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Research Article

A novel Brain Computer Interface for classification of social joint attention in autism and comparison of 3 experimental setups: A feasibility study

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HIGHLIGHTS

- A novel BCI paradigm interfaced with virtual reality for social skill training in autism.
- Successful statistical classification of joint attention events.
- Nautilus is the best performing system among the 3 tested ones.

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ABSTRACT

Background: We present a novel virtual-reality P300-based Brain Computer Interface (BCI) paradigm using social cues to direct the focus of attention. We combined interactive immersive virtual-reality (VR) technology with the properties of P300 signals in a training tool which can be used in social attention disorders such as autism spectrum disorder (ASD).
New method: We tested the novel social attention training paradigm (P300-based BCI paradigm for rehabilitation of joint-attention skills) in 13 healthy participants, in 3 EEG systems. The more suitable setup was tested online with 4 ASD subjects. Statistical accuracy was assessed based on the detection of P300, using spatial filtering and a Naïve-Bayes classifier.
Results: We compared: 1 – g.Mobilab+ (active dry-electrodes, wireless transmission); 2 – g.Nautilus (active electrodes, wireless transmission); 3 – V-Amp with actiCAP Xpress dry-electrodes. Significant statistical classification was achieved in all systems. g.Nautilus proved to be the best performing system in terms of accuracy in the detection of P300, preparation time, speed and reported comfort. Proof of concept tests in ASD participants proved that this setup is feasible for training joint attention skills in ASD.
Comparison with existing methods: This work provides a unique combination of 'easy-to-use' BCI systems with new technologies such as VR to train joint-attention skills in autism.
Conclusions: Our P300 BCI paradigm is feasible for future Phase I/II clinical trials **to** train joint-attention skills, with successful classification within few trials, online in ASD participants. The g.Nautilus system is the best performing one to use with the developed BCI setup.

1. Introduction

Electroencephalography (EEG) based brain-computer interfaces (BCI), represent widely studied communication technologies (Farwell and Donchin, 1988; Kleih et al., 2011; Mak et al., 2011; Wolpaw and Wolpaw, 2012). An online BCI can be defined as a closed-loop, composed of six main steps: brain activity measurement, preprocessing, feature extraction, classification, translation into a command and the presence of feedback inside the experiment (Lotte et al., 2015). Virtual reality (VR) has also been

Abbreviations: ASD, autism spectrum disorder; BCI, brain, computer interface; EEG, electroencephalography; VR, virtual reality.

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increasingly used in neuro-rehabilitation, in particular of motor control and has shown promising results (Astrand et al., 2014; Larson et al., 2014; Larson et al., 2011; Salisbury et al., 2016; Tankus et al., 2014). Concerning cognitive applications in the field of neuro-rehabilitation the use of combined VR and BCIs has mainly been used with children with attention deficit hyperactivity disorder (which includes the presence of frequent inattentive, impulsive and hyperactive behaviours (American Psychiatric Association, 2013)). For example, Cho et al. (2002) tested an attention enhancement system using a head mounted Virtual Reality device and EEG biofeedback to increase the attention span of children who have attention difficulties.

In (Wainer and Ingersoll, 2011; Wang and Reid, 2011) one can find a summary of several studies that have examined the feasibility and effectiveness of VR as a social skill training option for people with ASD (Bernard-Opitz et al., 2001; Mitchell et al., 2007; Ozonoff and Miller, 1995; Parsons et al., 2004). The majority of these studies focused on teaching emotion recognition and simple language skills such as learning vocabulary words and receptive language. More recently, Kandalaft et al. (2013) and Didehbani et al. (2016) tested the efficacy of a Virtual Reality Social Cognition Training tool in children with high functioning autism and measured changes in affect recognition, social attribution, and executive function pre and post training. These studies revealed some promising improvements in social capabilities of ASD subjects, but almost all of them pointed some problems in the translation of these improvements for the individuals' daily living joint attention skills, which represent 'real-world' life demands. Joint attention refers to the ability to share a common point of reference, e.g. the human capacity to coordinate attention cued by a social partner. Joint attention is pivotal in social information processing in learning situations.

Despite these limitations, several studies do postulate (Bekele et al., 2014; Georgescu et al., 2014; Wainer and Ingersoll, 2011), that the use of ecological, realistic and interactive virtual environments may be the solution for this typical generalization problem in the rehabilitation of social skills in ASD subjects to real life settings. Golan and Baron-Cohen (2006) proposed that the use of computerized intervention in ASD individuals permits the development of skills in a highly standardized, predictable, and controlled environment, while simultaneously allowing an individual to work at his own pace and ability level.

In this feasibility study we propose a novel virtual reality P300-based BCI paradigm that tries to couple the potentialities of ecological, realistic and interactive virtual environments with the attention related nature of the P300 brain waveform to create a cognitive training tool for ASD, for use in future efficacy Phase II clinical trials. The P300-based paradigm that we present here consists on an immersive environment were the subject must follow a non-verbal social agent cue (head turn) and direct his/her attention to the target object. The attentional mental state of the subject is monitored through the detection of oddballs, which leads to a P300 signal which allows giving feedback about his/her attentional focus. The P300 signal is a well-known neural signature of attention processes for detection of rare items in a stimulus series – oddball paradigm – (for a review see (Duncan et al., 2009; Patel and Azzam, 2005; Polich, 2007)). We decided to couple the training of joint attention skills to P300 signal because the latter is widely used in performance studies, and is related to integration of information with context and memory (Halgren et al., 1995). Moreover, with the automatic detection of P300 signals one can provide direct feedback about individual's attentional focus. This provides information that the subject can use to self-monitor his/her performance about where to look and subsequently allow ASD subjects to adjust behaviour. Given the repetitive nature of this type of oddball paradigm, and its operant learning properties, our motivation for the construction of this paradigm is based on the hypothesis that ASD subjects can assimilate joint attention skills by automating the response to the social cue that is given during the task we created. Joint attention is an early-developing social communication skill defined by the non-verbal coordination of attention of two individuals towards a third object or event (Bakeman and Adamson, 1984). People with ASD show severe deficits in joint attention abilities (Baron-Cohen, 1989; Baron-Cohen et al., 1997; Dawson et al., 2004; Klin, 2002; Leekam and Moore, 2001; Swettenham et al., 1998) which plays a critical role in social and language development (Charman, 1998).

From the target population's point of view, the comfort associated to the use of immersive technology plus the EEG setup is crucial because ASD subjects may show sensory hyper-reactivity (American Psychiatric Association, 2013). Thereby, it is important to reduce the time needed to prepare the BCI and virtual reality setup. This may help reduce stress levels and increase task compliance. Taking this into account, the use of active electrodes that do not require skin preparation may be an efficient way to reduce the EEG preparation time. The combined use of head mounted virtual reality setups with EEG acquisition devices is still a huge challenge due to the difficulties in coupling both systems in the same subjects. In this study, we addressed the feasibility of our novel P300 based paradigm with joint attention cues by comparing its performance and usability across 3 different 'easy-to-use' EEG systems coupled with a head mounted virtual reality setup. The objective was to find the most appropriate EEG system to use with this type of novel paradigm and then to test its feasibility online in ASD participants.

In sum, our study had two main goals: 1. to ascertain the usability of 3 distinct EEG setups to be used combined with a VR headset as part of a novel BCI system with a paradigm that uses social joint attention cues as an indicator of the target event; 2. to test its feasibility online in ASD participants as a prior step for future efficacy trials. Concerning this prior goal, we tested three distinct 'easy-to-use' EEG systems. The tests were conducted to verify the comfort and the time needed to use the VR P300-based BCI tool with each one of the EEG systems. The acquired EEG data were tested with the automatic BCI's P300 identification module to investigate which system showed better accuracy in which concerns BCI's performance.

We therefore first focused on a healthy participant cohort and finally performed exploratory assessments in four ASD subjects to prove the feasibility in a clinical setting.

2. Material and methods

This study and all the procedures were approved by the Ethics Commission of the Faculty of Medicine of the University of Coimbra (Comissão de Ética da Faculdade de Medicina da Universidade de Coimbra) and was conducted in accordance with the declaration of Helsinki. All participants were recruited from our database of voluntary participants, with no monetary compensation. All of them agreed and signed a written informed consent.

2.1. Participants

All healthy participants (n = 13, 7 males, 6 females, average age 22.5 years (SD = 1,8 years), range 21–26 years) had normal or corrected-to normal vision and no history of neuropsychiatric disorders.

Pilot studies with clinical participants included 4 young males with high-functioning Autism Spectrum Disorder (Full-Scale Intelligent Quotient [FSIQ] > 70; FSIQ: Mean = 106,75; SD = 17,85), ranging in age from 15 years to 22 years, average age 18.8 years (SD = 2,6 years). ASD diagnosis was assigned on the basis of the gold standard instruments: parental or caregiver interview (Autism

Fig. 1. Panoramic view of the virtual bedroom.

Diagnostic Interview – Revised, ADI-R (Lord et al., 1994)), direct structured subject assessment (Autism Diagnostic Observation Schedule, ADOS (Lord et al., 1989)), and the current diagnostic criteria for ASD according to the Diagnostic and Statistical Manual of Mental Disorders 5, DSM-5 (American Psychiatric Association, 2013).

2.2. Virtual environment and software details

The immersive virtual environment was presented to the participant via the Oculus Rift Development Kit 2 headset (from Oculus VR). Participants did not report any problems with the near vision conditions of the setup, due to the small distance between the headset display and the eyes. The virtual environment consists in a bedroom with common type of furniture (shelves, a bed, a table, a chair, and a dresser) and objects (frames, books, lights, a printer, a radio, a ball, a door, a window, and a laptop).

The room environment (Fig. 1) was designed with 3ds Max (from Autodesk Inc.) and SketchUp (from Trimble Navigation Limited). The objects in the room were obtained and adapted from 3D Warehouse (from Trimble Navigation Limited). The environment texture rendering was done in 3ds Max with Mental Ray 3D rendering software (from NVIDIA ARC GmbH). The stimulation software was written using the Vizard Virtual Reality Toolkit software (from WorldViz) and the real-time scene rendering was implemented using Vizard and Oculus Rift middleware software integration.

The communication between the stimulation and the EEG acquisition module (event markers and results of data processing) was achieved via a TCP/IP communication protocol. The TCP-IP protocol was chosen in order to allow the system to work in the future in separate computers, if the need arises, due to larger number of channels and/or sampling rate.

The overall system setup can be seen in Fig. 2.

The acquisition and the VR stimulus display was controlled by a single computer (Intel ® Core^{TM} i7-4710HQ CPU @ 2.50 GHz, 6 M Cache, up to 3.50 GHz, RAM: 16 Gb. graphics card: GeForce GTX 870 M, 1344 CUDA cores @ 941 MHz, 192 Bit memory interface @ 2500 MHz, 6 Gb of dedicated memory). Prior tests showed that the smooth rendering of the graphical VR stimulation is ensured, as well as the EEG acquisition.

2.3. EEG data acquisition

The tested systems were: 1) g.Mobilab+ (gTEC, Austria) with g.SAHARA active dry-electrodes and wireless transmission of the signal; 2) g.Nautilus (gTEC, Austria) with active electrodes that do not require abrasive skin treatment (completely wireless signal transmission); 3) V-Amp with wired actiCAP Xpress dry-electrodes (BrainProducts, Germany).

EEG data were recorded from the same 8 electrodes positions (C3, Cz, C4, CPz, P3, Pz, P4, POz) with all the systems. The reference positions were placed at the right ear. The ground positions was placed at the left ear, except with the g.Nautilus system (placed at AFz, because this could not be changed). Sampling rate was set at 250 Hz, the closest possible to predefined g.Mobilab sampling rate (256 Hz). Data were acquired notch filtered at 50 Hz and passband filtered between 2 Hz and 30 Hz. The filtering was performed via the proprietary Simulink HighSpeed Online Processing block modules for g.MOBIlab and g.Nautilus systems, and via MATLAB code for the Xpress system. Table 1 summarizes the acquisition settings for each system.

Participants took part in 3 EEG recordings, each one with one of the EEG systems, in random order, performing the same task. The number of trials resulting from each EEG recording is the same across all the setups, which gives a total number of events/trials per subject of 1600 trials $\times$ 3 acquisitions = 4800 trials. More details about the events are described in the next sections. In order to reduce the fatigue effect, and sequence effects, the order by which each system was tested was randomized between all the participants with the constraint that all systems had been tested in the first place the same number of times.

The time needed to place the cap on the volunteer's head was measured with a chronometer, as well as the time to place Oculus headset over the EEG caps, and the time to achieve the desired signal quality, using the same criteria. The time between the start and the end of the total session procedure was also recorded. Pilot recordings revealed that when the subject is still with the eyes opened and using active electrodes the EEG signal could be kept stable between $\pm 20\,\mu V$ and the impedances kept under 30 kΩ. We therefore defined the desired signal quality as the moment when the EEG signal was visually kept stable between $\pm 20\,\mu V$ more than 10 consecutive seconds, having the subject still and with the eyes opened. During the time to achieve the desired signal quality we explained the task to the participant and adjusted the positions of the electrodes and the contact with the scalp. With the g.Nautilus system, during this time we also placed the conductive gel.

Friedman Tests were conducted with a significance level set at 0,05 to compare the total session time, the time needed to place the cap on volunteer's head, the time to place the Oculus headset over the EEG caps, and the time to achieve the desired signal quality with each of the systems. These tests were followed by post hoc analysis with Wilcoxon signed-rank tests with a Bonferroni correction applied, resulting in a significance level set at $p < 0{,}017$.

At the end of the acquisitions we asked the participants which system was the most comfortable to use.

2.4. Proof of concept studies with clinical participants

The setup used in the pilot sessions with ASD individuals was chosen based on the results obtained from the tests with healthy subjects. As it will be shown in results section, the BCI configuration using g.Nautilus offered better signal reliability, faster setup preparation and more comfort to the participants. This way, ASD participants used the configuration with the above described g.Nautilus.

2.5. Paradigm and task

The participants were submitted to the calibration phase of the BCI. It is a fundamental step of a BCI system since the data and derived models of the filter and classifier resulting from this phase are used separately for training and test data, being in turn used in the BCI online phase (for the clinical proof of concept of this study).

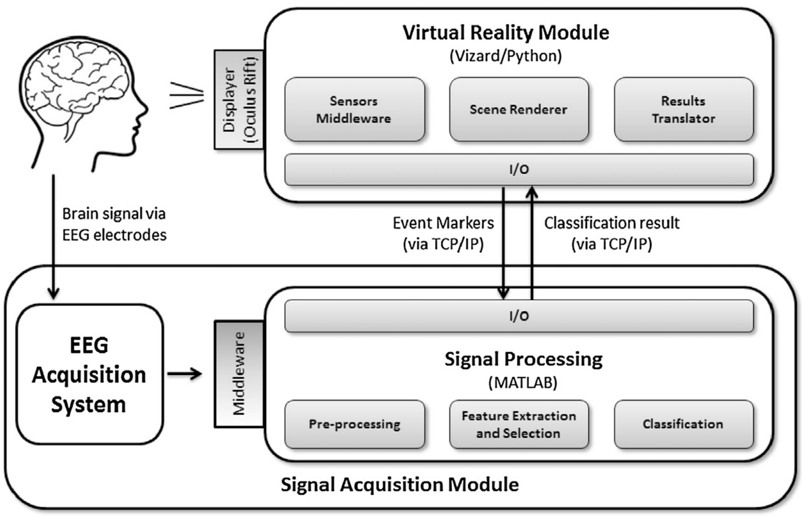

Fig. 2. BCI system integration.

Table 1
Acquisition systems characteristics.

Characteristics	Acquisition system		
	g.MOBIlab+	g.Nautilus	Xpress
Amplifier	g.MOBIlab+ 8 unipolar channels	g.Nautilus 16 Research Headset	V-Amp 16 unipolar channels
Cap	g.GAMMAcap[2] (10–20 system)		actiCAP Xpress cap (10–20 system)
Electrodes	8 active dry electrodes (g.SAHARAelectrodes) + 2 adhesive Ag/AgCl electrodes (GND and REF)	8 gel-based active electrodes (g.LADYbird) + g.LADYbird (GND) + g.GAMMAearclip (REF)	8 active dry electrodes (mushroom-headed QuickBits) + 2 T-shaped QuickBits (GND and REF)
Electrode positions	C3, Cz, C4, CPz, P3, Pz, P4, POz, GND: left ear, REF: right ear	C3, Cz, C4, CPz, P3, Pz, P4, POz, GND: AFz, REF: right ear	C3, Cz, C4, CPz, P3, Pz, P4, POz, GND: left ear, REF: right ear
Pré-amplifier	g.SAHARAbox – Active dry electrode driver box	–	–
Sampling rate	256 Hz	250 Hz	250 Hz
Signal transmission	Bluetooth 2.0	Bluetooth 4.0	USB 2.0
Middleware	g.MOBIlab+ Simulink HighSpeed Online Processing for MATLAB		TCP/IP Remote Data Access interface from BrainVision Recorder
Filtering	Notch: 50 Hz; 2Hz–30 Hz, 8th order Butterworth band-pass filter		Post-recording filtering: 2 Hz to 30 Hz 8th order Butterworth band-pass filter, 50 Hz Notch

This is a mandatory phase since the filter and the classifier are user-dependent. Only this way it is possible obtain the set of parameters that optimize the detection of P300 for each user.

The calibration phase of our BCI system is divided in two parts where the task is similar, but the instructions are slightly different.

First part (Fig. 3): This part had 10 blocks. Each block consisted in 10 sequential runs, and each such run consisted of flashing all of the 8 objects in the scene (green flashes) in a randomized order: 1. a wooden plane hanging from the ceiling; 2. a printer on a shelf; 3. a corkboard on the wall; 4. a laptop on a table; 5. a ball on the ground; 6. a radio on top of a dresser; 7. a picture on the wall; 8. books on a shelf. The highlight (flash) of each object occurred with a Inter-stimulus Interval of 200 ms. Each flash had the duration of 100 ms. The order which by all the objects were highlighted was random. This gives a total of 80 flashes (events) per block. In each block it was directly told to the participants to look to one of the already mentioned objects that would be flashed and count the number of times it would happen. The object that was explicitly mentioned to the user in this phase was the target one. The target object in each block was randomly chosen by the computer using the pseudo-random number generator Mersenne Twister algorithm, and was displayed only to the investigator on the laptop screen (the participant is wearing the Oculus device). Since the participant was only attending to the flashes of only one object per block, this event is the rarest one (target event probability of 1/8) and thus it generates the P300 brain response we aim to monitor. Here, by directly instructing the user to the target object during calibration, we intentionally remove potential errors identifying the target object related with social attention deficits that are present in ASD. At the end of each block it was asked to the participant to which object they looked (as a behavioural control). This part was designed to ensure the correct recording of each subject's P300 response, without interference of social cognition aspects. This is fundamental because the data from this part will be used as the training data of the filter and the classifier of the BCI system, explained in the next section.

Second part (Fig. 4): This part also had 10 blocks. In each block the participants were instructed to look to the virtual character's (avatar) face and attend to which of the objects it turned its head (joint attention cueing). The avatar then moved its head with a realistic and animated movement to one of the 8 objects already mentioned in the first part. The object to where the avatar turned its head was chosen randomly by the computer in each block using the pseudorandom number generator Mersenne Twister algorithm. Then they were asked about which object was chosen by the avatar. This cycle was repeated until the participant has given two consecutive correct answers. This response is meant to obligate the user to learn to read the social joint attention cue of the avatar and use this information correctly. In other words, these are the instructions for

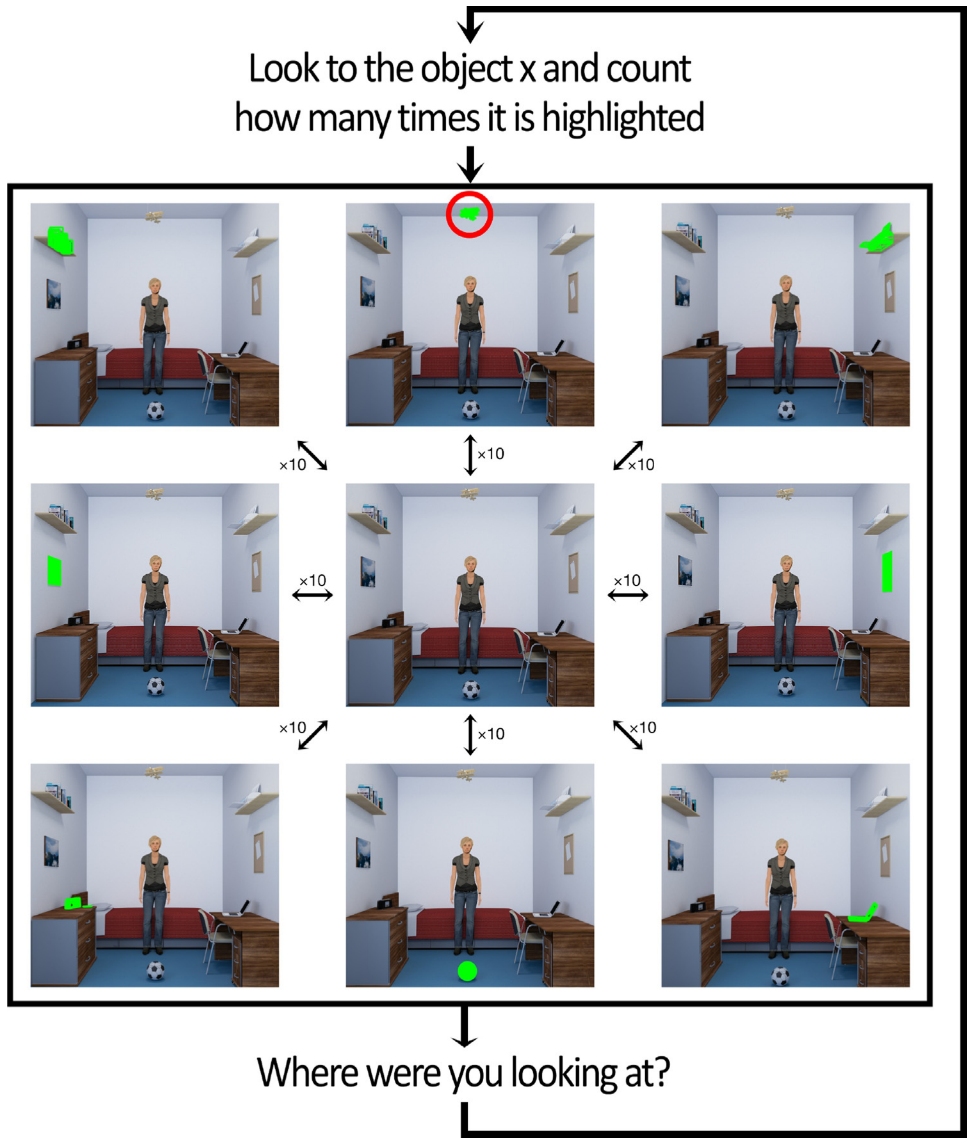

Fig. 3. Example of one block of the first part from the calibration phase of the BCI. Inside each block the same object never flashed two consecutive times. The randomization of the order of the objects highlighting was controlled in order so this never happened.

use of the BCI. It is crucial so the acquired data can be effectively used to properly test the classifier. After this, the participants were told to look to the object the avatar had chosen and count the times it was highlighted. This step is followed by 10 sequential runs of flashing all of the 8 objects in the scene (green flashes) in a randomized order. This gives a total of 80 flashes (events) per block. The object to which the avatar turned its head was the target object (event) of the block. Since the participant was only attending to the flashes of only one object per block, this event is the rarest one and thus it generates the P300 brain response we want to monitor. At the end of the objects highlighting period it was asked to the participant to which object they looked (as a behaviour control). This part was designed to add the joint attention training component of the online BCI paradigm. By introducing the ecological and immersive virtual reality environment and the realistic animation of avatars' head towards an object, as a cue to the target object, we intended to introduce the realistic component that can add joint attention mechanisms during social information processing. The understanding of this mechanism is fundamental so the participants can succeed in the online BCI task (performed in proof of concept tests with ASD individuals; see below) where the blocks are similar to the blocks of this second part but without the cycle of questioning to where the avatar turns its head. The participant must follow the head cue instantaneously and pay attention to the target object. In the online phase of BCI the P300 detection model created with the data from the calibration phase (explained in the next section) will be in charge to give the feedback about the attentional focus of each participant, at the end of each block (target object turns green if the user correctly directed their attention to it, or any non-target object turns red if the attention focus was one of them). This closed-loop ensures feedback about the attentional focus of the subject and its monitoring during the BCI game with no need for any explicit response, which helps keeping attention focused, critical for clinical applications.

2.6. EEG data analysis

Offline analysis of the data from the healthy subjects was performed using the C-FMS beamformer methodology proposed in Pires et al. (2011a,b), that cascades a spatial filter based on the Fisher Criterion (FC) with another spatial filter that maximizes the

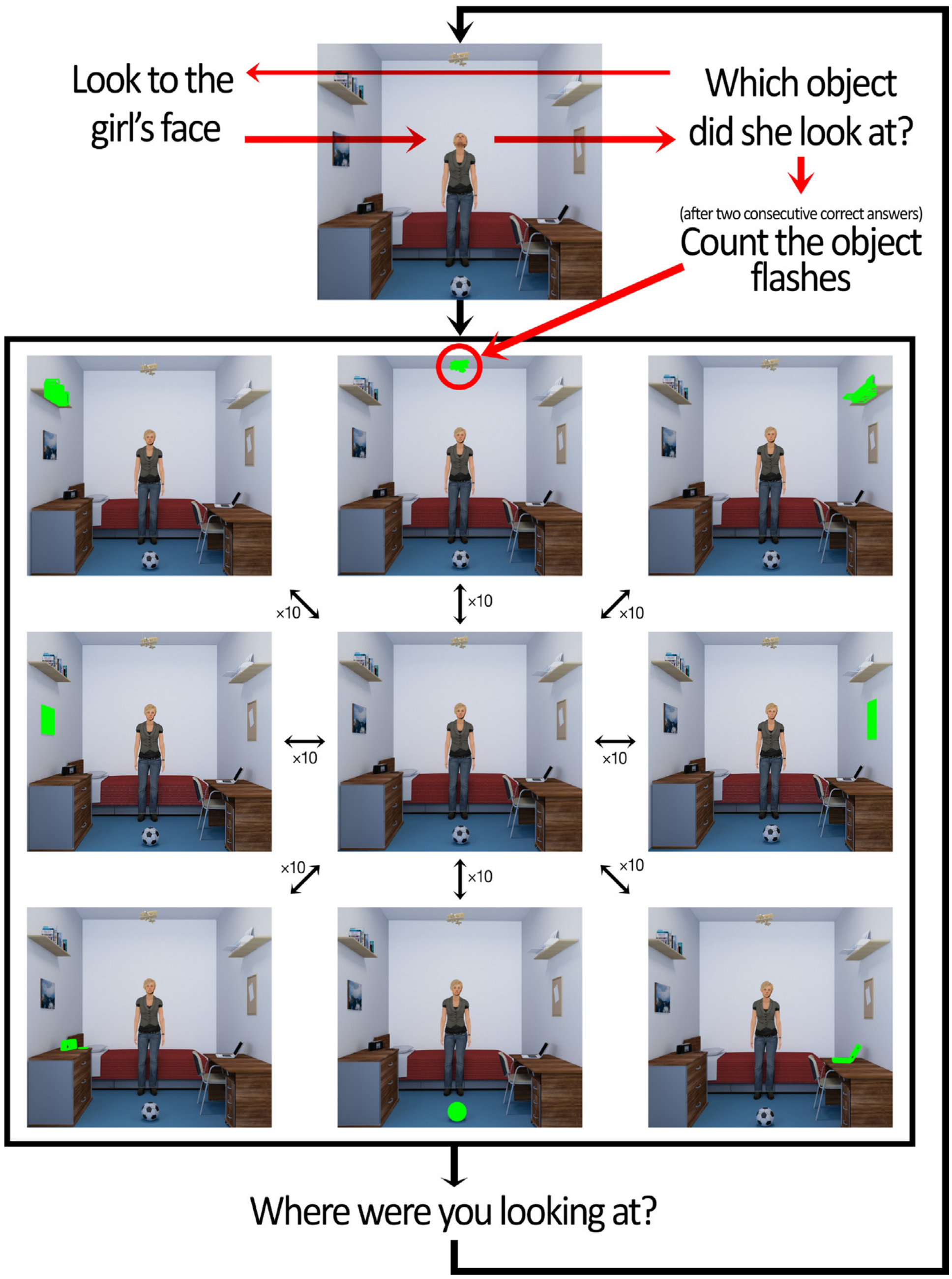

Fig. 4. Example of one block of the second part from the training phase of BCI. Inside each block the same object never flashed two consecutive times. The randomization of the order of the objects highlighting was controlled in order so this never happened.

ratio of signal power and noise power (Max-SNR) satisfying simultaneously sub-optimally both criteria (C-FMS beamformer).

The EEG data from both parts were segmented in epochs (related to each event of the blocks) of 1100 ms with a 100 ms pre-stimulus interval and a 1000 ms post-stimulus interval. Each epoch was normalized to zero mean and unit standard deviation. Each epoch is labeled as target or non-target accordingly to the trigger stored during the EEG acquisition and the target event of each block. From the events labels and the responses of the classifier for each event we could calculate the accuracy of the classifier responses.

From the structure of the tasks we get two datasets. We defined the data from the first part as the training dataset and the data from the second part as the test dataset. Both datasets have 10 blocks of data. Inside each block we have 10 runs of 8 distinct events from which only one is the target event (the target event of the block). This leads to a total of 800 epochs of data. This way we were able to test the classifier performance across different events averages (from single event to 10 event averages) inside each block.

The training dataset is used to compute the FC filter model. The FC filter is applied to the data and a first feature vector is obtained from the projection associated to the largest eigenvalue of FC filter. The Max-SNR filter model is calculated from the remaining projections. The filter is then applied to the same projections and a second feature vector is extracted from the projection associated to the largest eigenvalue of Max-SNR filter. The two feature vectors are concatenated (forming the C-FMS beamformer) and scored according to the r-square discrimination (square of the Pearson's correlation coefficient) between target and non-target events. Finally, a Naïve Bayes (NB) classifier is trained using the features

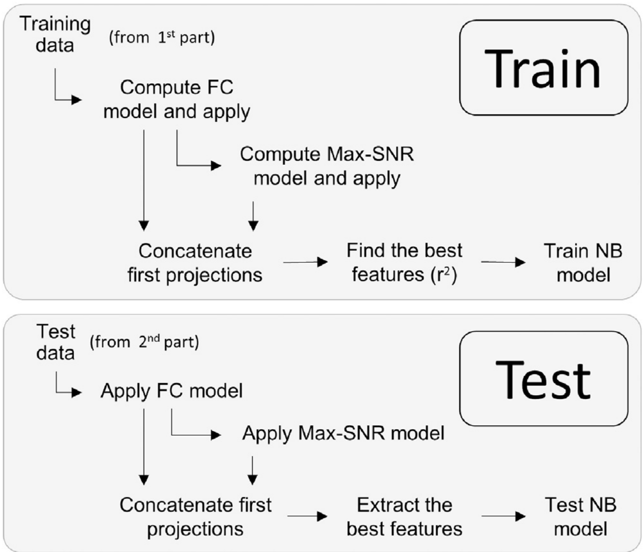

Fig. 5. Boxplot of the session times with the different systems.

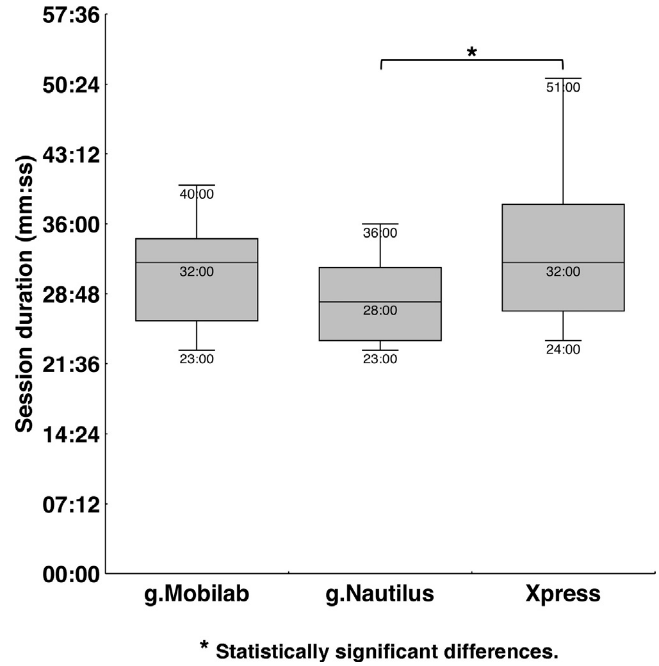

Fig. 6. Boxplot of the times needed to place the different systems' EEG caps.

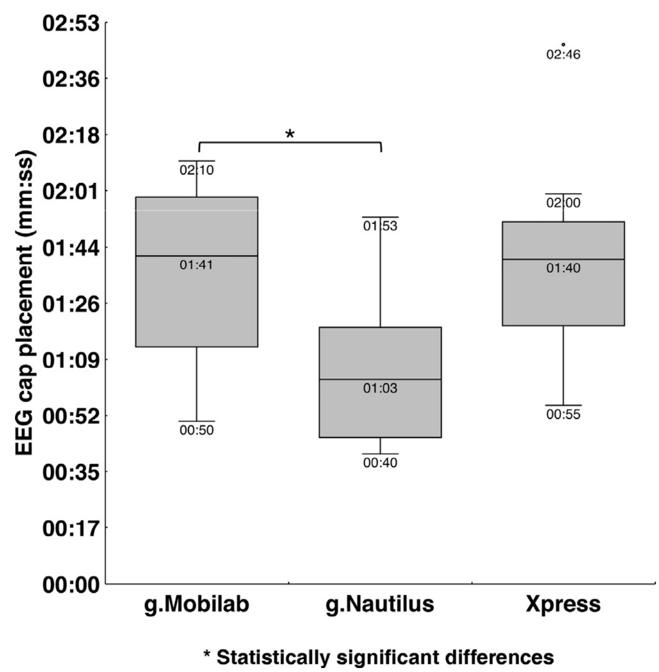

Fig. 7. Boxplot of the times needed to place the Oculus Rift headset over the EEG cap.

with higher r-square score and the best feature indices are also stored (Fig. 5).

Thereafter, the FC and Max-SNR filters calculated from the training dataset are then applied in cascade to the test dataset to obtain the vector of features. The features with the same indexes of the best features in the training dataset processing are used to test the NB classifier model. The decision about the attended object is obtained from the combination of the *a posteriori* probabilities returned by the NB classifier according to:

$$\#_{\text{object}} = \max_{j\in\{1,\ldots,8\}} \mathrm{P}^{j}_{+}$$

where P^{j}_{+} are the *a posteriori* probabilities associated to the events (index *j*, corresponding to the 8 objects). In other words, the method chooses the event most likely to be a target.

The classifier's accuracy of target object detection by run was computed with the data from the three systems, for each subject. The classification performance is assessed using the NB classifier. We tested several averages of events (from a single event to 10 event averages) to verify the influence of signal to noise ratio in the accuracy of the classifier.

The area under the curve of the accuracy levels across event averages was calculated to compare the global performance of the classifier across the different systems. A Friedman Test was conducted followed by Post hoc analysis with Wilcoxon signed-rank tests with a Bonferroni correction applied, resulting in a significance level set at $p < 0.017$.

3. Results

3.1. Tests with healthy subjects

The Friedman Tests comparing the measured times from all the 13 participants, for each of the 3 systems, revealed statistically significant differences in overal session time (Fig. 6), $\chi^2(2) = 5{,}320$, $p = 0{,}045$, in the time needed to place the EEG cap, $\chi^2(2) = 9{,}692$, $p = 0{,}007$, in the time needed to place the Oculus Rift headset over the EEG cap, $\chi^2(2) = 9{,}385$, $p = 0{,}009$, and in the time needed to signal stabilization, $\chi^2(2) = 7{,}538$, $p = 0{,}025$.

The post hoc tests with Bonferroni correction indicated that the sessions with the g.Nautilus EEG system (Mdn – 28 min = 1680 s) was significantly shorter than the sessions with the Xpress system (Mdn session time – 32 min = 1920seconds), $Z = -2{,}518$, $p = 0{,}008$.

There were no significant differences between the total session time with g.Mobilab (Mdn – 32 min = 1920 seconds) and Xpress (Mdn – 32 min = 1920 seconds), $Z = -0{,}735$ $p = 0{,}486$, neither between the session times with g.Nautilus and g.Mobilab, $Z = -1{,}297$, $p = 0{,}218$. It took less time to correctly place the g.Nautilus system's cap in the participants head (Mdn – 1 min and 3 s = 63 s) than all the others systems' caps (vs g.Mobilab: Mdn – 1 min and 41 s = 101 s, $Z = -2{,}342$, $p = 0{,}016$; vs Xpress: Mdn – 1 min and 40 s = 10 s, $Z = -2{,}132$, $p = 0{,}033$). There were no differences between the time to place the caps of g.Mobilab and Xpress systems, $Z = -0{,}769$, $p = 0{,}465$ (Fig. 7).

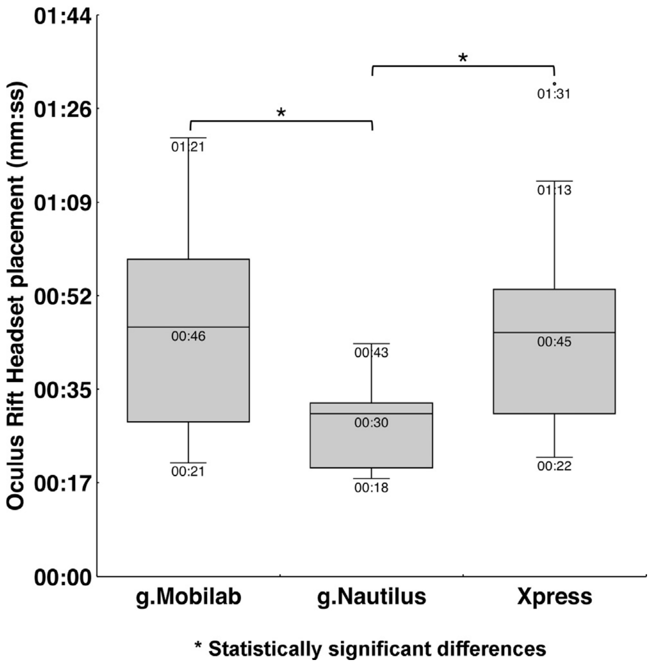

Fig. 8. Boxplot of the times for the signal stabilization occur.

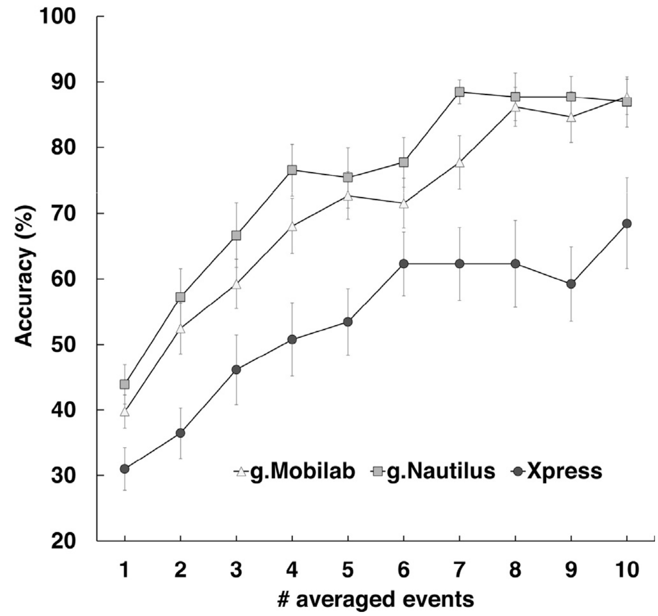

Fig. 10. Boxplot of the AUCs of accuracy levels across event averages, for each system.

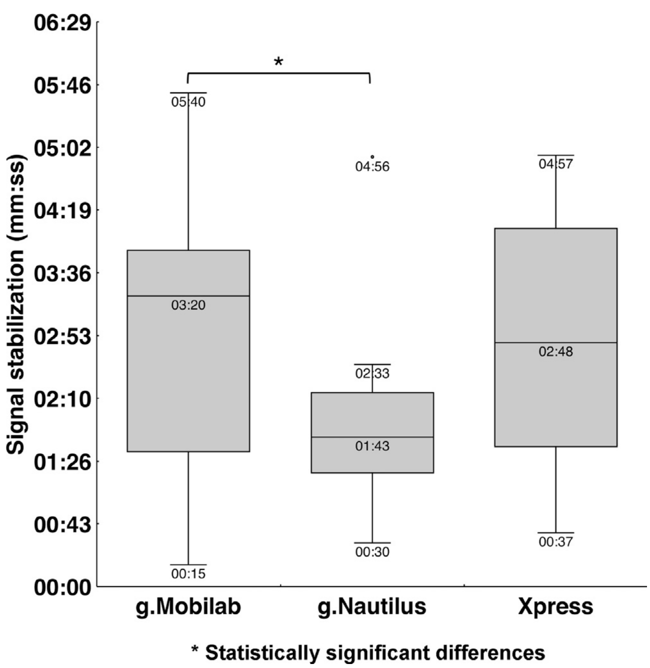

Fig. 9. Averaged accuracies and standard errors of the mean of object detection per block, with the signal from g.Mobilab, g.Nautilus and Xpress. Chance level is 12,5%.

Concerning the time needed to place the Oculus Rift headset over the EEG caps (Fig. 8), it was faster (Mdn – 30 s) to place when the participants were with the g.Nautilus cap on (vs g.Mobilab: Mdn – 46 s, $Z = -2{,}730$, $p = 0{,}004$; vs Xpress: Mdn – 45 s, $Z = -2{,}834$, $p = 0{,}003$. There were no differences when the participants were wearing g.Mobilab or Xpress, $Z = -0{,}280$, $p = 0{,}800$).

The comparison tests between the time needed for the EEG signal stabilization (Fig. 9) revealed that there were statistically significant differences between the times for signal stabilization of g.Nautilus (Mdn – 1 min and 43 s = 103 s) and g.Mobilab (Mdn – 3 min and 20 s = 200 s), $Z = -2201$, $p = 0{,}027$; but not between g.Nautilus and Xpress stabilization times (Mdn – 2 min and 48 s = 168 s), $Z = -1{,}748$, $p = 0{,}083$, nor between g.Mobilab and Xpress, $Z = -0{,}524$, $p = 0{,}635$.

Average accuracies of target object detection by block across event averages are summarized in Fig. 10. Even at the single trial level all systems were well above the 1/8 chance level.

Statistically significant differences were found between the AUCs of accuracy levels across event averages, $\chi^2(2) = 14{,}000$, $p = 0{,}001$. Post hoc tests unveiled that, globaly, the classifier performed significantly worse with the signal from Xpress: Median areas under the curve: g.Mobilab – 6,49; g.Nautilus – 6,88, Xpress – 5,09. Xpress vs g.Nautilus, $Z = -3{,}040$, $p = 0{,}001$; Xpress vs g.Mobilab, $Z = -2{,}900$, $p = 0{,}002$. The AUCs of g.Mobilab and g.Nautilus were not significantly different, $Z = -1{,}992$, $p = 0{,}048$ (Fig. 11).

Twelve participants pointed g.Nautilus as the most comfortable system to use with the VR setup, performing the BCI task. One participant preferred the g.Mobilab system.

3.2. Proof of concept in Autism Spectrum Disorder Participants

We took the opportunity to test the overall BCI configuration online in ASD participants. Based on the results shown in the previous section we picked g.Nautilus system to perform these experiments.

We were able to make four online sessions with four ASD subjects. Fig. 12 shows the accuracy of target object detection on calibration phase of BCI. The number of averaged events 1 and 2 was not tested in the calibration phase to prevent excessive elongation of the overall online session time.

The number of averaged events to use in the online phase of BCI was chosen from the results of each calibration phase: we selected the lowest number of averaged events with the accuracy levels above 87,5% (100% – 12,5%) or the lowest number of averaged events with the best possible accuracy.

Table 2 presents the detection accuracy of attention to the target object on the online phase of BCI using the number of averaged events chosen from each calibration phase. All participants were all well above chance.

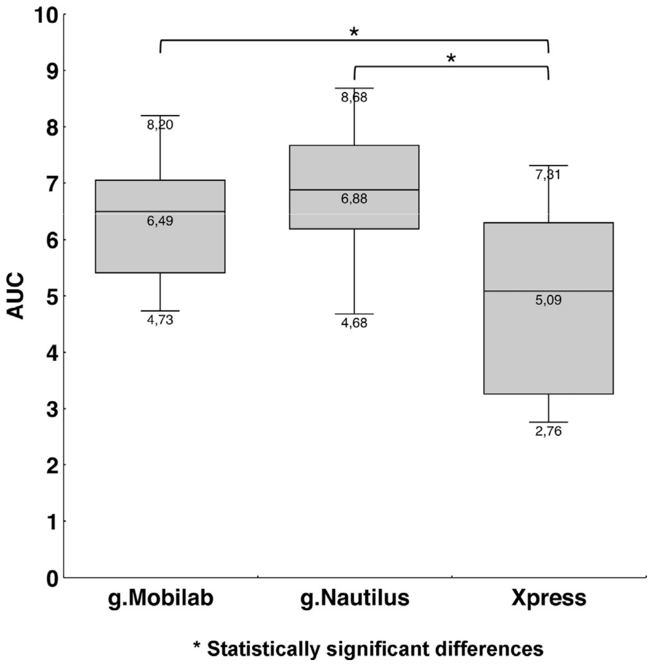

Fig. 11. Boxplot of the AUCs of accuracy levels across event averages, for each system.

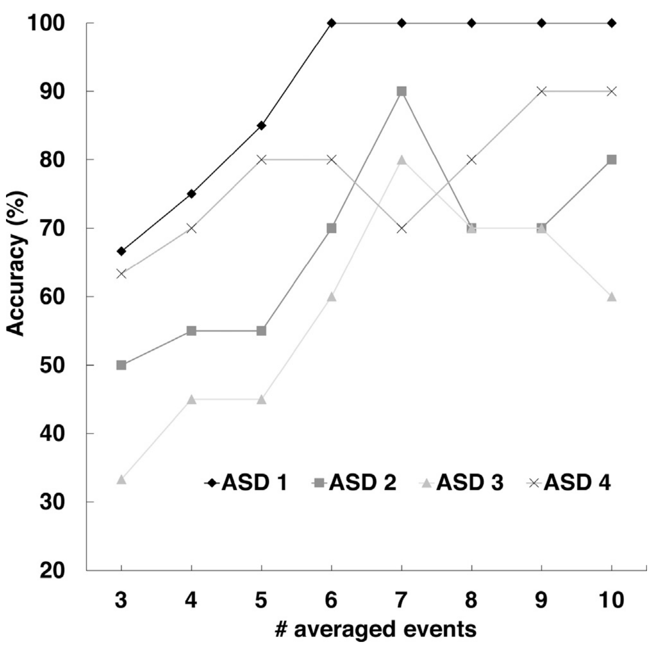

Fig. 12. Accuracies of target object detection across different number of averaged events per block on calibration phase, for each ASD participant. Chance level is 12,5%.

Table 2
Accuracy of detection of attention to the target object on the online phase and the number (#) of averaged epochs for each ASD subject that performed the online BCI sessions.

ASD subject	Target object detection accuracy[1]	# averaged events
ASD1	0,34	6
ASD2	0,72	7
ASD3	0,36	7
ASD4	0,46	9

[1] Chance level: 0.125.

4. Discussion

This study had 2 main goals: 1. To develop a novel BCI with a paradigm that uses social joint attention cues as an indicator of the target event and ascertain the usability of 3 distinct EEG setups to be used combined with a VR headset; 2. Test this setup with an emphasis on comfort and usability with healthy subjects, and to test its feasibility online in ASD participants, for application in a future efficacy testing Phase I/II trial.

Regarding the comparisons tests in healthy participants two systems performed well above chance even at the single trial level. Tests with EEG data from each system revealed an overall better performance with the signal from g.Nautilus and g.Mobilab as compared to the signal derived from Xpress. A possible explanation might be that in the latter case artifacts are more likely during the recordings possibly because of stability of Xpress electrodes pin configuration or because of the wires that connect them to the amplifier. The Xpress‘ electrodes single pin configuration seemed to be less effective in maintaining stable contact with the skin to obtain good signal quality. A slight move of the subject (e.g.: turn the head to look to the target object) makes the wires stretch, move the electrodes and, eventually, even make them occasionally lose contact with the skin. Because Xpress electrodes have only one pin they are prone to leave their position and hardly return to the original one. In contact, despite the fact that g.Mobilab electrodes are also dry electrodes and have wires connected to the transmitter, their 8 pin configuration makes it possible the electrodes to tilt and drag, which makes them less prone to lose contact with the skin.

The mean accuracy of 80% after 4 trials averages with the g.Nautilus system shows the possibility of using this paradigm with this setup in an applied setting to give direct feedback about the attentional focus of the subject. Nonetheless these accuracy values are significant having into acount the scene complexity and the relatively high probability of target occurrence in relation to the usual target probability in someof others P300 based BCI paradigms (Guan et al., 2004; Pires et al., 2011a, 2012; Townsend et al., 2010). One could possibly increase the accuracy rates by reducing the target event probability since the lower the probability of the target event the higher the amplitude of P300 wich, in turn, is one of the most relevant features for P300 detection (Croft et al., 2003; Mars et al., 2008; Polich et al., 1996). One way to do this would be increasing the number of objects flashing in the bedroom. We decided to keep the high probability of the target event by choosing only 8 objects in the room to have a fair tradeoff between the scene realism and the performance of the BCI. This decision was also suported by the already mentioned sensory hypersensitivity of the potential target population of the system. Having a big number of flashes in front of their eyes might disturb the ASD subjects and decrease the adherence to the task. Increasing the number of objects in the scene would also increase the total number of events of the task and thus the total time. It might negatively affect the attention levels of the subject due to the fatigue acumulation during the task.

In terms of the usability of all the experimental setups, globally, the sessions with the g.Nautilus EEG system were shorter than with other systems. During the acquisitions with Xpress and g.Mobilab and by monitoring the online EEG plot we noticed that the electrodes had lost their contact with the scalp sometimes. It was often necessary to correct these faults, pausing the task and adjusting the electrodes positions. This might have contributed to the larger range of session duration times of Xpress and g.Mobilab and contributed to the statistically significant longer sessions of Xpress sessions as compared to the sessions with g.Nautilus.

Concerning recording time g.Nautilus showed to be the easiest EEG system to use together with the remaining BCI apparatus since it was quicker to place its cap than the g.Mobilab cap, and it was quicker to place VR headset over g.Nautilus cap than the other systems' caps. Despite the fact that these differences were only of some seconds, they are still quite important considering the BCI's target population. ASD subjects may have an hyper-reactivity to sensory stimulation so it is important to minimize the direct contact with the participant. These results together with the narrower range of g.Nautilus' signal stabilization time constraints (* Statistically significant differences.

Fig. 8 indicates an overall lower direct contact time with the users of the BCI when the g.Nautilus system is used.

We believe that some technical factors related to EEG systems' configuration might have influenced the usability differences between all systems. The electrode configuration of Xpress and g.Mobilab system complicated the cap placement. Each Xpress electrode have one pin with mushroom heads designed "to ensure a stable contact with the scalp even if the sensors are not completely perpendicular to the surface" (Brain Products, 2014). However, when placing the cap, the pins often caused unwarranted pressure on the participants' scalp and sometimes even discomfort. So, we had to carefully raise from the skin each electrode that was causing such discomfort to the participant and only then move the cap to the correct position. Regarding g.Mobilab electrodes the same happened but less frequently because these electrodes have 8 pins instead of a single one. It distributed the forces applied in the scalp which reduced the potentially inflicted discomfort. Besides that, the electrode pins of both systems revealed to be not the best to have the VR headset elastic bands over them. The bands increase the pressure on the electrodes which caused additional discomfort to the participant when placing the Oculus system, which required extra care, and implied an increase of the time needed to place the Oculus Rift headset over the electrodes caps.

The differences between the stabilization times of g.Nautilus and g.Mobilab suggest that the use of the gel optimizes the stabilization of the EEG signal. Additionally, the differences between overall sessions times of g.Nautilus and Xpress support the idea that it is still worth to use gel in these applications, because it reduces the occurrence of the loss of contact between the electrodes and the skin during the EEG acquisitions. We have experienced that this often occurs with the Xpress system. This is reflected in the overall session time with Xpress and in the respective differences to the g.Nautilus. With the gel, we did not have to interrupt the session to reestablish the contact between the electrodes and the skin and this is why the overall session time with g.Nautilus is inferior. At the same time, the gel reduces the skin impedance which justifies the best classification results (best signal-to-noise ratio).

4.1. Online tests in ASD participants

The configuration with g.Nautilus was tested online with ASD subjects and proved to be well accepted by these participants. The task was performed without any problems, and the BCI classifier was able to correctly identify the attention marker well above the chance level in the online sessions, with all the four ASD participants. This means they understood the task and learned to read the joint attention social cue and use the information to correctly direct their attention to the target object. This is noteworthy and proves the potential for a possible BCI based training tool to improve joint attention impairments. Future Phase I/II clinical trials should be done to prove the efficacy of this potential training tool.

5. Conclusions

We have developed a P300 BCI paradigm that introduces joint attention social cues to the participants. We showed that it is possible to introduce this kind of cues in immersive and realistic P300 based paradigms and that those cues can be effectively used. The results of the offline tests indicate significant classification results, even within few trials, and suggest the feasibility of online BCI sessions using this type of joint attention social cues as an indicator of the target object. We could show that it is feasible to use this paradigm online with autistic participants with joint attention impairments. The next step should be to investigate, within the scope of a clinical trial, the possibility of training joint attention skills of ASD subjects based on such social cueing to target events in the BCIs. At the same time, it was possible to test the feasibility of introducing virtual reality in this kind of applications.

Among the compared systems, the g.Nautilus system is the more suited system and was chosen as the final BCI setup for clinical testing. It is less intrusive to the participants and ensures good signal reliability. Among the three EEG systems compared, the criteria suggest that the g.Nautilus is better placed to afford a quicker setup and a better classification performance which in turn are good characteristics of a BCI planned to be used with ASD population. These characteristics might reduce the probability of hypersensitivity responses by the potential target population

This work highlights the importance to test the usability of these 'easy-to-use' EEG systems with new technologies such as VR to increase the cognitive rehabilitation possibilities, in particular the ability to follow social cues, in clinical populations.

In sum, we have shown that joint attention signals (critical in autism, which is a social attention disorder) can be used in a BCI. The introduction of realistic social cues and immersive setups in BCI paradigms is a novelty and this study also showed the feasibility of this new approach in autistic participants. In the future similar setups could be used to train and test efficacy of joint attention skills in ASD population within the context of clinical Phase I/II clinical trials.

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Disclosure

The authors report no conflict of interest

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