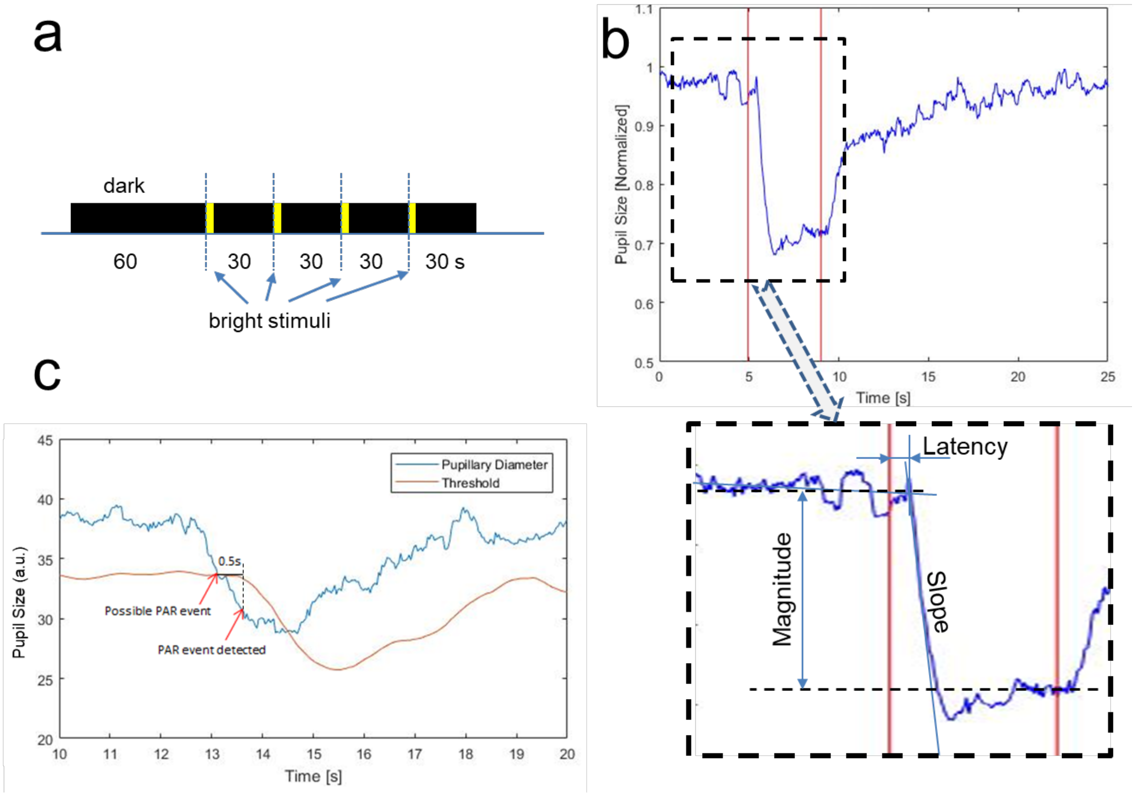

Figure 2. Methodological illustrations. a) Pupil light reflex assessment protocol. Four bright stimuli, lasting 4 s are delivered during an otherwise completely dark visual field.; b) Pupil light reflex. The pupil size is normalized to the basal level (dark condition). The red vertical lines indicate start and end of the 4-s lasting light stimulus. The tracing represents the average of 4 responses. The magnification below is used to show the parameters extracted from the curve; c) Detection of the pupil accommodative response. The threshold level (brown) is obtained from the pupil size signal smoothed by a moving average (0.8-s size), delayed by 0.8 s, and attenuated by 10 %. A valid pupil constriction is detected whenever the pupil size remains below threshold for at least 0.5 s.

3 Results

3.1 First Visit: PLR and PAR characterization results

The patient’s pupil exhibited a clear response to the light stimulus (**Fig. 2b**), presenting a mean magnitude of constriction of 30.96 ± 5.0% of the basal value (corresponding to the dark condition), a mean latency of 510 ± 63.5 ms, and a speed of constriction of 58 ± 20.4%/s.

The accommodative task was easily performed by the patient and the PARs were present and clearly identifiable (**Fig. 1S**), in spite of ocular instability due to nystagmus. On average, mean PAR amplitude was 26 ± 6 % of basal pupil diameter (corresponding to the focus-on-far-target condition). The observed minimum and maximum PAR amplitude values were 19 % and 33 % respectively.

Thus, the results from the first visit showed preserved pupillary function and demonstrated the capacity of the patient to produce clear PARs by voluntary shifting the visual focus on the near target.

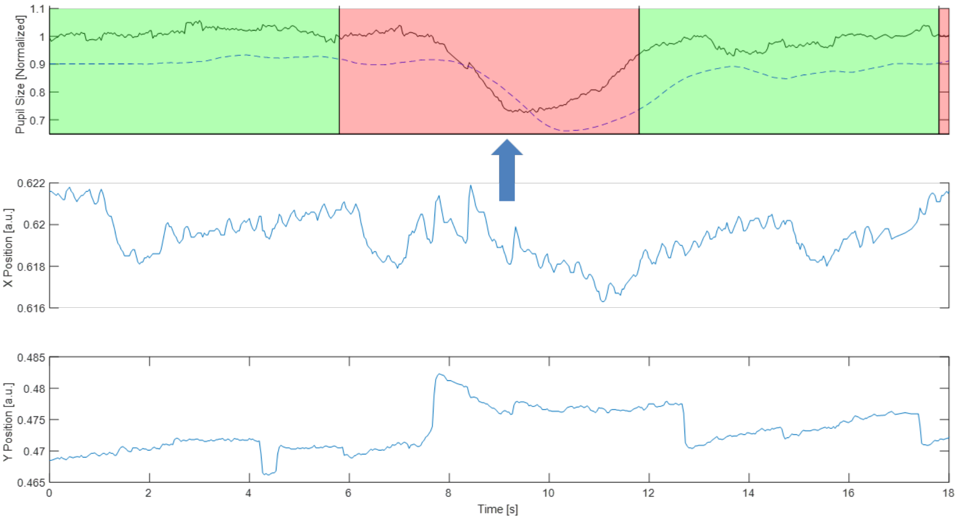

Figure 3. Representative response to one of the posed questions (question #8). From top to bottom: pupil size (black continuous line) and threshold (blue dashed line), horizontal eye position (increase = rightward movement), vertical eye position (increase = upward movement). On the top panel green and red time intervals indicate the time when the scanning bar was passing over the YES and the NO option, respectively, on the tablet display. The arrow indicates the time of detection of the pupillary constriction (pupil size remaining below threshold for at least 0.5 s) Note the presence of periodical (respiratory) oscillations on the horizontal eye movement and of nystagmus on the vertical eye movement

3.2 Second Visit: Communication trial results

The patient could easily answer the ten questions after the brief training performed. Figure 3 shows an example of the recordings of pupil size along with horizontal and vertical eye movements during the correctly given response to question #8. Note the persistent vertical nystagmus, as well as a vertical eye movement around the 9th second, possibly associated to the gaze switch on the near target. The associated PAR was, instead, quite insensitive to nystagmus interference and was, therefore, well visible. In this trial, the PAR was detected by the algorithm after 8 seconds, and indicated a correct answer (“Yes”). The recordings from all trials are reported in supplementary Figs. 2S-11S.

Table 1 Patient’s performance in the communication protocol.

Question (expected answer)	*Correctly answered*	*Response time (s)*
1) Is your name -SUBJECT’S NAME-? (yes)	*Yes*	22

2) Is your name – WRONG SUBJECT'S NAME? (no)	*Yes*	4
3) Are we in Australia? (no)	*No*	19
4) Are we in Italy? (yes)	*Yes*	11
5) Are you a man? (yes)	*Yes*	7
6) Are you a woman? (no)	*Yes*	13
7) Is there anyone else besides you in this room? (yes)	*No*	7
8) Are you the only person in this room? (no)	*Yes*	8
9) Are you over 18? (yes)	*Yes*	2
10) Are you under 18? (no)	*Yes*	4

Table 1 reports the patient's performance over the whole communication protocol. The response accuracy over the 10 trials was quite good. Response accuracy with real-time detection was 80%, with a mean response time for correct responses of 8.9 s. Two questions, #3 and #7, received a wrong response. However, off-line examination of the recordings showed that a correct response was first attempted by the patient but the PAR was not detected because too short-lasting (#3, Fig. 5S) or too small (#7, Fig.9S); a second attempt or spontaneous oscillation in pupil size was then detected but wrongly interpreted for occurring too late (i.e, in the wrong time interval). Original recordings may be examined in Figs 5S and 9S.

4. Discussion

We have here presented a device prototype which implements the detection of pupillary constrictions to drive a commercial and customizable scanning-selection AAC interface. As a proof of concept, the device was tested on a brainstem stroke patient unable to autonomously use other AAC devices. The patient immediately learned how to use the device and, on the same session of device presentation, correctly answered 8 out of 10 questions with obvious answer. While the probability of randomly answering at least 8 correct "Yes or No" questions out of 10 is 5.47%, the performance of the test, achieving an accuracy of 80% in its very first implementation, was above the 70% accuracy mark, which is considered adequate by today's standards for AAC communication [20].

The PAR was recently proposed as a possible mean of binary communication [13,15] and its magnitude and robustness were investigated in an ecological study addressing the influence of different factors such as eye illuminance, type of visual targets, mono/binocular vision, etc. [13]. In the present study an AAC prototype is implemented, based on a commercially available and customizable interface.

The patient involved in the present study could not use standard eye tracking. Due to the persistent nystagmus, enduring failure in attempting to use AAC eye-pointing devices increased his aversion towards that type of solutions. On the contrary, he immediately learned to control the pupil size by the simple accommodative task.

The present approach offers several advantages compared to current alternatives, such as EEG-based BCIs [10,21,22], which generally require long-lasting preparation by experienced operators, expensive equipment, as well as extensive patient training with unfamiliar devices and procedures.

1) The hardware, comprised of the pupil tracker, the passive near target and the tablet (far target), is easy to set up and can be easily positioned even by persons that lack a specific technical background, such as care givers, and family members [23]. In the present version a PC is still necessary to implement the PAR detection algorithm but future implementations may embed this feature within the eye-tracking system, thus further simplifying the overall usability.

2) The operative task, i.e. switching the focus from a far to a near target is an extremely simple and familiar task, that we have daily practiced during our whole life. As such it does not require any learning, although some practice with the device may be necessary to get acquainted with the slowness of the pupillary constriction and the delay introduced by the system for its detection.

3) The patients in the need of these AAC devices may fatigue easily when confronted with new devices, tasks, and interfaces and they generally benefit of the possibility to maintain the same interface they are used to [24]. In this respect the present prototype has the advantage of presenting a visual interface (the tablet equipped with the Grid 3 software) which they may be already familiar with, since it is widely diffused and compatible with many eye-tracking-based AACs.

4) The cost of this prototype is less than a tenth of other AAC systems in the market (less than 1500 dollars).

5) A final consideration concerns the origin of pupillary constriction, which is mediated by the vegetative (parasympathetic) system and, in principle, does not require a functional somatomotor system. In fact, even in the absence of eye movements, which are performed by extraocular (skeletal) muscles, switching the focus form a far to a near target remains monocularly possible, as far as the far and near targets are aligned with the gaze of the eye under study [13]. This aspect is of particular relevance considering that pupil functionality may be preserved in conditions that prevent eye-tracking-based communication, e.g., when the somatomotor system is heavily impaired, as with advanced amyotrophic lateral sclerosis [25,26] and when normal eye movements are disturbed, as with the nystagmus here observed [10,27].

The current prototype system also presents limitations. First of all, it requires intact visual function, at least on one eye, and a functional pupil. Secondly, there is a delay in PAR detection with respect to the intended switch of focus. In fact, the PAR has a delayed and slower development, compared to vergence movements (e.g., develops with a latency of about 0.3-0.4 s from a visual stimulus [28]). In addition, the secondary PAR recognition criteria (0.5 s of minimum PAR duration) and further acquisition and processing delays introduce a delay of 0.5-0.8 s before the PAR is detected. Thus, a delay of about 1 s needs to be accounted for, to timely drive the change in focus with respect to the position and speed of the scanning bar of the AAC interface.

In this respect, off-line analysis revealed that the two wrong answers were actually correct answers, undetected because of small magnitude or short duration of the PAR. This suggests that an even higher communication accuracy could be achieved with more practice. In fact, patient proficiency often increases with practice, as task repetition favors automatic behavior over voluntary cortical control, which results in faster and more precise task execution [29].

In a recent study, another alternative approach was proposed to grant a communication possibility to patients in the transition from the LIS to the CLIS condition [24]. By means of electrooculography the last residual activity of extraocular muscles could be detected and exploited to implement customized AAC devices to 4 ALS patients [24]. We here observe that, while their approach could be effective, even in the absence of vision and of non-functional pupil, it would have probably failed with the present patient, due to the disturbances introduced by the nystagmus.

4.1 Limitations of the study and conclusions

The evidence presented in this study is not exhaustive. Firstly, results from single-case studies are always poorly generalizable. Secondly, one would like to test the PAR-based approach with a much larger set of questions. Thirdly, verifying the presence of PAR in these patients over only two months may be not enough to establish how reliable is this approach in the long term. Unfortunately, the sudden worsening of the patient prevented us from performing further testing.

Despite these limitations, the collected evidence proves the efficacy of this novel approach [13]. The adoption of a general purpose AAC interface allows for easy customization of the communication possibilities. In fact, although the scanning selection was here used in its simplest configuration to operate a binary choice, the Grid 3 interface may be configured to operate on multiple choices and navigate over different menus, potentially giving access to text writing, internet browsing, domotic actions, etc.

In conclusion, the presented PAR-based prototype may constitute a convenient alternative to cortical (EEG-based) brain-computer interfaces for patients who can no longer rely on AAC based on tracking of eye movements [30,31].

5. Acknowledgments

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Some of the authors (CdS and SR) hold a patent that partly covers the described prototype

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