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NEUROPLASTIC AND BEHAVIORAL CHANGES FOLLOWING PRISM ADAPTATION

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Introduction

Prismatic or Prism adaptation (PA) is a particular visuomotor procedure that through the deviation of visual field and a motor task influences brain activity (Redding & Wallace, 2006). Initially developed 1998, when Rossetti et al. study showed an improvement of neglected hemispace exploring emineglected stroke patients, the number of studies focused on PA was greatly increased.

The PA effects were investigated in healthy subjects as well as in patients in different tasks targeting different cognitive functions. A large number of applications of PA procedure was developed in the different studies but the majority of the procedures includes a movement task during the wearing of lenses that deviate the visual field of the subjects. Functional magnetic resonance (fMRI) studies have showed, prevalently, a recruitment of cerebellum and parietal cortex during PA procedure. Moreover, recent evidences (Bracco et al., 2017) have shown an increase of motor cortex activity during the task.

The present work presents the results of a series of experiments aimed at identifying new applications of PA.

The work is structured in three chapters.

In the first chapter we will present an overview of PA thought analysing the different techniques, settings, and neuro-correlates of the procedure.

In the second chapter we will be present a brief analysis of the pre-existing literature about PA and postural effects, followed by an experimental work about baropodometric and hand strength changes after PA.

In the third chapter we will present an experimental work about the effects of PA in Phonemic Fluency and discuss the main results with reference to pre-existing literature about PA effects in cognitive function.

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1. Prism Adaptation

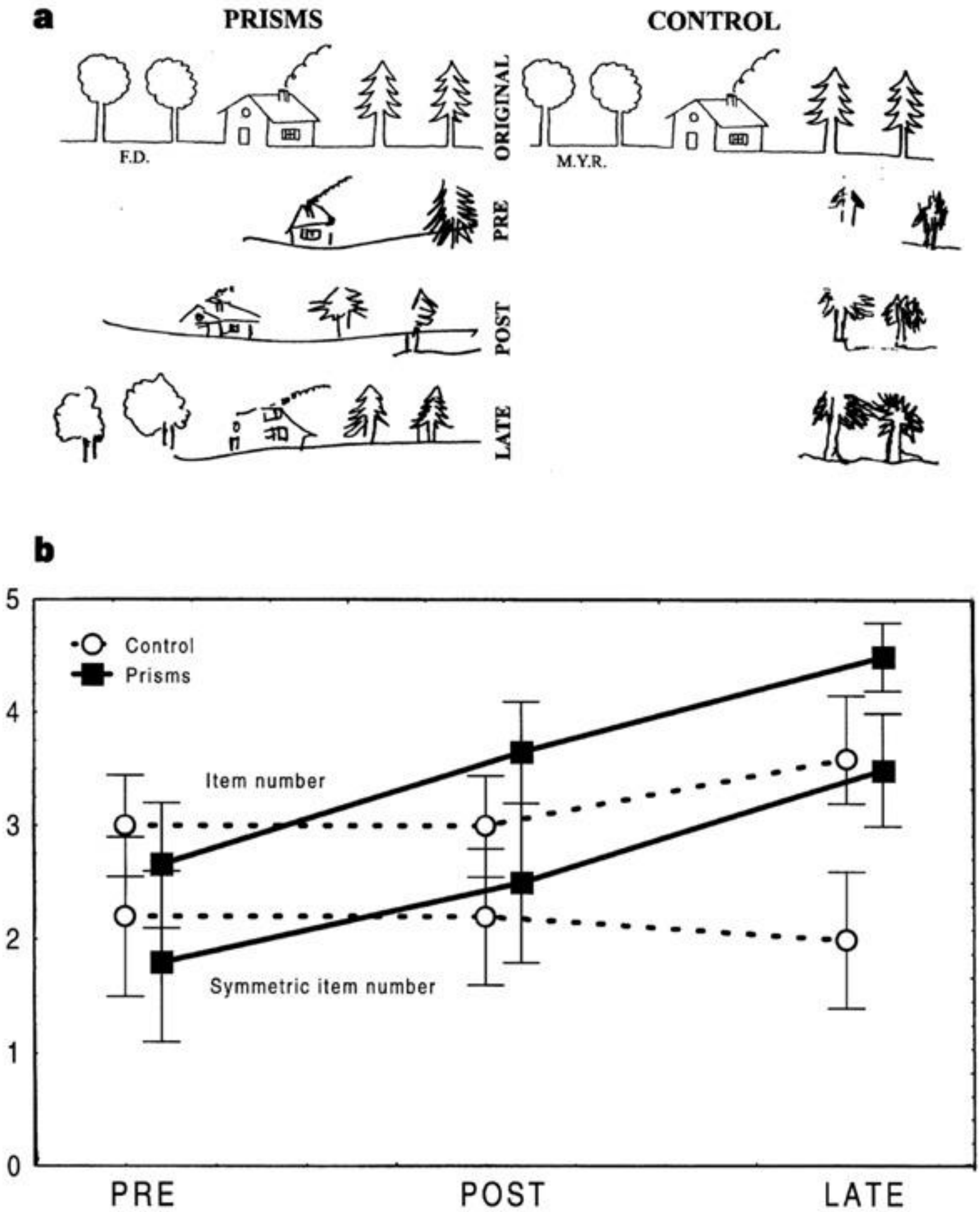
Prism adaptation is a procedure that exploits the capacity to adapt the movement to reach an object, prevalently with pointing, following a modified viewing condition. Through lenses that shift the visual field to the left or right space, the researchers can study how visuomotor adaptation during a target-directed reaching movement task can influence brain activity and consequently cognitive functions.

Prismatic lenses were developed principally in ophthalmology to rehabilitate strabismus and diplopia and can be fitted in plastic structure to make wearable glasses for subject. These lenses are composed by two refractory surfaces of isotropic material (i.e., glass, plastic, etc.), one of which is inclined to perform an angle named refractory angle or apex. This prism lens refracts the light from the thick side (base) and deviate it from the apex. The orienting of prism deviation is referred to the apex direction: if the apex direction is to right the objects and the field of view viewed through this lens are shifted to right. This deviation is often expressed in degree or centimetres (angle of deviation). The refractory power of prism is expressed in dioptres (1 dioptre is an apparently linear deviation of 1 cm over an object at 1m of distance). More dioptres correspond to a bigger deviation of the field of view. The distortion of the view is not perceived by subjects until they try to perform an action; as a result, on first trial of pointing while wearing prismatic lenses, the action may be wrong or hard to complete. This is principally related to a difference between the standard perceived position of the target and the visual field deviation induced by the lenses. In fact, pointing movements performed with glasses cause a movement error that the subjects correct after some trials through a recalibration of the visuomotor system to the new coordinates generated by the visual field deviation. When glasses are removed, in subjects persist an effect of adaptation to the new coordinates despite to the absence of the visual field deviation. This after effect is visible because subjects while pointing or throwing make an error in the direction opposite to that of visual field deviation. This phenomenon is called aftereffect and generally it disappears after few trials if subjects have the possibility to see the trajectory of their movement.

The first study that directly reports the effects to an adaptation of a visual field distortion was driven in 1897 by the psychologist George M. Stratton (Stratton, 1897). Stratton wore a pair of mirrored glasses that inverted the field of view for 7 days. He reported a gradual adaptation of the visuomotor system to the new condition in daily activities. At the end of the 7 days, he reported a total adjustment to the new condition, followed by spatial aftereffects.

During the 20s century, other studies investigated the effects of visual field deviation in visuomotor functions (e.g., (Beebe, 1933; Ewert, 1930; Himel, 1988; Tuan & Jones, 1997). A great boost to interest in this research field, in particular in prism lenses use, was driven by a study of Rossetti et al. in 1998 (Rossetti et al., 1998). In this study the authors investigated how rightward prism deviation of the visual field can improve the rehabilitation of neglect in right hemispheric brain damaged patients. A sample of 12 patients was randomly assigned to a prism group or to a control group. All patients performed a pointing task wearing glasses: in the prism group, subjects wore 10-degree rightward lenses; in the control group, subjects wore flat lenses. The prism group showed a big improvement on neuropsychological tests compared to control group, in particular in the exploration of the left hemispace (fig 1).

Fig 1



a- sample of Gainotti copying test result in pre post and late exposure after prismatic adaption. b- Mean number of item and symmetrically item dawn by subjects. (Rossetti et al., 1998)

Following this evidence reported by Rossetti et al., a large number of studies started to deeply investigate how prismatic adaptation works and the different fields of application of the procedure even outside the domain of spatial neglect in stroke patients.

1.1 Overview of Prism adaptation study

A brief research query as "prism adaptation" or "prismatic adaptation" in the mostly important scientific search engines or databases produces over 130 results related to neurosciences field only on the last ten years[1]. The large interest of this research topic is strictly related to the easiness and large applicability of Prism adaptation procedure (PA). PA effect was investigated in rehabilitation of different post stroke symptoms as hemispatial neglect (Facchin et al., 2019; Farnè et al., 2002; Fortis et al., 2010; Frassinetti et al., 2002; Luauté et al., 2006; Ronga, Franza, et al., 2017; Rossetti et al., 1998) dysgraphia (Rode, Pisella, et al., 2006) and imbalance (T. C. W. Nijboer et al., 2014; Tilikete et al., 2001). Moreover, PA application was investigated in healthy subjects to generate pseudo-neglect effects (Colent et al., 2000; Jackson & Newport, 2001), to improve cognitive and motor performance (Martin et al., 2001; Schintu et al., 2018; Striemer & Borza, 2017; Tottenham & Saucier, 2004). Finally, a lot of researches with healthy subjects and patients focused to analyse and investigate how PA procedure works.

One of the most influential works about the mechanisms that underlie prism adaptation is a review of Redding and Wallace of 2006 (Redding & Wallace, 2006). PA is quite exclusively linked to calibration and recalibration of workspace and environmental coordinates. The calibration of movement to reach an object is the result of a large number of exogenous and endogenous information regarding the task to be performed. For example, in order to reach an object placed in front of subjects, they must perform a rapid analysis about distance, shape,

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[1] Pubmed and Scopus search: "prism adaptation" or "prismatic adaptation" Filters: Abstract, Full text, Journal Article, From 1998 to 3000/12/12, Humans, English, Adult: 19+ years- 25/02/2020

obstacle, and information on “how to perform the task” that come from previous similar experiences. The recalibration is related to a new calibration process from the same task with new information. When the new upcoming information is strictly exogenous, the recalibration is rapid; when the exogenous information interferes with endogenous information, learned movement and task schemes, the recalibration process is slower and more linked to a trial-and-error learning paradigm. Another mechanism underlying PA is the alignment process which transforms spatially coded position from one coordinate system into another. For example, this process adjusts the different spatial information between sensory and motor systems, like limb position and visual information. Moreover, spatial alignment is slower than calibration. Recalibration can be accomplished in the early few trials during a PA exposure task, quite bit more trials to be accomplished.

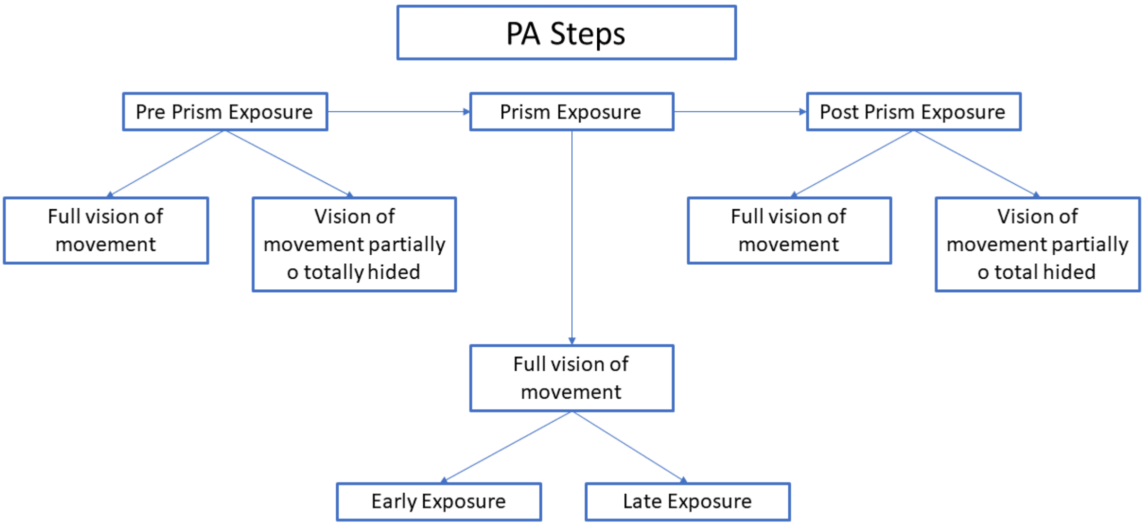
To perform PA, these two processes are involved through movement task directed to an object. The most common task is pointing to a target in which subjects are placed in a front different type of settings apparatus to perform the adaptation. Regards settings, most common is to place one or more targets in front of subjects who have to point with a hand to these targets.

There are different phases during PA: Pre-Prism Exposure, Prism Exposure and Post-Prism Exposure. Pre- and Post-prism exposure are the phases when data are collected, and often these phases can be divided in a full vision (closed-loop) of movement during task and partially or total hided vision (open-loop) of movement during task. The full vision of movement during task data collection and measurement is performed to take baseline data and as practice of the task. The task performed with vision of movement partially or totally hided (Bultitude et al., 2017) is specifically performed to take baseline to analyse the effects of recalibration after prism exposure (often called “PA after effects” or only “after effects”).

The task used in these two steps may differ from the prism exposure phase or may be the same, for example in Rossetti 1998’s study, to measure the PA adaptation after effects were performed a straight-ahead pointing task Pre- and Post-Prism Exposure, despite to a target directed pointing task performed during the exposure phase. In other study the experimental task was maintained the same during all the procedure (Frassinetti et al., 2009; Magnani et al., 2012). This difference in PA protocol in studies are principally related to different aims, but in last years, when PA is used as rehabilitation intervention, the dominant protocols are pointing tasks with a target to reach (Hugues et al., 2021; Magnani et al., 2021; Matsuo et al., 2020).

Regarding the Prism exposure phase, it can be defined as the steps when subjects are exposed to the deviation of the visual field. This step can be furthermore divided in early and late exposure. In the early exposure phase, subjects make errors related to the new coordinates generated by the distortion of the visual field. The late exposure phase is characterised by an absence of pointing errors during the last trial of the task with the visual field distortion. The exposure phase is divided in these two phases to analyse if and how subjects recalibrate their visuomotor system to the visual field distortion. (Fig 2).

Fig 2



Generally used PA procedure in large part of studies

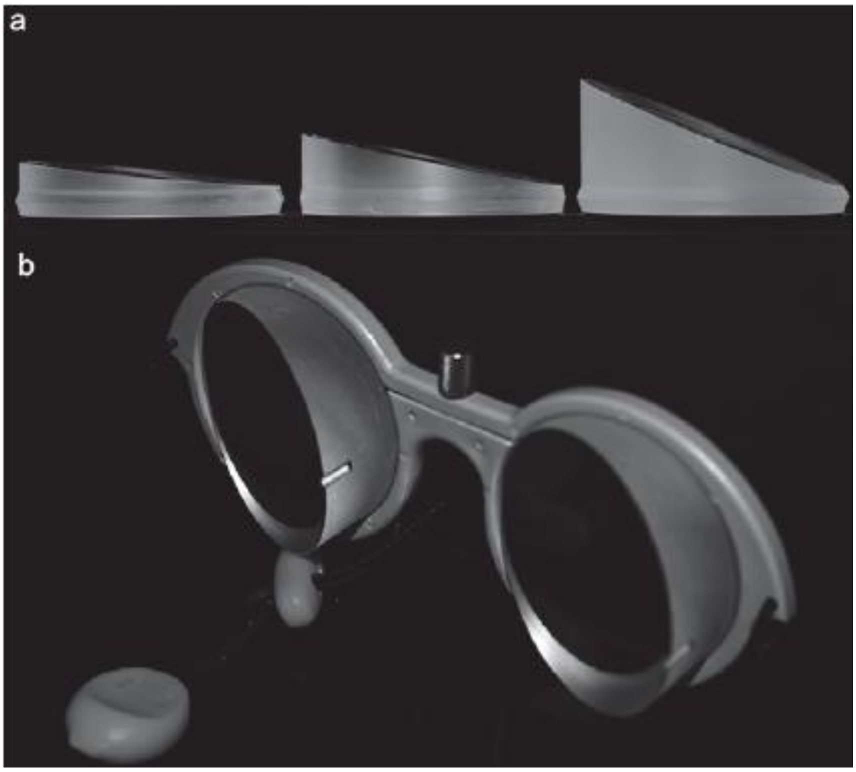
1.2 Lenses, tasks settings and targets

Despite the large number of studies regarding PA protocol and rehabilitation, lenses, task settings and targets used in different protocols can be grouped in different category.

1.2.1 Lenses

Regarding the lenses used in large part of studies we can find wedge prism and Fresnel lenses. Wedge prisms are the most widely used (e.g., (Berberovic et al., 2004; Michel et al., 2007; Panico, Sagliano, Nozzolillo, et al., 2018; Rode, Klos, et al., 2006; Shimizu et al., 2020), even if the shape is not always described in the studies. This type of lenses is commonly applied in glasses frame to easy suit on the participant head (e.g., Facchin et al., 2013; Hugues et al., 2021) (Fig. 3).

Fig. 3



a- wedge prism of 5, 10 and 20 dioptres. b- lenses in glasses frame. (Facchin et al., 2013)

Fresnel lenses are more economical and easier to set up and can be described as a thin laminar piece of refractory material applied over glasses (Fernández-Ruiz & Díaz, 1999; Mizuno et al., 2011). The particular sawtooth microprism structure deviate the vision, but over 5 dioptres vertical stripes become visible (Prablanc et al., 2019).

Prism adaptation is performed with the deviation of visual field perceived thought the direction of the apex side of prism lenses, the rightward or leftward deviation and PA effects increase with increase of lenses dioptres (Facchin et al., 2013; Striemerthe et al., 2016).

1.2.2 Tasks

As said before, the large part of studies reported the use of pointing task to perform and measure PA, but there are different and interesting procedures implemented in the different studies.

1.2.2.1 Pointing task

Speaking about the pointing task in PA, it can be performed in different ways. To describe the task briefly, the subjects, human or primates, perform a movement with a finger directly to a target. In the majority of cases, it is possible to define this task as a closed loop task (when there is a visual information available for the subject) but it can also be performed as an open loop task (in this case no visual information available) (Bracco et al., 2017, 2018; Magnani, Caltagirone, et al., 2014). Moreover, the pointing task can be performed as a simply straight-ahead pointing task: in this case, subjects must perform a movement pointing in front of their subjectively perceived midsagittal plane (Guinet & Michel, 2013; Hatada et al., 2006; Herlihey et al., 2012; Ronga, Sarasso, et al., 2017).

1.2.2.2 Others tasks

Throwing a ball directly to a target to perform PA had a quite large interest in literature (Blau et al., 2009; Fernandez-Ruiz et al., 2003; Fleury et al., 2021; Moreno-Briseño et al., 2010). In one study of Martin et al. (Martin et al., 2002), 8 participants throwed a ball to a target pre-, during and post-prism exposure. Prism adaptation was made by a leftward (“base right”) Fresnel lens deviation.

Regarding walking during PA, few studies investigated this movement task. In this case the participants must walk in a specific direction pre-, post- and after prism exposure (Alexander et al., 2013; Morton & Bastian, 2004; Nemanich & Earhart, 2015). Finally, few studies have performed PA trough an eye movement task (T. Nijboer et al., 2010; Ronga, Franza, et al., 2017; Ronga, Sarasso, et al., 2017), line bisection task (Fortis et al., 2011; Herlihey et al., 2012) or daily life activities (Fortis et al., 2013).

1.2.3 Settings and targets

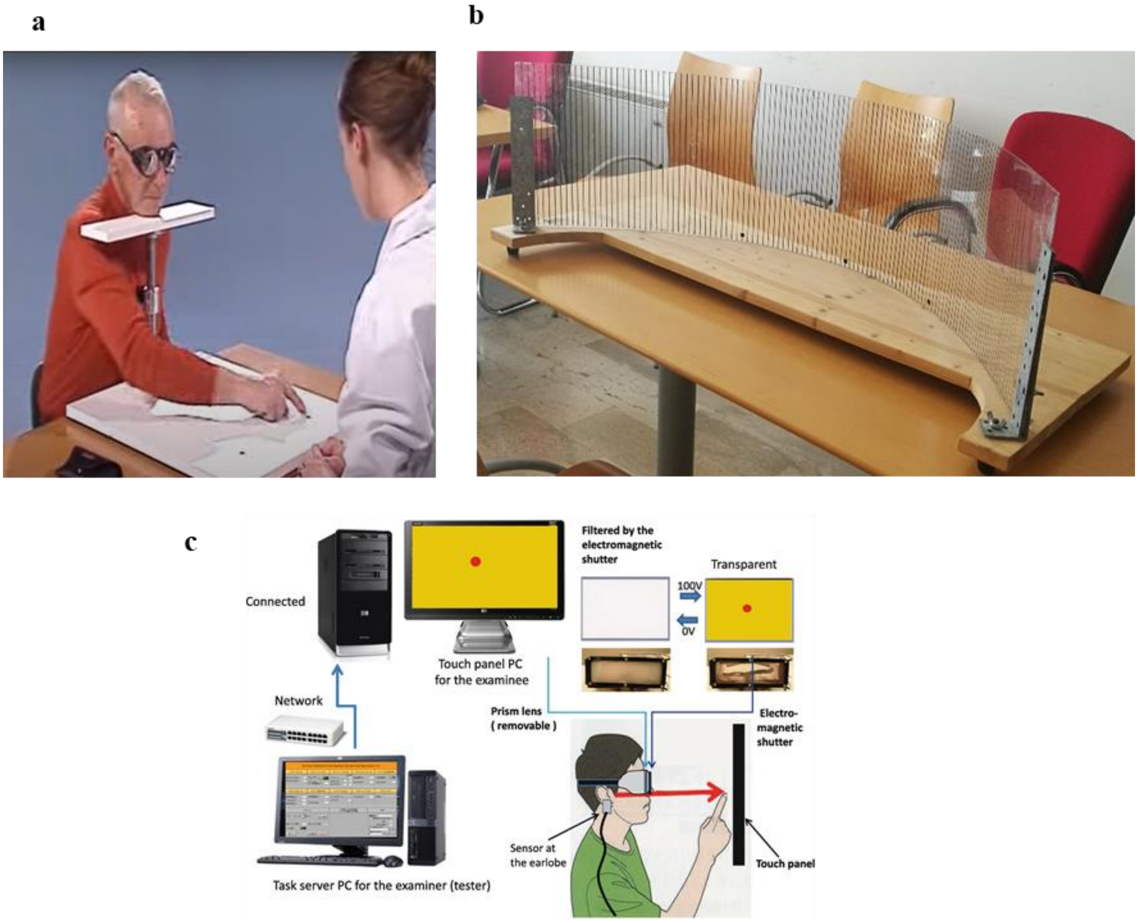
Setting and target in PA are the most intriguing and challenging topics to discuss. In fact, different group of researchers developed different setting and targets to perform the PA.

One of the most used set ups is the “desk set up”. This setup, prevalently, requires that the participants are seated in front of one side of a table or desk, while the experimenter sits on the other side. The targets are prevalently two points drawn on desk or on surface cover (i.e., paper), one on left and one on right of the participant’s midsagittal plane (Bornschlegl et al., 2012; Jackson & Newport, 2001; Michel et al., 2019; Rossetti et al., 1998, 2004; Schintu et al., 2014, 2018).

Another large used setting is the “box”, with different variant. This setting is often made by wooden or plastic box opened in participant side; in the other side, the experimenter shows a target, like a pen or a laser dot, that subject must reach with pointing task. In literature there are different variance of this set up, in example with curved surface that following visual angle, with automated target appearing or with electro sensitivity surface used to register pointing position (Angeli et al., 2004; Bracco et al., 2017, 2018; Gaveau et al., 2018; Magnani, Caltagirone, et al., 2014; Magnani et al., 2010, 2013a, 2013b; Redding & Wallace, 2001, 2008; Yoon et al., 2014).

Last big category of set up for PA adaptation is related to the use of computer touchscreen to perform the pointing task direct to showed targets (Gilligan et al., 2019; Kintzel et al., 2015; Panico, Sagliano, Grossi, et al., 2018; Striemer et al., 2016; Vocat et al., 2011). (Fig 4).

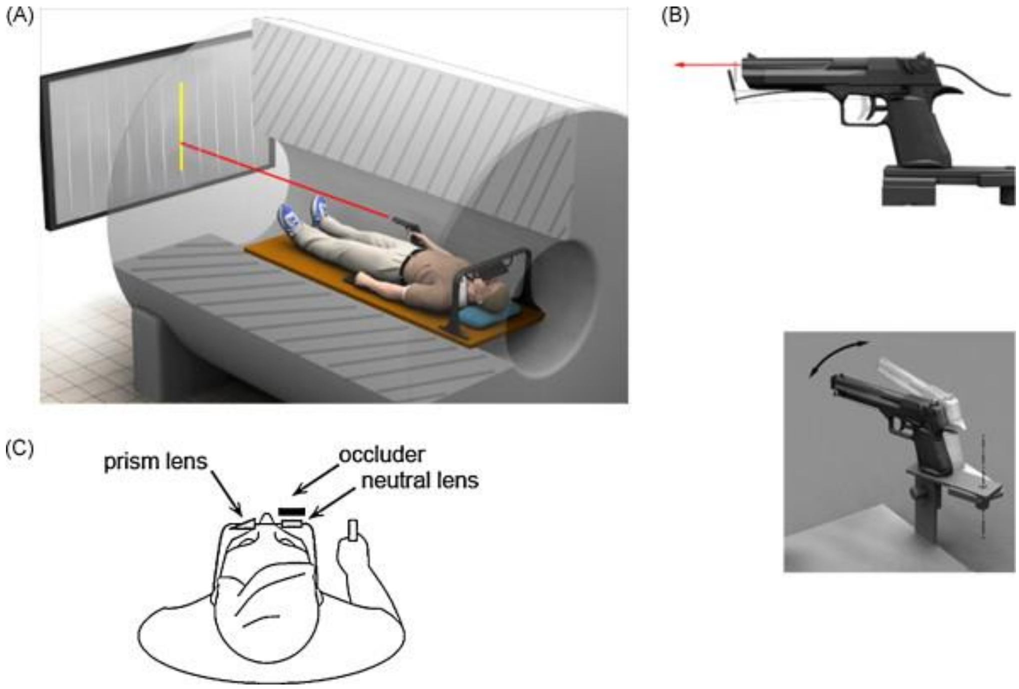
Fig 4



PA procedure settings: a-Desk set up; b- Bracco et al. (Bracco et al., 2017) **box set up; c-example of touch screen set up** (Mizusawa, 2021)

One last interesting original set up is the fMRI set up of Chapman et al. (Chapman et al., 2010). The researchers developed this set using a monitor posed in front of the scan bed that was still visible to participants through a mirror system that allowed the vision in lying position. To perform the PA was used a singular leftward deviating lens that could be moved in one or the other eye. The task was performed using a laser pointer applied over a toy pistol that could be moved horizontally. This special set up allowed to take the fMRI scan with the head immobility of the participants.

Fig 5



Original fMRI set up for investigate brain activity of PA during scan. (Chapman et al., 2010)

1.2.4 Special Virtual Reality (VR) PA

A new interesting way to perform PA is through virtual reality devices. These interesting technologies can easily simplify the set up and the use of the PA in rehabilitation. There is not much literature on this topic but all the existing studies have confirmed the efficacy of the PA through virtual reality environments and devices (Adams et al., 2018; Cho et al., 2020; Gammeri et al., 2020; Wilf et al., 2021). A study of Romos et al. (Ramos et al., 2019) showed a greater after effects in virtual reality PA as compared with classical procedures. 20 healthy participants underwent to a classical PA with a pointing task and a virtual reality version of it. To simulate the deviation the authors skewed and rotated the camera, the participants performed the pointing task using a virtual reality controller. Their results showed a larger after effects in post exposure phase in virtual reality condition than in classic PA condition, furthermore larger effects were shown in the rotated camera deviation condition.

1.3 Neural bases

PA as a visuomotor task is directly related to the associated brain area networks related to the visuomotor functions. Starting from the Rossetti's study, the results showed in right brain neglect patients a possible correlation with parietal cortex and PA.

A neuroimaging study of Luautè et al. (Luauté et al., 2009) revealed a complex pattern of brain activation during PA. A sample of 14 healthy right-handed participants (mean age = 23 years) performed PA during fMRI scan and wearing a 10° leftward lens during exposure phase only in one eye (7 participants wearing lenses on right eye and 4 on left eye). An activation of the superior temporal gyrus and sulcus, right superior parietal lobule, left and right inferior parietal sulcus, left parietal lobule, left anterior intraparietal sulcus, left parieto-occipital sulcus and cerebellum was shown during prism exposure. Moreover, to investigate a de-adaptation phase, the authors analysed the brain activity in pre-exposure vs post-exposure phases and the activity during the early exposure in contrast with the late exposure, showing and increase of activity in inferior parietal lobule and left anterior intraparietal sulcus. To summarise, these results showed a direct involvement of posterior parietal cortex in visuospatial error detection as recalibration, an involvement of the cerebellum in spatial mapping, movement coordination and spatial realignment, and of the superior temporal sulcus in spatial cognition changes as PA aftereffects.

One interesting study that investigated the relation between cerebellum and PA was that of Pisella et al. (Pisella et al., 2005). The authors investigated how a patient with left cerebellar lesion and left superior ataxia adapts to PA. The patient underwent PA under 4 different conditions: rightward PA using the right hand, rightward PA using the left hand, leftward PA using the right hand, leftward PA using the left hand. The results showed an absence of adaptation to leftward PA as compared with rightward PA with both hands. This evidence shoved a lateralized involvement of cerebellum to PA deviation side. To deeply investigate this evidence, a more recent study of Panico et al. (Panico et al., 2016) showed how the cerebellum is involved in PA. The authors applied a PA to a sample of 26 healthy participants with 11 degrees of rightward lenses deviation. During PA, cathodal cerebellar transcranial direct current stimulation (tDCS) was applied over the right cerebellum in real and sham stimulation conditions. The participants that received a real stimulation showed a worst accuracy and a slower readaptation, providing more recent evidence of the role of the cerebellum in PA.

1.3.1 Motor cortex activation

Motor cortex is directly involved in PA adaptation procedure.

An interesting result is the activation of the motor cortex ipsilateral to the deviation of the visual field. The study of Magnani et al. (Magnani, Caltagirone, et al., 2014) was the first that directly investigated how prismatic adaptation exerts direct effects on motor cortex excitability. They recruited 14 right-handed healthy subjects that performed PA. Seven subjects underwent to a leftward deviation and 7 to rightward deviation. Cortical activity was investigated through a short intracortical inhibition and short intracortical facilitation transcranial magnetic stimulation (TMS) protocol, recording motor evoked potentials through surface electrodes placed over the first dorsal interosseus muscle.

The authors reported an increase of motor cortex activity in both hemispheres for both deviation sides. Left prism deviation specifically increased left motor intracortical facilitation while right prism deviation specifically increased right motor intracortical facilitation, as tested with paired TMS using 10 ms interstimulus intervals.

Another interesting study about motor cortex activation trough PA was conducted by Bracco et al. (Bracco et al., 2017). The aim of this work was to examine the effects of a combination of techniques that increase the activity of motor cortex. They combined an anodal (tDCS) on M1 with a rightward PA adaptation; the excitability was measured trough the motor evoked potential recorded following TMS of M1. The recruited sample consisted of 34 healthy subjects: 16 received rightward PA and M1 anodal tDCS, 9 participants underwent only rightward PA, 9 subjects underwent only under right M1 anodal tDCS. The authors found an increase of cortical excitability in M1 in the PA only and in the tDCS only group. Interestingly, they found a decrease of cortical excitability when the two techniques were combined.

These results show that PA exerts similar effects on motor cortical excitability as anodal tDCA and that the combination of the two methods activates homeoplastic plasticity effects.

2. Balance, posture and PA

The recalibration during PA can be associated to a change in visuospatial environment mapping and body position representation and this evidence can explain how PA influences the posture and gait in participants (Michel et al., 2003; Tilikete et al., 2001). Michel et. al. (Michel et al., 2003) investigated the effects of PA on body posture in healthy subjects. 14 right-handed healthy participants underwent to PA with rightward or leftward deviation in the exposure phase. Participants showed rightward bias in postural control with closed eyes after leftward deviation. As the authors discuss this may be related to readaptation on internal body scheme perception. Moreover, PA induced an activation of the motor cortex ipsilateral to visual field deviation, but this activation wasn't directly converted as an increase of muscular strength or muscular activity.

In the following paragraph we will present an experimental work that investigated PA effects in plantar pressure and handgrip strength in a group of healthy participants. The work will provide further evidence that PA directly influences the internal body schema perception and representation and a new finding in decrease of muscular strength in the opposite side of lenses deviation.

2.1 Investigating prismatic adaptation effects in handgrip strength and in plantar pressure in healthy (Bonaventura et al., 2020)

Introduction

In the last decades, prismatic adaptation (PA) effects have been widely investigated either in visuomotor processes (Clarke & Crottaz-Herbette, 2016; Danckert et al., 2008) and higher-level cognitive domains (Magnani et al., 2013b). PA induces a lateral displacement of the visual field, enhancing cortical activity in the hemisphere ipsilateral to the lenses deviation side (Magnani, Caltagirone, et al., 2014), an activation involving both posterior brain regions of the dorsal stream (i.e. occipito-parietal cortex) and anterior regions, mainly in the frontal cortex.

This pattern of neuromodulation explains why PA has also been used to study the physiological mechanisms of postural control, in both neurological patients (Padula et al., 2009; Tilikete et al., 2001) and healthy subjects (Michel et al., 2003). An aspect of body posture particularly suitable to be studied with PA is the weight distribution among feet, that allows a symmetrical distribution of plantar pressure (Vianna & Greve, 2006) in terms of reaction force to the ground (Orlin & McPoil, 2000). Plantar pressure is controlled by both subcortical (Kolb et al., 2001; Massion, 1992) and higher-level brain mechanisms, such as the elaboration of an internal model of the body (Gurfinkel & Levick, 1991) and attention processes (Woollacott & Shumway-Cook, 2002).

PA could also be useful to study and modulate processes associated to regulation of muscle strength. Remarkably, hand strength relies on sensorimotor processes that regulate corrections and adjustments depending on the executed force task (Ehrsson et al., 2017; Filimon, 2010). Attentional resources, directionally shifted by PA, are also involved in regulating feet and hand movements. Indeed, a reduction of muscle force has been found when attention is shared between hand and leg (Takebayashi et al., 2009).

Relevant differences occur between the parameters of hand strength and plantar pressure distribution in terms of hemispheric asymmetries and activated regions in each hemisphere. Indeed, stronger involvement of anterior regions (i.e., motor cortex) is required to control hand strength (Siemionow et al., 2000). On the other hand, posterior brain regions (i.e., parietal cortex) might be more involved in regulating pressure distribution among feet, allowing the access to an internal model of the body and the control of its position in the space (Slobounov et al., 2005). Another point concerns hemispheric asymmetries in postural control and muscle strength. Previous studies have shown a right hemisphere pivotal role on balance control and body posture in stroke patients (Fernandes et al., 2018; Ishii et al., 2010) as well as in healthy subjects (Cioncoloni et al., 2016; Zhavoronkova et al., 2012). Conversely, motor control of each hand symmetrically depends on the activation of the contralateral brain hemisphere (Ferbert et al., 1992).

In this line, previously reported rightward-PA effects (i.e., right hemisphere activation) on body posture have been explained in terms of modulation of higher level cognitive processes (Shiraishi et al., 2008), subserved by posterior regions of the right dorsal stream (Magnani et al., 2013b). For instance, in a previous study, rightward-PA has been shown to rebalance the abnormal body weight distribution and therefore, the posture bias of patients after cerebrovascular accident (Padula et al., 2009). The authors suggested that the rebalance in body weight distribution occurred through a PA-induced modulation of higher order processes of spatial orientation related to parietal lobe (Padula et al., 2009).

A previous study investigating changes in body sway in two groups of healthy subjects reported a forward displacement of the center of pressure (CoP) after both leftward and rightward PA (Michel et al., 2003). Authors suggested that the observed changes in CoP reflected a displacement in the projection of body pressure, reflecting a change in body scheme. Unluckily, whether these effects extended directly to weight distribution among feet was not investigated. Additionally, asymmetries between plantar pressure and hands were not explored. Overall, to date, no studies have investigated whether PA might affect hand strength through modulation of anterior regions of the dorsal stream (Bracco et al., 2017; Rogers et al., 2009).

Indirect evidence might be found in neurophysiological and electrophysiological studies showing that PA modulates oscillatory activity over motor cortex (M1) as well as motor evoked potentials' amplitude (Bracco et al., 2017; Magnani, Caltagirone, et al., 2014).

The present study aimed at exploring interhemispheric asymmetries in the PA effects on hand strength and plantar pressure distribution. To this end, we evaluated hand strength and baropodometric functions immediately before and after leftward vs. rightward PA in two groups of healthy subjects. Since PA affects either sensorimotor and higher-level attentive processes modulating the dorsal stream activity (Clower et al., 1996; Tsujimoto et al., 2019), wearing prisms could affect both hand and feet functions. Specifically, since body posture depends more on posterior dorsal stream regions of the right hemisphere (Cioncoloni et al., 2016; Parkinson et al., 2010; Zhavoronkova et al., 2012) while hands strength is controlled by left and right motor cortices (Fan et al., 2017), we expected 1) changes in body posture occurring only after rightward PA; 2) changes in hand strength following either leftward and rightward PA.

Material and methods

Participants

Forty-six (male= 23; mean age= 25±3 years) right-handed healthy participants were randomly assigned to a leftward Prismatic Adaptation group (l-PA; n=23; mean age= 26±3.92 years) or a rightward Prismatic Adaptation group (r-PA; n=23; mean age= 25±1.87 years). The l-PA group wore a 20° left shifting prismatic lenses and the r-PA group wore a 20° right shifting prismatic lenses. Participants handedness was assessed using the Edinburgh Handedness Inventory (Oldfield, 1971).

Exclusion criteria were prior diagnosis of psychiatric disease, brain injury, acute orthopaedic injury, pregnancy, depression, not corrected vision impairment or other neurologic diseases. Four subjects were excluded from the experiment: one subject due to pregnancy and three subjects due to knees’ injuries. The study was in compliance with the Helsinki declaration. Participants were informed about the experimental procedures and provided their written informed consent to voluntarily participate in the experiment. Experimenter and participants were both naïve to the experimental hypothesis tested. Table 1 shows participants demographic characteristics.

Table 1.

	l-PA group (n=23)	r-PA group (n=23)
Age (years)	25±1.87	26±3.92
Years of education	17±1.27	17±1.85
Handedness	62%±0.23	66%±0.2
Weight (kg)	63.52±13.36	62.05±11.41
Height (cm)	167.65±10.55	170±9.85

Sample Demographic characteristics. Legend: l-PA = leftward prismatic adaptation group. r-PA = rightward prismatic adaptation group

Experimental design

Baropodometric and handgrip measurements were collected twice: the first time before PA (Pre-PA) and the second after PA (Post-PA). The delay between the first and the second measurement was ~15 min, that is in the frame time of the PA effects (McIntosh et al., 2019; Schintu et al., 2014).

Postural assessment

Baropodometric evaluation was conducted using the freeMed®posturographic system (Sensor Medica®; Guidonia Montecelio, Roma, Italia), consisting of the freeMed®Maxi platform and the freeStep®software. Signal was digitalized at a sampling frequency of 50 Hz. The baropodometric test, lasting 5 sec, was performed in a sound-isolated room. Each participant was required to stand barefoot in orthostatic stance on the platform with the head in neutral position, gazing forward, arms along the trunk and feet placed side-by-side with both heels in line. The following parameters were considered: rearfoot/forefoot and total plantar pressure (%); rearfoot/forefoot and total surface area (cm2).

Handgrip test

Each participant performed 3 trials of 3 sec of maximal isometric handgrip on a mechanical dynamometer (KernMap model 80K1 - Kern®, Kern & Sohn GmbH, Balingen, Germany), alternatively with the dominant and the non-dominant hand, with 3 min rest between each trial. The subjects performed the handgrip test while seating in a chair, back at 90º angle with sacrum, shoulder blades immobilized to the backrest, head in neutral position, gazing forward, and elbow joint positioned at a 90º angle, as recommended by the American Society of Hand Therapists (Spijkerman et al., 1991). The best performance out of the 3 trials (kg) was included in the statistical analyses.

PA procedure

We followed the same PA procedure as in previous studies (Bracco et al., 2017; Magnani, Caltagirone, et al., 2014). Subject sat in basic position (right index finger at the sternum) in front of the concave side of a curved Plexiglas panel at a distance of 57-cm. The panel was graded with vertical lines corresponding to the degrees of the visual angle (covering a total visual angle of 120°). Three vertical lines of the panel were marked to indicate central position (0°), left position (21° to the left), right position (21° to the right). During PA, the experimenter, facing the opposite side of the panel, randomly pointed in one of the three marked positions of the panel.

The task required to point with the right index finger the panel point indicated by the experimenter and then return to the basic position. Pointing accuracy was collected in five experimental conditions: pre-exposure, blind pre-exposure, early exposure (first 9 trials while wearing prisms), late exposure (last 9 trials while wearing prisms), blind post-exposure (after prisms removal). In the blind exposure conditions the pointing task was performed with hidden arm. Prismatic lenses were worn only during the exposure condition.

Exposure condition included 90 trials, while the other conditions included 30 trials. All the trials were equally and randomly distributed in the three marked positions of the panel.

Data analysis

Analyses were conducted on the mean accuracy of the 5 experimental conditions: pre-exposure, blind pre-exposure, early exposure, late exposure, blind post-exposure. Prismatic adaptation was analysed using a 5×2 repeated measures ANOVA, with Condition (all 5 experimental conditions) as within-subjects factor and Group (l-PA vs. r-PA) as between-subjects factor.

Handgrip

Handgrip performances were analysed using a 2×2×2 repeated measures ANOVA with Time (pre-PA vs. post-PA) and Hand (left vs. right) as within-subjects factors and Group (l-PA vs. r-PA) as between-subjects factor.

Plantar Surface Area

Total plantar surface data were analysed using a 2×2×2 repeated measures ANOVA with Time (pre-PA vs. post-PA) and Feet (left vs. right) as within-subjects factors and Group (l-PA vs. r-PA) as between-subjects factor.

Forefoot/rearfoot plantar surface data were analysed using a 2×2×2×2 repeated measures ANOVA with Feet (left vs. right), Time (pre-PA vs. post-PA) and Area (forefoot vs. rearfoot) as within-subjects factors and Group (l-PA vs. r-PA) as between-subjects factor.

Plantar Pressure

Total plantar pressure data were analysed using a 2×2 ANOVA, with Time (pre-PA vs. post-PA) as within-subjects factor and Group (l-PA vs. r-PA) as between-subjects factor. Since changes in pressure distribution in one foot are accompanied by proportional changes in the other one (i.e., the two variables negatively correlate), analyses have been conducted only on pressure distribution in the right foot. Namely, whether pressure on the left foot increases, it proportionally decreases on the right foot. Similarly, forefoot plantar data were analysed using a 2×2×2 ANOVA with Time (pre-PA vs. post-PA) and Feet (left vs. right) as within-subjects and Group (l-PA vs. r-PA) as between-subjects factors. As for total pressure distribution among feet, whether pressure on the forefoot increases, pressure distribution in the rearfoot proportionally decreases, therefore analyses were conducted only in the forefoot data.

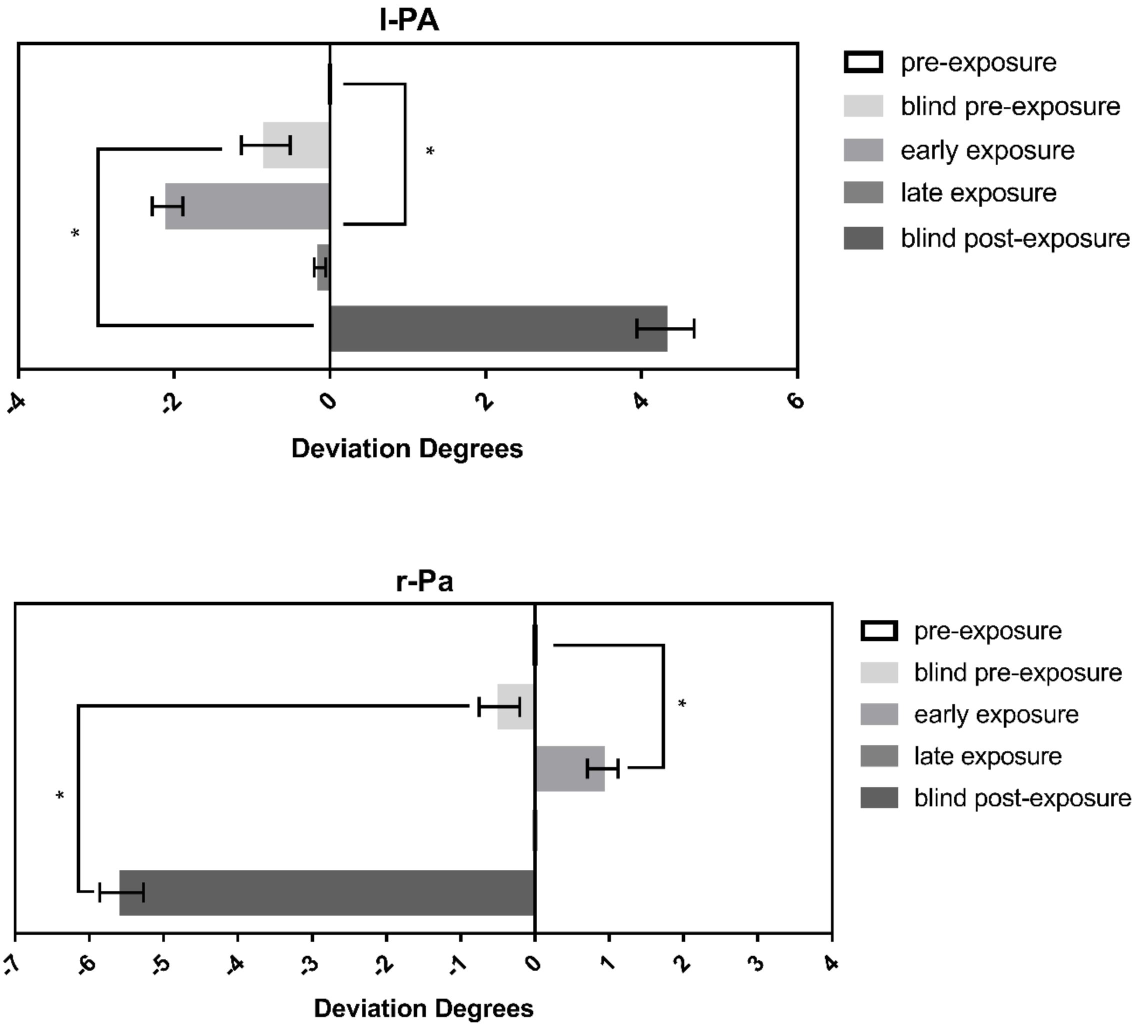
Bonferroni post-hoc tests were used to test main effects and interactions when appropriate. All the analyses were conducted using IBM SPSS Statistics software 23 (International Business Machines Corporation, Armonk, New York, United States).

Results

Prismatic adaptation

Figure 1 shows prismatic adaptation for l-PA and r-PA group across the five experimental conditions. ANOVA showed significant effects of the factors Group [F(1,44)= 46.776; p<.001; ηp2=.325] and Condition [F(4,41)= 5.108; p=.029; ηp2=.104] and a significant Group×Condition interaction [F(4,41)= 662.583; p<.001; ηp2=.938]. Lenses deviation was reflected by the difference between pre-exposure and early exposure trials, either in the l-PA (p<.001) and in the r-PA (p<.001) groups. Conversely, due to subjects' adaptation to prismatic deviation, no differences were found between pre-exposure and late exposure neither in the l-PA (p=.085) nor in the r-PA (p=1) group. The presence of after effect was confirmed by a significant difference between blind pre-exposure and blind post-exposure either in the l-PA (p<.001) and in the r-PA (p<.001) group (Figure 1).

Figure 1



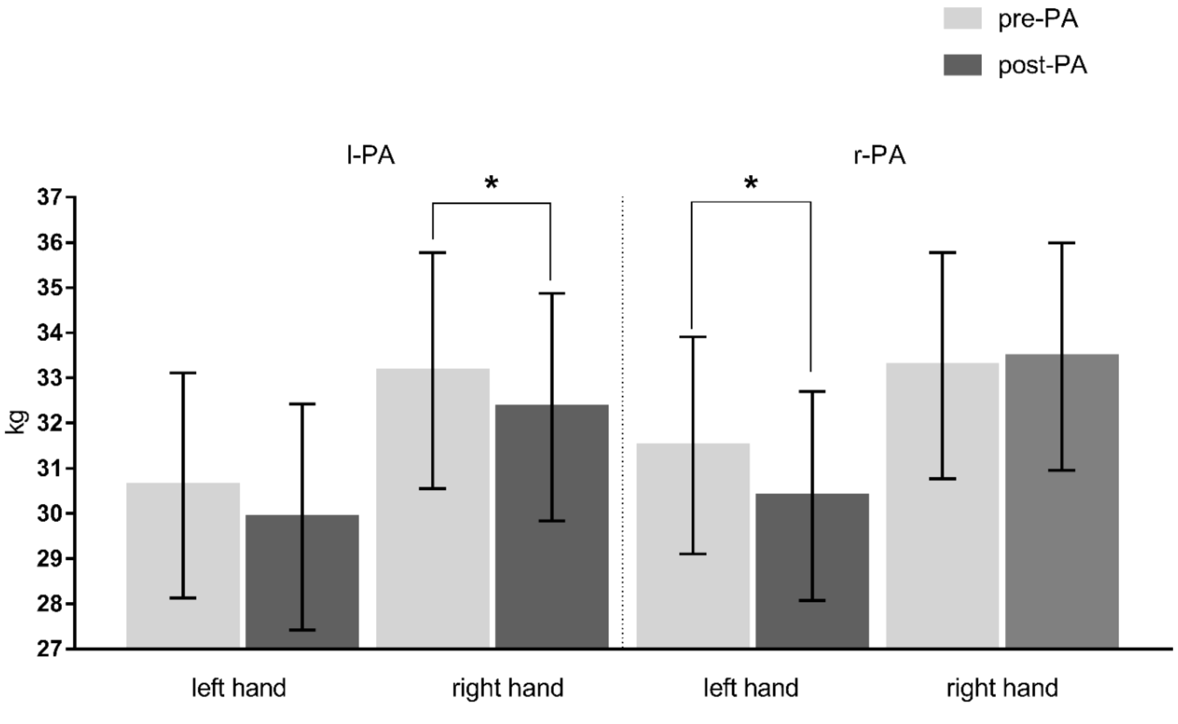
Means pointing displacement during Prismatic Adaptation in the five experimental conditions across groups (leftward prismatic adaptation group and rightward prismatic adaptation group). Legend: l-PA= leftward prismatic adaptation group; r-PA= rightward prismatic adaptation group; Error bars= Standard error of mean; *p<.001

Negative values indicate leftward pointing displacement, positive values indicate rightward pointing displacement.

Handgrip

Figure 2 shows handgrip performance for the left and the right hand during the first and the second measurement across l-PA and r-PA groups. ANOVA revealed significant main effects of the factors Hand [F(1,44)=37.730, p<.001, ηp2=.441] and Time [F(1,44)=8.205, p=.006, ηp2=.157] while the factor Group [F(1,44)=.035, p=.853, ηp2= .001] and the interaction Hand×Time [F(1,44)=3.345, p=.074, ηp2= .071] were not significant. The interaction Hand×Time×Group was significant [F(1,44)=4.659, p=.036, ηp2=.096]. Post-hoc tests revealed that l-PA reduced right hand strength (33.160 vs. 32.352, p=.034) and r-PA reduced left hand strength (31.506 vs. 30.389, p=.006) (Figure 2).

Figure 2



Differences in handgrip strength (left and right) means values before and after prismatic adaptation (pre- PA, post-PA) across groups (leftward prismatic adaptation group and rightward prismatic adaptation group). Legend: l-PA = leftward prismatic adaptation group; r-PA = rightward prismatic adaptation group; pre-PA= before prismatic Adaptation; post-PA= after prismatic adaptation; Error bars = Standard error; * p<.05.

Plantar Surface Area

ANOVA on the total plantar surface area revealed a significant effect of the factor Feet [F(1,44)=12.576, p=.001, ηp2=.222], while the factors Time [F(1,44)=.137, p=.713, ηp2=.003] and Group [F(1,44)=2.917, p=.095, ηp2=.062] were not significant. The interaction Feet×Time was significant [F(1,44)=6.846, p=.012, ηp2=.135], the interaction Feet×Time×Group was not significant [F(1,44)=.179, p=.674, ηp2=.004].

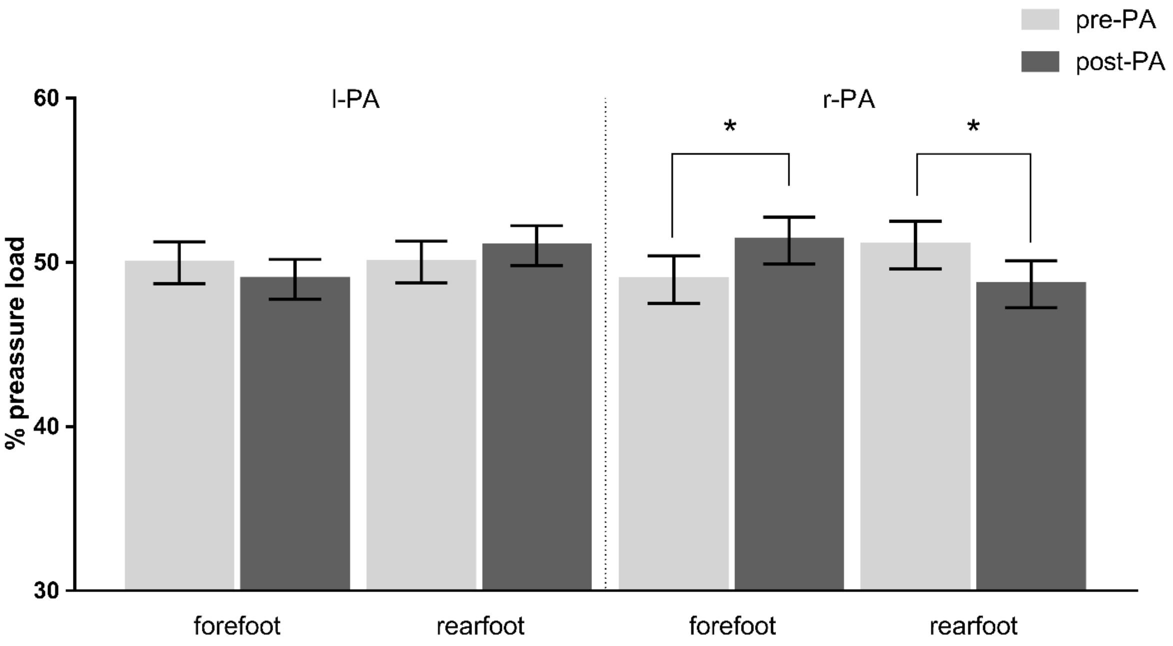
ANOVA on the forefoot/rearfoot plantar surface area revealed a significant effect of the factors Feet [F(1,44)=118.368, p<.001, ηp2=.729] and Area [F(1,44)=12.582, p<.001, ηp2=.222], and no effect of the factors Time [F(1,44)=.102, p=.751, ηp2=.002] and Group [F(1,44)=2.895, p=.096, ηp2=.062]. The interaction Feet×Area [F(1,44)=4.305, p=.044, ηp2=.089], Time×Area [F(1,44)=6.417, p=.015, ηp2=.127], Feet×Time×Group [F(1,44)=5.806, p=.029, ηp2=.104] were significant. None of the post hoc tests revealed significant differences (all p values> .05).

Plantar Pressure

ANOVA on the total plantar pressure revealed a significant effect of the factor Time [F(1,44)=6.887, p=.012, ηp2=.135] and not of the factor Group [F(1,44)=1.028, p=.316, ηp2=.023] neither of the interaction Time × Group [F(1,44)=.969, p=.330, ηp2=.022]. Post-hoc tests on the main factor of Time revealed a decrease of plantar pressure on the right foot (49.537 vs. 48.006, p= .012) after PA, regardless of the lenses deviation side. There was no significant difference among the pre-PA measurements (all p values>.05).

Figure 3 shows forefoot/rearfoot plantar pressure distribution in the l-PA and r-PA groups during the first and the second measurement. ANOVA on the forefoot/rearfoot plantar pressure revealed that neither the main factor Time [F(1,44)=.987,p=.326, ηp2=.022] nor the factor Feet [F(1,44)= 1.978,p=.167, ηp2=.043] were significant, whereas the interaction Time×Group was significant [F(1,44)=5.847, p=.020, ηp2=.117]. The post-hoc tests revealed an increase in forefoot plantar pressure (48.947 vs. 51.342, p=.020) in both feet after r-PA (Figure 3).

Figure 3



Feet pressure distribution (forefoot/rearfoot) before and after prismatic adaptation (pre- PA, post-PA) across groups (leftward prismatic adaptation group and rightward prismatic adaptation group).

Legend: l-PA = leftward prismatic adaptation group; r-PA = rightward prismatic adaptation group; pre-PA= before Prismatic Adaptation; post-PA= after Prismatic Adaptation; Error bars=Standard error; * p<.05.

Discussion

The main result of the present study was that PA differently affected muscle strength and plantar pressure depending on the side of prismatic deviation. Namely, we found a significant decrease in muscle strength in the hand contralateral to the lenses deviation side after either leftward or rightward PA. A forward displacement of plantar pressure of both feet was found selectively after r-PA.

As a secondary result, we found a decrease of plantar pressure on the right foot after PA, regardless of the lenses deviation side. This effect could be explained by a compensatory postural adjustment activated by the visuomotor unbalance determined by PA, and leading to greater pressure on the non-preferred foot in order to obtain body stabilization. Further studies would better address asymmetries between dominant and non-dominant foot in body stabilization following visuomotor perturbation.

This is the first study investigating the effect of PA on handgrip strength and plantar pressure.

We suggest that the weakening of strength we observed in hands depends on inhibitory processes taking place both during the handgrip task and PA. Namely, it has been shown that PA induces an enhancement of excitability levels of M1 ipsilateral to the lenses deviation side (Bracco et al., 2017; Magnani, Caltagirone, et al., 2014), whereas, due to interhemispheric inhibitory processes, excitability levels in the contralateral M1 decrease (Martín-Arévalo et al., 2018). On the other hand, during muscle contraction, activity in the M1 contralateral to the tested hand increases, while excitability levels in the M1 ipsilateral to the tested hand decrease (Naccarato et al., 2006; Ward et al., 2007). It has been reported that the inhibition of M1 ipsilateral to the activated hand lasts until muscles contractions of medium-intensity are reached; when maximal voluntary contractions (MVC) are reached, the pattern of activation changes (Shibuya, 2011; Shibuya et al., 2014). Studies using near-infrared spectroscopy and functional magnetic resonance imaging have shown that M1 contralateral to the tested hand is activated when muscle strength is exerted from 20% to 60% MVC and then cortical reactivity reaches a plateau. At this point, higher muscle contractions (i.e., above 60%) are obtained through activation of the M1 ipsilateral to the tested hand, that complements activation of the contralateral one (Shibuya, 2011; Shibuya et al., 2014). Noteworthy, in our task 100% of the

MVC was required. This implies that the contribution of the M1 ipsilateral to the tested hand was pivotal in order to execute the grip task. We suggest that PA disrupted the recruitment of the M1 ipsilateral to the tested hand since this was inhibited by interhemispheric inhibitory processes occurring during PA (Martín-Arévalo et al., 2018).

In other words, PA inhibited the hemisphere contralateral to the lenses deviation side, thus preventing M1 recruitment to exert 100% of MVC during the handgrip task. If so, one should expect that PA either increase or decrease handgrip depending on the level of muscle contraction. Further studies will better address this issue.

In sum, these results do not contradict studies reporting an enhanced cortical activation in M1 ipsilateral to the lenses deviation side (Magnani, Caltagirone, et al., 2014). In particular, our findings add evidence to previous studies investigating PA effects with TMS over M1 and reporting that PA induces changes in excitability levels of M1 ipsilateral to the lenses deviation side (Magnani, Caltagirone, et al., 2014).

However, for hand strength weakening, we cannot exclude the occurrence of homeostatic plasticity phenomena, a natural neuron mechanism that reduce neuron’s activity to prevent overstimulation and cells damage (Tien & Kerschensteiner, 2018). Indeed, the combination of M1 activation induced by motor grip and PA might have caused a suppressive effect and a consequent hand strength reduction (Turrigiano & Nelson, 2004). In particular, a previous study has shown that PA excitatory effects may be reversed whether they are administered immediately after a conditioning excitatory paradigm of transcranial direct current stimulation (Bracco et al., 2017). Further studies combining behavioural with neurophysiological measures of M1 activation (i.e. analysis of motor evoked potentials) could better clarify this issue.

In addition to hand strength reduction, we found a selective plantar pressure forward displacement after r-PA but not l-PA. This result adds evidence to a previous study (Michel et al., 2003)reporting a forward displacement of the center of pressure (CoP) after both l-PA and r-PA, showing that r-PA may induce a shift either of the vertical projection of the center of pressure (as measured with stabilometry) and of the plantar pressure in terms of interaction between feet and ground reaction force (as measured with baropodometry)(Orlin & McPoil, 2000). However, unlike Michael et al., we did not find an effect on plantar pressure after l-PA. Besides differences in the measurements (baropodometry vs. stabilometry), a methodological issue may account for this lack of result. Namely, in our study subjects performed an additional pointing task to measure PA after effect (blind post-exposure) (Welch, 1974). Since subjects were prevented to watch their arm moving in order to adjust the pointing bias, an access to body postural representation was probably strongly needed (Longo & Haggard, 2010). We may speculate that the blind post-exposure caused a stronger modulation of the right hemisphere in order to retrieve internal and extra-personal body space representation (Shiraishi et al., 2008) and to correct for the arm shift. Activation of the right hemisphere is potentiated after r-PA but not after l-PA (inducing left hemispheric activation). This could explain the plantar pressure displacement selectively observed following right PA. This hypothesis finds confirmation in previous studies showing that body sway and body weight distribution among feet are regulated by the internal body representation, linked to attentive process (Michel et al., 2003; Shiraishi et al., 2008) taking place mostly in the right brain hemisphere (Cioncoloni et al., 2016; Parkinson et al., 2010; Zhavoronkova et al., 2012).

These findings suggest that PA may induce the recalibration of representation of space (Rossetti et al., 1998) and of body space (Michel et al., 2003). Further studies might explore the link between the direction of the PA induced shift in body posture and PA deviation side. parkin

In conclusion, our results suggest that PA exerts effects on body posture and hand strength relying on different mechanisms. The PA effects on hand strength would be related to modulation of interhemispheric inhibition of sensorimotor processes, involving both hemispheres. On the other hand, the PA effects on body posture would be related to modulation of higher-level processes such as body representation, involving mainly the right hemisphere.

3. PA and cognitive effects

Although the majority of the studies on PA procedure are aimed at investigating visuomotor or visuospatial effects in healthy participants and in patients, some studies investigated more cognitive effects, for example reward based learning (Schintu et al., 2018), mental alphabet line (Nicholls et al., 2008b) or hypnotisability after PA (Menzocchi et al., 2015). One interesting study was conducted by Frassinetti, Magnani & Oliveri (Frassinetti et al., 2009). The authors recruited 12 right-handed healthy participants to investigate how PA modulates time perception. Participants performed, pre and after PA with leftward or rightward lenses deviation, 2 experimental tasks, a reproduction time task and a half time bisection task about a visual stimuli presentation time. Participants showed, after rightward deviation, a significant underestimation of time duration, whereas, after leftward deviation, they showed a significant overestimation of time duration. These results suggest that PA changes in visual spatial representation can also influence the representation of time, i.e. a function strictly linked with spatial representation.

In the next paragraph we will present an experimental study made in our lab about the effects of the PA in phonemic fluency that showed interesting results about other possible application of the procedure.

3.1 Improvement of phonemic fluency following leftward prism adaptation (Turriziani et al., 2021)

Introduction

Prism adaptation (PA) is a form of visuomotor adaptation to displaced vision and it has been shown to modulate a wide range of behaviours in addition to the well-known application in patients with right hemispheric lesion and spatial neglect (Michel, 2016; Redding & Wallace, 2006; Rossetti et al., 2019).

The majority of observations indicate that prism adaptation acts both on space representation as well as on other features interacting with it. For example, in healthy subjects leftward PA induces a sort of left minineglect, counteracting the physiological leftward bias called pseudoneglect (Jewell & McCourt, 2000; Oliveri, Rausei, et al., 2004). PA cognitive effects have also been reported in visual search (Vangkilde & Habekost, 2010), endogenous and/or exogenous orienting of attention (Striemer & Danckert, 2010b), spatial/temporal representation (Anelli & Frassinetti, 2019; Frassinetti et al., 2009; Magnani et al., 2010, 2011, 2013b; Magnani, Frassinetti, et al., 2014; Oliveri et al., 2013), visually guided actions (Striemer & Danckert, 2010a), auditory representation (Michel et al., 2019), chronic pain (Christophe et al., 2016), constructional disorders (Rode, Klos, et al., 2006) and reward-based learning (Schintu et al., 2018). Lateralized effects of PA have been reported to be dependent on the age, being more evident in young adults (Magnani et al., 2020).

Visuomotor adaptation elicited by PA can also induce modulation of frontal areas ipsilateral to prism deviation. Magnani et al. (Magnani, Frassinetti, et al., 2014), in a study using paired-transcranial magnetic stimulation (TMS) in healthy subjects, first reported modulation of excitatory brain circuits on the motor cortex specific to the direction of the visual shift induced by prismatic lenses: left-deviation PA increased excitation of the left motor cortex, while right-deviation PA increased excitation of the right motor cortex, as tested with the amplitude of motor evoked potentials.

Bracco et al. (Bracco et al., 2017) reproduced these findings in a study combining TMS, transcranial direct current stimulation (tDCS) and PA in healthy subjects. Prism adaptation increased excitability of the motor cortex ipsilateral to the deviation, as tested with TMS, in a manner similar as anodal tDCS did. The combination of the two interventions (i.e., PA and anodal tDCS) induced homeostatic plasticity effects, reducing motor cortical excitability. The same research group (Bracco et al., 2018) showed that prism adaptation induces an increase of the power of beta oscillations in the frontal areas of the hemisphere ipsilateral to the optical deviation during motor preparation but not visual attention tasks.

These findings may suggest that prism adaptation can strengthen the activation of a brain network ipsilateral to the deviation, with effects that could have an impact on the cognitive functions subserved by that network. This view suggest that left PA could modulate subjects' performance on linguistic tasks recruiting left hemispheric areas. Related to this, left PA has been reported to activate the left dorsal attentional system and to increase interhemispheric inhibition from the left to the right hemisphere (Schintu et al., 2016). A role of increased right hemispheric inhibition in phonemic fluency tasks has been reported with rTMS in healthy subjects (Smirni et al., 2017). Moreover, PA reduces connectivity between the Default Mode Network and the inferior frontal gyrus (Wilf et al., 2019), thus increasing activation of the inferior frontal gyrus during specific tasks. The inferior frontal gyrus is involved in different components of phonological fluency, including phonological working memory and the motor articulatory processes associated with it, through the connections of area 44 with premotor cortex(Nixon et al., 2004). These inter- and intra-hemispheric connectivity changes could be associated to boosting of phonemic fluency following left PA.

In the present study, we tested these predictions by investigating the effects of left vs. right PA in modulating phonemic fluency tasks. We chose to investigate phonemic fluency because it shows a strong left hemispheric lateralization in frontal areas(Gutierrez-Sigut et al., 2015) and it has been studied with other, neuromodulatory, techniques (Smirni et al., 2017).

Phonemic fluency tasks require search, access, selection, retrieval and pronunciation of as many words as possible in a restricted time, based on a predefined criterion of a target letter. Therefore, fluency tasks are included in many neuropsychological batteries in that they probe cognitive functions at the interface between language and executive processing. As such, phonological fluency can be impaired in a variety of clinical populations, including aphasia and dementia(Baldo et al., 2010; Metternich et al., 2014; Rodríguez-Aranda et al., 2016).

We predicted that adaptation to a leftward optical deviation should increase subjects' performance compared to adaptation to rightward optical deviation and to no adaptation conditions.

Results

Both leftward prism adaptation (L-PA) and rightward prism adaptation (R-PA) groups underwent a neuropsychological assessment to exclude that the results on phonemic fluency task post-PA were correlated to other cognitive functions.

There was no significant difference in the performance of the L-PA and R-PA groups on the cognitive baseline tasks: Digit Span (forward ($F_{1,28} = 0.24$, $p = 0.78$; backward $F_{1,28} = 1.35$, $p = 0.26$), SDMT ($F_{1,28} = 0.22$, $p = 0.64$), MFPT ($F_{1,28} = 0.85$, $p = 0.36$), Stroop test ($F_{1,28} = 1.70$, $p = 0.21$), RAPM ($F_{1,28} = 0.68$, $p = 0.32$).

Effects of prism adaptation on phonemic fluency task

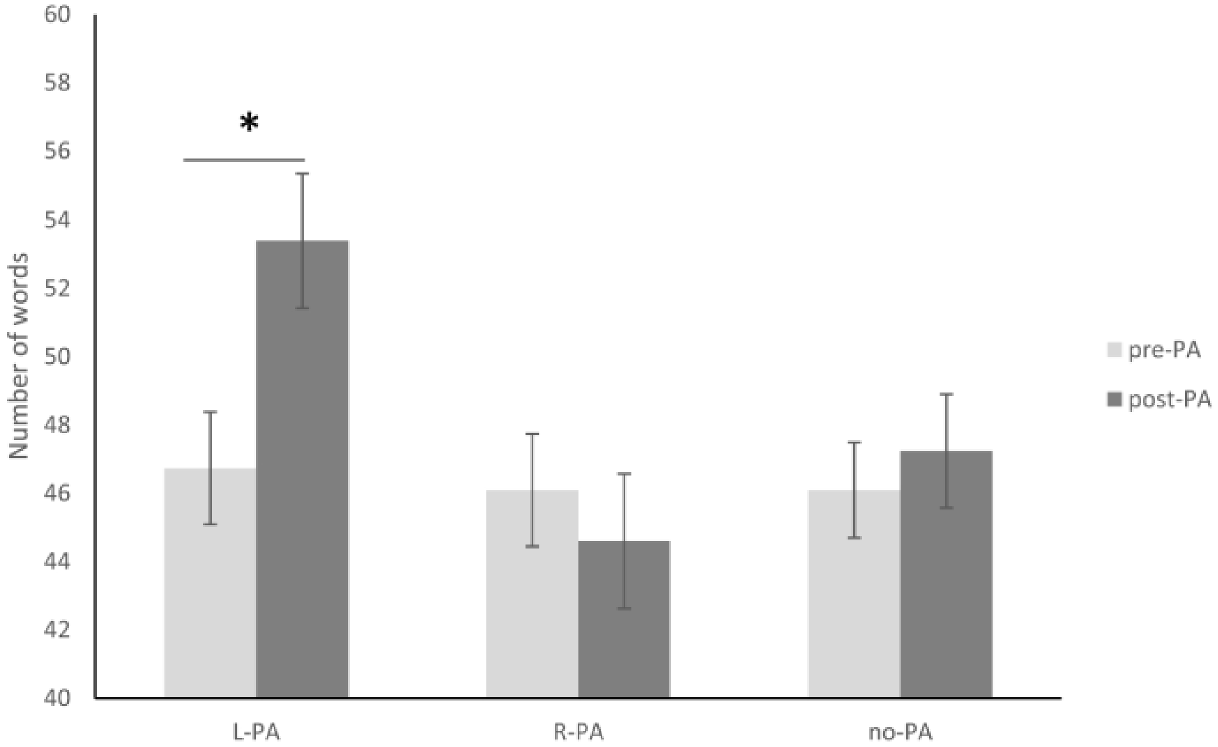
To compare the verbal fluency of participants at baseline (pre-PA), a one-way ANOVA with Condition (L-PA, R-PA, no-PA) variable was performed on the number of words produced in the phonemic fluency tasks. The analysis did not show significant differences ($F_{2,48} = 0.04$, $p = 0.95$, $\eta p^2 = 0.002$) suggesting that performance on the phonemic fluency task was similar for the three groups (L-PA = 46.73; R-PA = 46.09; no-PA = 46.57).

To investigate whether leftward and rightward PA differently modulate the phonemic fluency, a 3 × 2 repeated measures ANOVA was conducted on the number of words produced, with the variables Session (pre-PA, post-PA) as within subject factor and Condition (L-PA, R-PA, no-PA) as between subjects factor.

The ANOVA revealed a significant effect of Session ($F_{1,48} = 5.28$, $p = 0.02$, $\eta p^2 = 0.09$) indicating an overall increase in the words produced in the post PA session. The main effect of Condition ($F_{2,48} = 2.15$, $p = 0.12$, $\eta p^2 = 0.078$) did not reach statistical significance. As shown in Fig. 1, there was a significant Session × Condition interaction ($F_{2,48} = 7.64$; $p = 0.001$,

$\eta p^2 = 0.24$). L-PA significantly increased the number of words produced as compared with baseline (pre-PA = 46.73 vs. post-PA = 53.38; $p = 0.003$, $\eta p^2 = 0.48$). In contrast, R-PA did not significantly modulate phonemic fluency as compared with baseline (pre-PA = 46.09 vs. post-PA = 44.6, $p = 0.34$, $\eta p^2 = 0.06$). The number of words produced following left PA was higher than that following right PA ($p < 0.01$).

Figure 1:



Phonemic fluency performance before and after prism adaptation (pre-PA, post-PA) across groups (L-PA group, R-PA group and no PA group). L-PA significantly improves the performance on phonemic fluency task.

Additionally, we investigated whether PA affected the grammatical class of the words (nouns or verbs) produced in the phonemic fluency task.

An ANOVA was performed on the number of nouns and verbs produced in the phonemic fluency task, with Session (pre-PA, post-PA) and Type of word (noun, verb) as within-subjects' factors and Condition (L-PA, R-PA, No-PA) as between-subjects factor. The analysis revealed a significant main effect of Type of word ($F_{1,28} = 468.61$, $p = 0.000$, $\eta p^2 = 0.94$) indicating the production of higher number of nouns (mean = 43.33) than verbs (mean = 5.58). The Session × Type of word ($F_{1,28} = 10.87$, $p = 0.003$, $\eta p^2 = 0.28$), Session × Condition ($F_{1,28} = 4.84$, $p = 0.03$, $\eta p^2 = 0.14$) and Session × Type of word × Condition ($F_{1,28} = 5.73$, $p = 0.02$, $\eta p^2 = 0.17$) interactions were significant.

L-PA increased the number of produced nouns (pre-PA = 42.33 vs. post-PA = 50.33, $p = 0.003$, $\eta p^2 = 0.48$) but not of verbs (pre-PA = 5.80 vs. post-PA = 6.0, $p > 0.05$, $\eta p^2 = 0.06$). R-PA did not modulate nouns (pre-PA = 40.13 vs. post-PA = 40.33, $p = 0.92$, $\eta p^2 = 0.08$) and verbs (pre-PA = 5.80 vs. post-PA = 5.50, $p = 0.95$, $\eta p^2 = 0.01$) fluency.

The Session ($F_{1,28} = 3.19$, $p = 0.08$, $\eta p^2 = 0.10$) and Condition ($F_{1,28} = 2.29$, $p = 1.14$, $\eta p^2 = 0.76$) main effects and Type of word × Condition ($F_{1,28} = 2.54$, $p = 1.22$, $\eta p^2 = 0.08$) interaction did not reach statistical significance.

These findings indicate that leftward PA increases the phonemic fluency of nouns but not of verbs whereas rightward PA does not modify the production of any type of words.

To investigate whether leftward or rightward PA differently modulate the motor articulatory component involved in linguistic tasks, an ANOVA with the variables Session (pre-PA, post-PA) as within subject factor and Condition (L-PA, R-PA, no-PA) as between subjects factor was conducted on the mean number of syllables (number of syllables/number of words) produced in the phonemic fluency task.

The ANOVA did not reveal main effects of Session ($F_{1,28} = 1.88$, $p = 0.18$, $\eta p^2 = 0.06$) and Condition ($F_{1,28} = 0.18$, $p = 0.67$, $\eta p^2 = 0.006$). A significant Session × Condition interaction ($F_{2,48} = 4.71$, $p = 0.038$, $\eta p^2 = 0.14$) was found, revealing that L-PA significantly increased the number of syllables produced (pre-PA = 2.77 vs. post-PA = 2.84, $p = 0.02$, $\eta p^2 = 0.52$). R-PA did not significantly modulate the number of syllables (pre-PA = 2.76 vs. post-PA = 2.73, $p = 0.34$, $\eta p^2 = 0.01$).

These findings indicate that leftward PA increases not only the absolute number of words produced but also the production of words formed by a greater number of syllables.

Prism adaptation

Error reduction

The ANOVA showed a significant effect of Condition ($F_{1,28} = 47.85$, $p = 0.0001$, $\eta p^2 = 0.20$) and a significant Session × Condition interaction ($F_{2,48} = 38.07$, $p = 0.0001$, $\eta p^2 = 0.62$). The Session main effect was not significant ($F_{1,29} = 1.03$, $p = 0.34$, $\eta p^2 = 0.03$). Post-hoc analyses showed that, for both groups, the pointing displacement in the pre-exposure condition was significantly different from that in the early-exposure-condition (L-PA $p = 0.001$, R-PA $p = 0.006$).

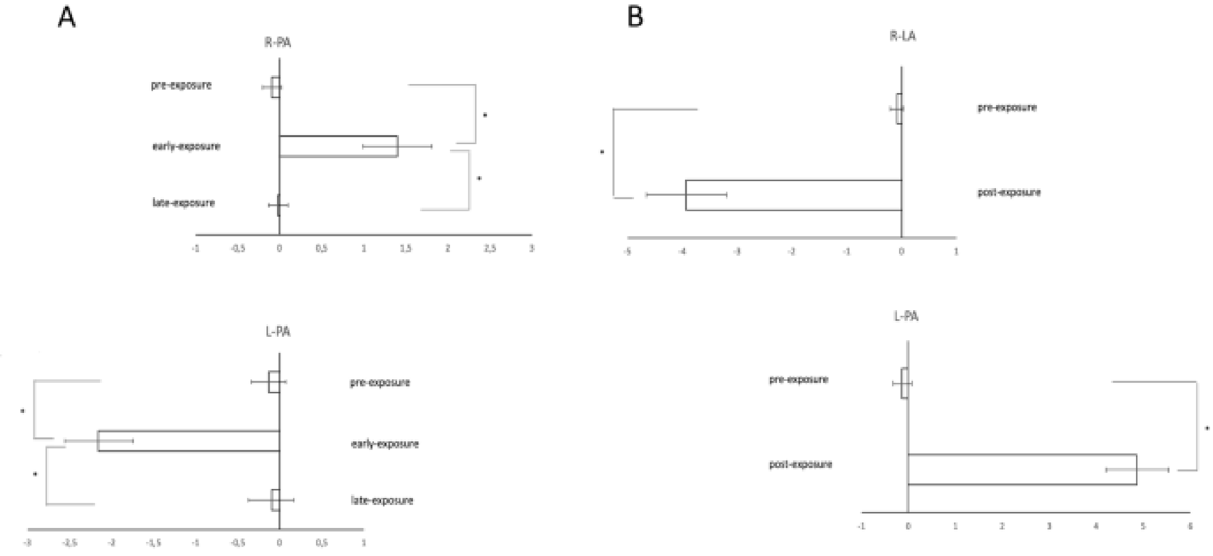
Conversely, due to subjects' adaptation to prismatic deviation, no differences were found between visible pointing in the pre-exposure and late exposure conditions, neither in the L-PA ($p = 0.99$) nor the in the R-PA ($p = 0.99$) group.

Aftereffect

The ANOVA revealed significant effects of Condition ($F_{1,29} = 219.57$, $p = 0.000$, $\eta p^2 = 0.88$) and Session × Condition interaction ($F_{1,48} = 192.54$, $p = 0.000$, $\eta p^2 = 0.86$). Session main effect was not significant ($F_{1,29} = 3.28$, $p = 0.08$, $\eta p^2 = 0.10$).

The presence of aftereffect was confirmed by a significant difference between pre-exposure and post-exposure in both the L-PA ($p = 0.0001$) and the R-PA ($p = 0.0001$) groups (Fig. 2).

Figure 2



Prism adaptation parameters: (A) error reduction for R-PA (top) and L-PA (bottom); (B) aftereffect following R-PA (top) and L-PA (bottom). The values indicate mean pointing displacement in the four experimental conditions across groups. L-PA = leftward prism adaptation group; R-PA = rightward prism adaptation group; Error bars = standard error of mean; *p < 0.05. Negative values indicate leftward pointing displacement, positive values indicate rightward pointing displacement.

Discussion

The present study was aimed at investigating the effects of leftward vs. rightward PA in a phonemic fluency task.

The main results show that leftward PA is associated with improved phonemic fluency performance in healthy subjects when compared with either baseline (i.e., no optical deviation) or rightward PA. Improved phonemic fluency was evident either in terms of the number of words produced and in the number of syllables for each word. The increase in phonemic fluency following leftward PA was mainly evident for the grammatical category of nouns.

These results are unlikely to be explained by practice effects. Parallel forms of the task were used in baseline and post-PA sessions, although one target letter was common in the two fluency tasks; moreover, the control condition in the no-PA group failed to document significant increases in phonemic fluency performance across repeated sessions.

To our knowledge, this is the first study documenting facilitation of a linguistic task by prism adaptation, i.e., a procedure traditionally associated with modulation of spatial cognition or cognitive functions linked to spatial components.

According to some findings, suggesting that prism adaptation possibly increases excitability of frontal and parietal areas ipsilateral to the deviation side (Bracco et al., 2018; Magnani, Frassinetti, et al., 2014; Schintu et al., 2016), we may interpret the present results as probably reflecting activation of left hemispheric brain regions that are also associated with phonemic fluency tasks. In this field, neuroimaging and neuropsychological studies show that phonemic fluency recruits a left lateralized network including inferior frontal gyrus, motor cortices, anterior cingulate, temporal regions, superior parietal cortex, hippocampus, thalamus and cerebellum (Abrahams et al., 2003; Biesbroek et al., 2016; Costafreda et al., 2006; Gourovitch et al., 2000; Phelps et al., 1997; Robinson et al., 2012). All these areas are part of a dorsal language network (Hickok & Poeppel, 2007) encompassing the left fronto-temporal arcuate fasciculus (Blecher et al., 2019), a finding consistent with the articulatory component of the phonemic fluency tasks. On the other hand, the motor articulatory component in linguistic tasks is associated with recruitment of motor cortical circuits (Oliveri, Finocchiaro, et al., 2004). The increase in the number of syllables produced for each word is also consistent with the recruitment of frontal motor areas (Wildgruber et al., 2001).

The literature shows modulation of other brain regions, in addition to frontal ones, by prism adaptation. Neuroimaging and neurophysiological studies support the idea that PA affects the visual attention and sensorimotor networks, including the parietal cortex and the cerebellum (Chapman et al., 2010; Clower et al., 1996; Danckert et al., 2008; Luauté et al., 2009). The activation of the parietal cortex and the cerebellum has been related to error reduction and realignment during prism adaptation. The anterior cingulate cortex is also activated in an early error-correcting phase (Danckert et al., 2008). Interestingly, parietal cortex and cerebellum are also activated during phonological fluency tasks (Ben-Yehudah & Fiez, 2008; Mariën et al., 2014).

It is therefore possible that phonological fluency modulation is also controlled by the parieto-cerebellar network, activated during the spatial realignment.

The grammatical class effect encountered in phonemic boosting following leftward PA, with greater production of nouns than verbs, could depend on different factors. A neuroanatomical account posits that verb processing is mainly supported by the left frontal cortex while noun processing is supported by left temporal regions (Cappelletti et al., n.d.; Damasio & Tranel, 1993; Daniele et al., 1994; Shapiro et al., 2006). On the other hand, other evidence suggests that left frontal, parietal and temporal areas are similarly correlated with the noun and verb processing (Crepaldi et al., 2011; Luzzatti et al., 2006; Tranel et al., 2001).

Another possibility is linked to differential effects of PA on neural oscillations. In fact, while PA increases beta power in motor cortices ipsilateral to prismatic deviation(Bracco et al., 2018), verb retrieval is associated with beta suppression in motor areas(Pavlova et al., 2019).

Modulation of a phonemic fluency task by leftward prism adaptation fits the general idea that cognition is grounded on sensorimotor interactions.

A rTMS study (Smirni et al., 2017) showed that low-frequency rTMS of the right inferior frontal gyrus increased subjects' performance in phonological fluency tasks. The results were interpreted as reflecting plastic neural changes in the left lateral frontal cortex induced by low frequency rTMS, suppressing interhemispheric inhibitory transcallosal interactions. Interestingly, an electrophysiological study reported that leftward PA increases transcallosal interhemispheric inhibition from the left to the right primary motor cortex(Martín-Arévalo et al., 2018). The results of the present study may, therefore, be also associated to modulation of transcallosal inhibition, with a reduction of activity of homologous regions of the right hemisphere, as in the reported rTMS study (Smirni et al., 2017).

Previous findings reported that rightward prism adaptation does not produce significant cognitive changes in healthy subjects (Berberovic & Mattingley, 2003; Colent et al., 2000; Fortis et al., 2011; GOEDERT et al., 2010; Michel et al., 2003; T. Nijboer et al., 2010; Schintu et al., 2014, 2017; Striemer & Danckert, 2010b), (but see Bracco et al., 2018; Crottaz-Herbette et al., 2014) for neurophysiological changes of brain activities in healthy adults). The authors interpreted this asymmetry of prism adaptation effects as related to the right hemisphere dominance in visual attention networks (de Schotten et al., 2011; Kucyi et al., 2012). This dominance would explain the phenomenon of leftward attentional bias called pseudoneglect. Indeed, leftward PA can counteract pseudoneglect, while rightward PA would be less efficient in shifting attention further towards the left hemispace. Therefore, one may think that the selective effects of leftward optical deviation on phonemic fluency could also be linked to the modulation of spatial factors selectively in this condition. On the other hand, since sensorimotor aftereffect and cognitive effect act at different levels, they are not consistently reported together, as suggested by other experiments exploring the effects of leftward PA in both healthy subjects and neurological patients. Schintu et al. (Schintu et al., 2018) reported modulation of left hemisphere dopaminergic activity in healthy subjects following leftward PA, without differences in the amount of sensorimotor effects induced by leftward vs. rightward PA. Frassinetti et al. (Frassinetti et al., 2009) first documented underestimation of time perception following leftward PA, a finding consistently replicated in other studies and correlated with the amount of sensorimotor effects (Anelli & Frassinetti, 2019; Magnani et al., 2010, 2013b, 2020; Magnani, Frassinetti, et al., 2014). In neurological patients, leftward PA has been shown to reshape visuospatial representation in left brain damaged patients with right neglect (Bultitude & Rafal, 2010; Crottaz-Herbette et al., 2019; Facchin et al., 2017). In other cases, spatial aftereffects following leftward PA were reduced (Ronchi et al., 2019) in patients with left brain damage.

The influence of spatial components on linguistic representations has been reported in the literature. Turriziani et al. (Turriziani et al., 2009) described attentional representational biases in semantic judgments in healthy subjects, similar to those observed for the processing of space and numbers. Spatial manipulation of semantics was linked to the activation of specialized attentional resources located in the left hemisphere, and it was selectively modulated by left parietal rTMS. One could argue that there could be an influence of spatial factors also in the phonemic fluency task. This task requires to produce as many words as possible in a restricted time based on the predefined criterion. A leftward spatial bias has been reported for mental representations of alphabet lines. This bias is counteracted by leftward but not rightward PA (Nicholls et al., 2008a). Therefore, assuming that the representation of alphabet letters could be spatially organized in a left-to-right pattern, it could be hypothesized that in the present study leftward PA has shifted attention to the right space and facilitated focusing of attention to the ending letter targets (i.e., “S”). Although the hypothesis is intriguing for future, at present it only remains speculative and further, dedicated, studies, will be necessary to test this prediction.

If confirmed and extended to clinical populations of neurological patients, the present findings could help to devise a novel type of rehabilitation approach for cortical dysfunctions involving the left hemisphere. In this field, since fluency tasks lie at the interface between language and executive functions, and can be impaired in numerous neurological disorders, this behavioural rehabilitative approach could have a huge clinical impact for a variety of disorders. On the other hand, future application in patients should take into account the different interactions of side of PA with side of cerebral lesion and age of the patients (Magnani et al., 2010, 2011; Oliveri et al., 2013).

Methods

Subjects

Fifty-one healthy females (mean age: 24.8 ± 2.4 years) volunteered to participate in these experiments. All participants were Psychology students, native Italian speakers, right-handed, had a normal or corrected-to-normal vision and reported no history of neurological or psychiatric disease.

Thirty subjects were randomly allocated in the experimental group (mean age: 25.04 ± 2.5 years). Participants were assigned to a leftward Prism Adaptation group (L-PA; n = 15; mean age = 23.69 ± 1.88 years) or a rightward Prism Adaptation group (R-PA; n = 15; mean age = 23.86 ± 2.59 years). Participants handedness was assessed using the Edinburgh Handedness Inventory (Oldfield, 1971).

In the control group, there were 21 right-handed healthy participants (mean age = 25.04 ± 2.51 years).

All subjects gave written informed consent for participation in the study that was approved by the ethical committee of the University of Palermo (approval n. 25/2020). The experiments were done in accord to the principles of Declaration of Helsinki.

Neuropsychological assessment

The experimental group underwent a neuropsychological evaluation. Digit Span forward and backward (Monaco et al., 2013), Symbol Digit Modalities Test (Nocentini et al., 2006) (SDMT), Modified Five Point Test (Cattelani et al., 2011) (MFPT); a short version of the Stroop Colour-Word Test (Caffarra et al., 2002), Raven's Advanced Progressive Matrices (Raven, 1982).

Phonemic fluency tasks

Two phonemic fluency tasks, standardized for the Italian population, were used (Carlesimo et al., 1996; Novelli et al., 1986). Both tasks require participants to generate as many words as possible starting with a given letter within 1 min, excluding proper nouns and words differing only for the suffix. Thus, the dependent variable was the number of words generated in 1′. In one of the two phonemic fluency tasks, the 3 letters used were “F” “A” “S”. In the second task, the 3 letters used were “F” “P” “L”.

Prism adaptation procedure

The procedure for PA was similar to that adopted in previous studies (Frassinetti et al., 2009; Magnani et al., 2011, 2020; Oliveri et al., 2013).

For PA, prisms of 20 prismatic diopters, inducing a leftward or rightward shift of the visual field depending on the rotation of the lenses, were used.

During PA, subjects were seated at a table in front of a box (height = 30 cm, depth = 34 cm at the center and 18 cm at the periphery, width = 72 cm) that was open on the side facing the subjects and on the opposite side, facing the experimenter. The experimenter placed a visual target (a pen) at the distal edge of the top surface of the box, in one of three possible positions (randomly determined on each trial): a central position (0°), 21° to the left of the center, and 21° to the right of the center. Subjects were asked to keep their right hand at the level of the sternum and to point toward the pen using the index finger of the same hand; the experimenter recorded the end position of the subject's pointing direction.

In the invisible pointing trials, the arm was totally covered by a black sheet and the subjects did not see any part of the trajectory of the arm.

In the visible pointing trials, the arm was covered only in the proximal part and the subjects could see the last third of the trajectory of the pointing movement.

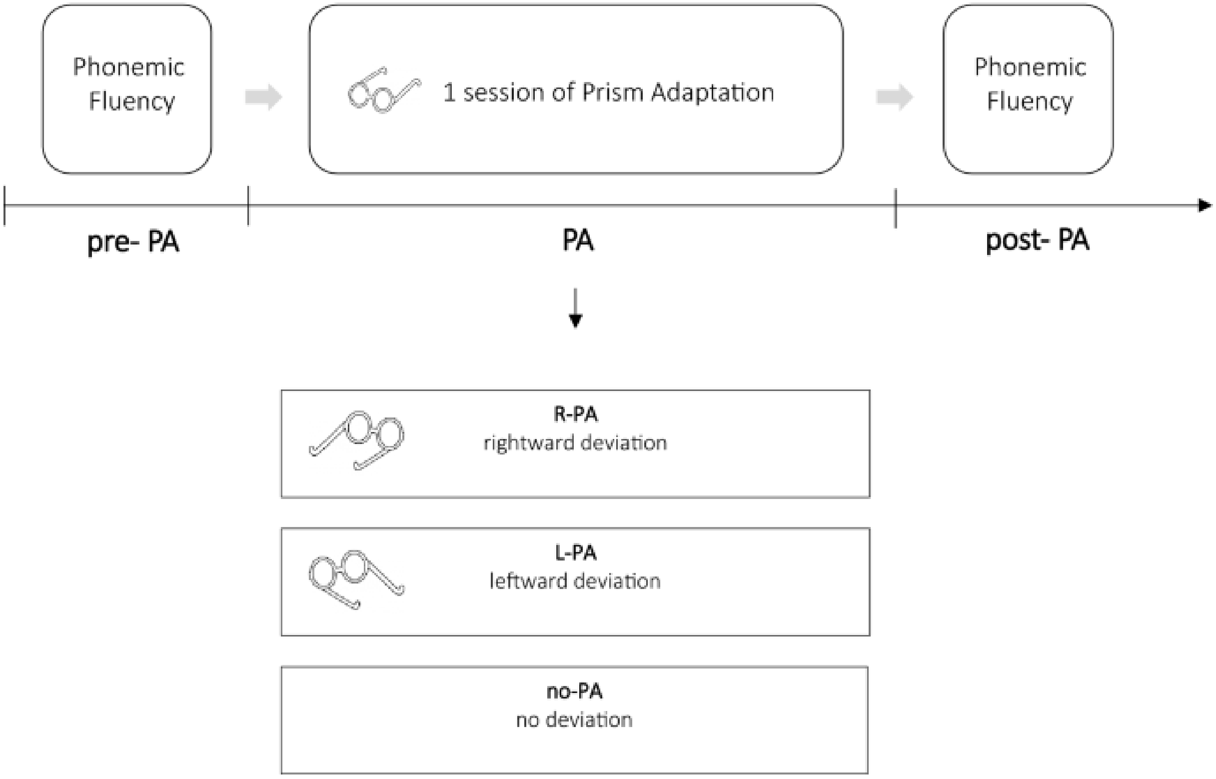
The pointing task was performed in three experimental conditions: pre-exposure, exposure and post-exposure. In the pre-exposure condition, 60 trials were administered, 30 in visible pointing and 30 in invisible pointing. In the exposure condition, 90 trials in visible pointing were administered; subjects wore prismatic lenses that induced a 20° shift of the visual field to the right or to the left. In the post-exposure condition, 30 trials in invisible pointing were administered immediately after removal of the prisms (Magnani et al., 2020).

All the trials were equally and randomly distributed in the three marked positions of the panel.

Experimental procedure

Both the L-PA and the R-PA groups and the control group participated in two testing sessions over two separate days, with an interval of 7 days between sessions (Fig. 3).

Fig 3



Schematic representation of the experimental design.

In the first testing session, the two experimental groups were given the cognitive baseline tasks and the phonemic fluency task (FAS or FPL). In the second testing session, the two experimental groups were first administered the PA procedure (L-PA or R-PA), immediately followed by one of the two phonemic fluency tasks. The control group was administered one of the two phonemic fluency tasks (FAS or FPL) in the first testing session. In the second testing session, the control group was administered the other fluency task. The order of administration of the two phonemic fluency tasks was counterbalanced across groups and randomly assigned.

Statistical analysis

Phonemic fluency task

Behavioral data were analyzed with an ANOVA, with Condition (L-PA, R-PA, No-PA) as between-subjects factor and Session (pre-PA, post-PA) as a within-subjects factor. Post-hoc analyses were conducted with Tukey's test. Effect size is reported as partial eta square.

Prism adaptation

Error reduction

To verify whether subjects adapted to prism deviation, showing an error reduction following rightward or leftward deviation, we compared their displacement measure in the pre-exposure (visible pointing) condition with that of the first three (early- exposure condition) and the last three trials (late-exposure condition) of the exposure condition (more details on this procedure can be found in(Magnani et al., 2020)). A difference between a pre-exposure condition and the early-exposure condition is expected due to the rightward or leftward displacement induced by prism exposure. On the other hand, no difference is expected between the pre-exposure and the late-exposure condition in the assumption of an almost perfect error reduction. The dependent measure in this analysis was the mean displacement (expressed as degrees of visual angle) of subjects' visible pointing. An ANOVA was conducted with Group (L-PA; R-PA) as between-subjects and Condition (pre-exposure, early-exposure and late-exposure) as within-subjects variable. Whenever necessary, post hoc comparisons were conducted using Tukey's test. Effect size is reported as partial eta square.

Aftereffect

We compared the subjects' displacement in the invisible pointing in the pre-exposure and post-exposure conditions. If, after prism exposure, subjects point to the direction opposite the displacement induced by the prism, a difference is expected between the pre- and the post-exposure conditions (aftereffect). The dependent measure was the mean displacement (expressed in degrees of visual angle) of the subjects' invisible pointing responses in the pre-exposure condition and the post-exposure condition (Magnani et al., 2020). An ANOVA was conducted with Condition (L-PA; R-PA) as between-subjects and Session (pre-exposure, post-exposure) as within-subjects variable. Whenever necessary, post hoc comparisons were conducted using Tukey's test. Effect size is reported as partial eta square.

4. Conclusion

PA is an intriguing procedure and, how was showed in this work, this procedure has a large range of applicability and different approaches. Moreover, there aren't much studies that tried the effects of this procedure in daily life activity or sport practice. Probably all the sports strongly related to a visuomotor target reaching and coordination tasks can show more and new interesting evidence of the application an adaptation to a visual field deviation.

Starting from realignment and recalibration the effects of PA, was discussed how an activation of visuomotor system (motor cortex, parietal cortex and cerebellum) and neuroimaging studies evidences confirmed this activation

There is still not much clarity about terminology used to describe the procedure and a lot of difference about settings, but in all the studies the opposite to lenses deviation after effects was showed in participants, healthy or not. Furthermore, was showed how the time to move this technique to new technologies, like virtual reality headset, is arrived. Regard this, will could be easier to perform PA with all the participants, adapt the "prism" power and perform more ecological task, but, until now there aren't much works on this.

Our research had showed how the application field of PA aren't exhausted. The interesting effects of PA in muscular strength was only evidenced by our study and a more deeply investigation, in example with fMRI or electroencephalography can better explain these results and help to understand how this process can be used in different rehabilitation procedure, not only with stroke patient. Finally, the results of PA in number of produced words open the topic an applicability of this procedure in a large number of language function and task.

In conclusion, PA adaptation produced and continue to produce a large number of evidence, studies and application that can allow to think that there is much more to investigate and understand how a deviation of visual field and simple task as pointing to a target can deeply have effects in humans cognitive function and brain activity.

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