Brain correlates of adaptation to multifocal contact lenses

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comib OPTICS AND OPTOMETRY RESEARCH CENTER UNIVERSITY OF MILANO BICOCCA

Disclosure

Fabrizio Zeri
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Associations and retail

ASSOTTICA (consulting relationships and speaker honoraria)
Grand Vision (consulting relationship)

Instruments

CSO (research support)
Nikon (consulting relationship)

Contact Lenses-Eye drops

Alcon (research support, consulting relationships and speaker honoraria)
Bausch & Lomb (consulting relationships and speaker honoraria)
Cooper Vision (consulting relationships and speaker honoraria)
Johnson & Johnson (consulting relationships and speaker honoraria)
Schalcon (consulting relationships)

Ophthalmic lenses

Essilor (speaker honoraria)
Hoya (research support, consulting relationship)

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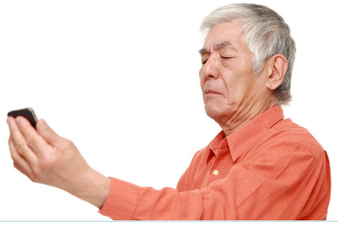
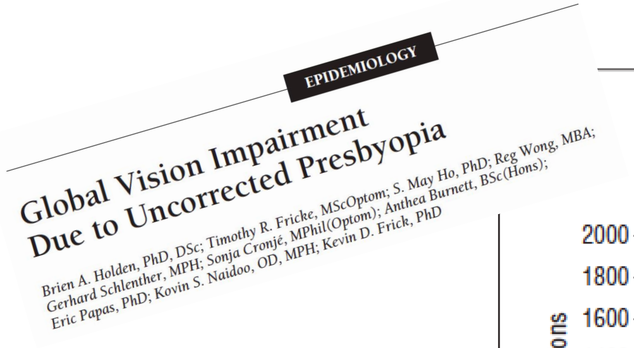


Prevalence of Functional Presbyopia

From 43.8% in southern and eastern Asian countries to 83.0% in western Asia, Australia, New Zealand, North America, and Europe. (Holden et al, 2008)



EPIDEMIOLOGY

Global Vision Impairment Due to Uncorrected Presbyopia

Brien A. Holden, PhD, DSc; Timothy R. Fricke, MScOptom; S. May Ho, PhD; Reg Wong, MBA; Gerhard Schlenther, MPH; Sonja Cronjé, MPhil(Optom); Anthea Burnett, BSc(Hons); Eric Papas, PhD; Kovin S. Naidoo, OD, MPH; Kevin D. Frick, PhD

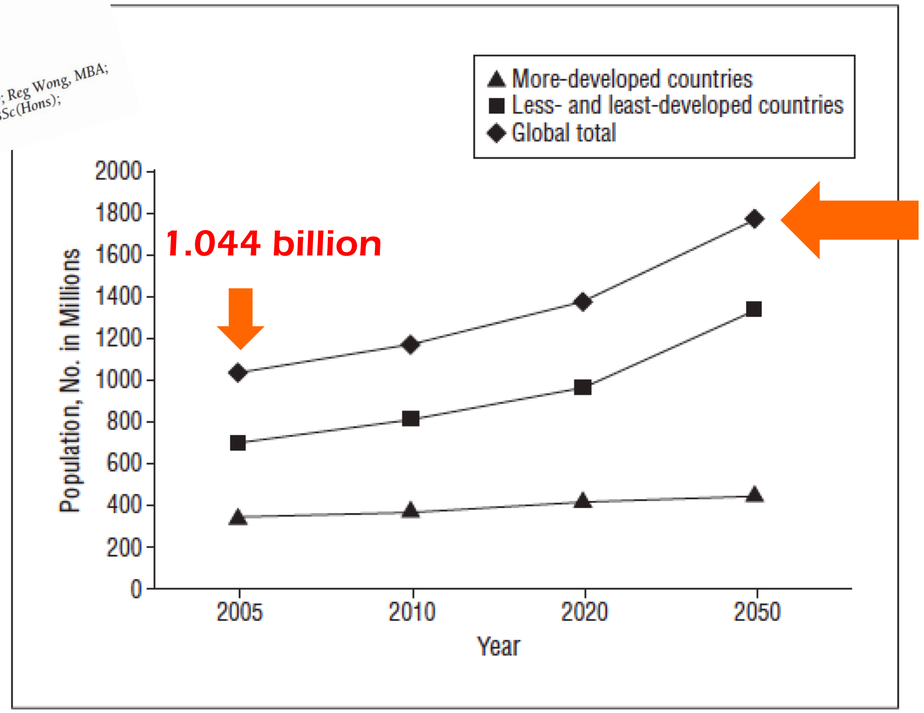
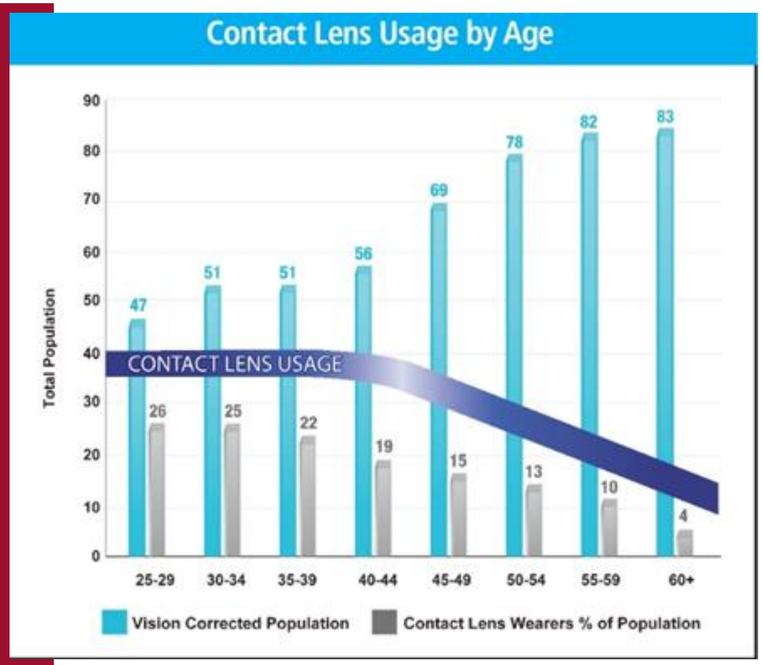
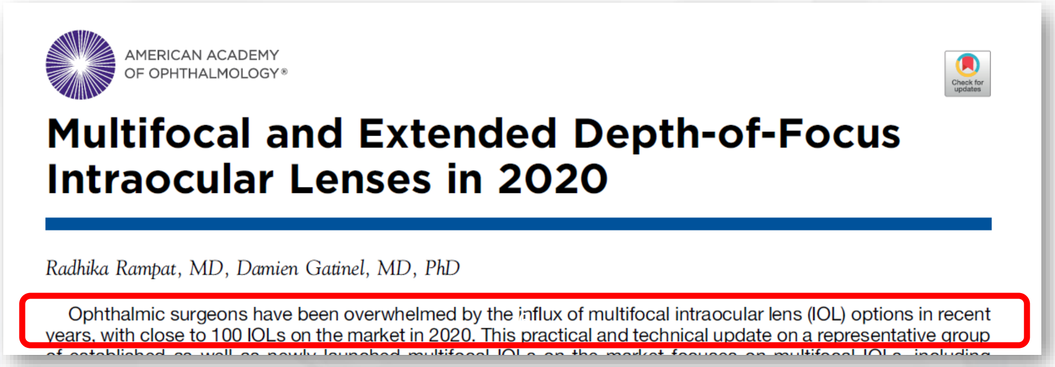


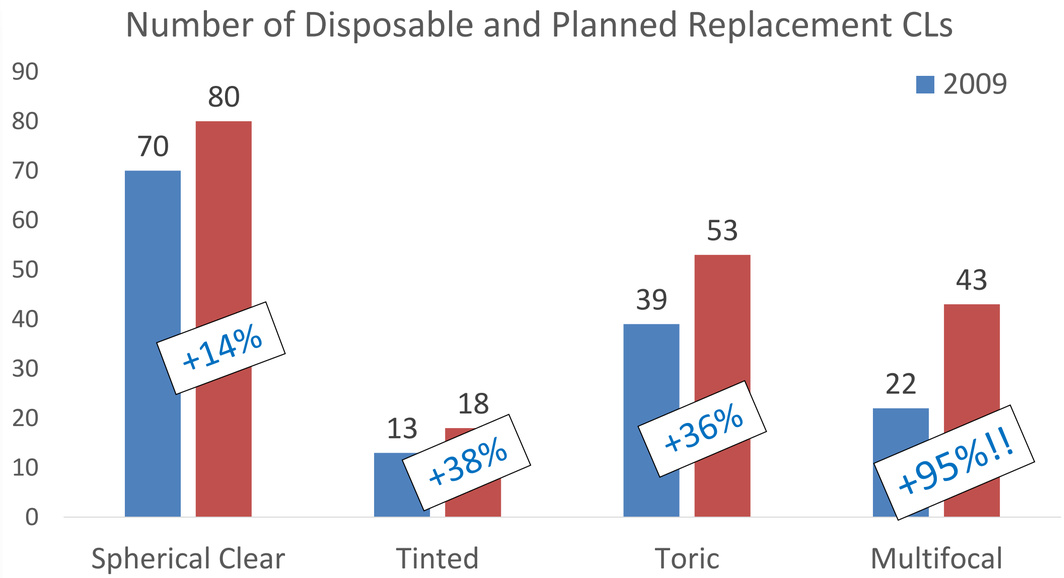
Figure. The predicted number of people with presbyopia from 2005 to 2050.

"The presbyopia dilemma"



(Akerman, 2010)





The adaptation to multifocal contact lenses (MCLs)

ORIGINAL ARTICLE

J Optom 2010;3:51-59

Depth-of-Focus and its Association with the Spherical Aberration Sign. A Ray-Tracing Analysis

Ravi C. Bakaraju[1-3], Klaus Ehrmann[1-3], Eric B. Papas[1-3] and Arthur Ho[1-3]

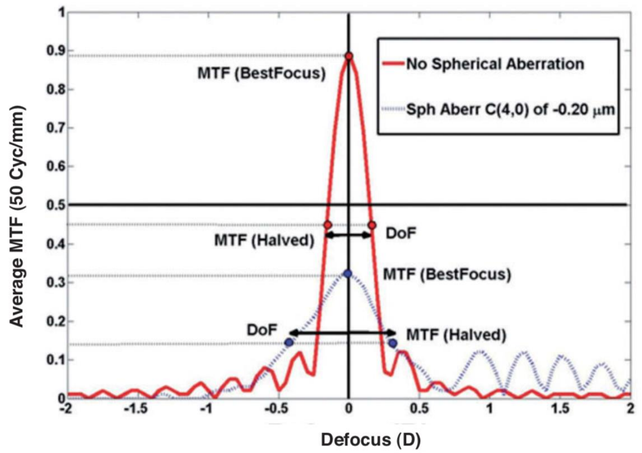


FIGURE 1
Through-focus MTF both for an aberrated and an unaberrated schematic eye model. Depth-of-focus (D) is defined as the defocus range for which the MTF stays above 50% of its maximum value. The red bold line represents the unaberrated system, while the blue dashed line represents a model with -0.20 µm of spherical aberration (Zernike coefficient C(4, 0)).

- MCLs use the simultaneous-image principle to correct presbyopia, but the spherical aberration induced by this method compromises the MTF of the optical system at the best focus, causing a contrast sensitivity loss.
- Many people adapt very quickly and effectively to MCLs, whereas others tolerate these lenses very badly and reject them.
- The brain mechanism supporting MCL adaptation is not well understood

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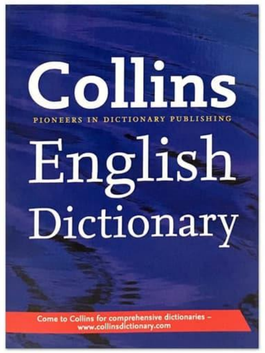
Electrophysiological measurements

Electrophysiology (from Greek ἤλεκτρον, ēlektron, "amber" [see the etymology of "electron"]; φύσις, physis, "nature, origin"; and -λογία, -logia) **is the study of the electrical properties of biological cells and tissues**. It involves measurements of voltage changes or electric current or manipulations **on a wide variety of scales from single ion channel proteins to whole organs like the heart**. In neuroscience**, it includes measurements of the electrical activity of neurons**, and, in particular, action potential activity. Recordings of large-scale electric signals from the nervous system, such as electroencephalography, may also be referred to as electrophysiological recordings. They are useful for electrodiagnosis and monitoring.

WIKIPEDIA
The Free Encyclopedia

the branch of physiology dealing with the
electric phenomena associated with the body and its functions



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Electrophysiological measurements

Modality	Abbreviation	Body part	Commo
electrocardiography	ECG or EKG	heart (specifically, the cardiac muscle), with cutaneous electrodes (noninvasive)	Very co
electroatriography	EAG	atrial cardiac muscle	Uncomm
electroventriculography	EVG	ventricular cardiac muscle	Uncomm
intracardiac electrogram	EGM	heart (specifically, the cardiac muscle), with intracardiac electrodes (invasive)	Somew
electroencephalography	EEG	brain (usually the cerebral cortex), with extracranial electrodes	Somew
electrocorticography	ECoG or iEEG	brain (specifically the cerebral cortex), with intracranial electrodes	Somew
electromyography	EMG	muscles throughout the body (usually skeletal, occasionally smooth)	Very co
electrooculography	EOG	eye (entire globe)	Somew
electroretinography	ERG	retina specifically	Somew
electronystagmography	ENG	eye via the corneoretinal potential	Somew
electroolfactography	EOG	olfactory epithelium in mammals	Uncommon
electroantennography	EAG	olfactory receptors in arthropod antennae	Not app
electrocochleography	ECOG or ECochG	cochlea	Somew
electrogastrography	EGG	stomach smooth muscle	Somew
electrogastroenterography	EGEG	stomach and bowel smooth muscle	Somew
electroglottography	EGG	glottis	Uncomm
electropalatography	EPG	palatal contact of tongue	Uncomm
electroarteriography	EAG	arterial flow via streaming potential detected through skin[2]	Uncomm
electroblepharography	EBG	eyelid muscle	Uncomm
electrodermography	EDG	skin	Uncomm
electrohysterography	EHG	uterus	Uncomm
electroneuronography	ENeG or ENoG	nerves	Uncommon
electropneumography	EPG	lungs (chest movements)	Uncommon
electrospinography	ESG	spinal cord	Uncommon
electrovomerography	EVG	vomeronasal organ	Uncommon

•Electroretinography (ERG)

Recording of mass electrical response of the retina when it is stimulated by light (e.g. a flash). It is recorded by placing an electrode in contact with the cornea or around the eye under the eyelid. The response is complex as many cells of various types contribute to it and varies according to whether the eye is dark or light adapted, the colour and size of the stimulus, the health of the retina, etc. (Millodot, 2014)

•Electroencelography (EEG)

The EEG is an electrophysiological technique for the recording of electrical activity arising from the human brain. Given its exquisite temporal sensitivity, the main utility of EEG is in the evaluation of dynamic cerebral functioning. (Britton et al, 2016)

Event-related potential (ERP)

evoked potentials" or "event-related potentials" (ERP) refer to changes in the patterns of activation produced by specific stimuli

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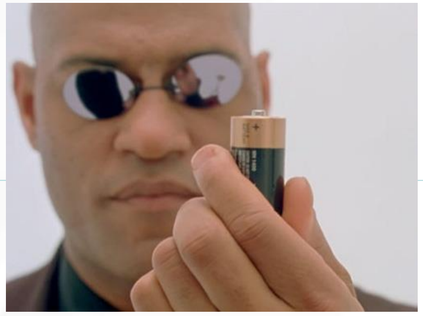
Electrophysiological measurements: EEG



The brain does not produce electricity!

The EEG represents the collective behavior of cortical neurons (Kandel, Schwartz, Jessell 2000) (summed electrical activities of populations of neurons)

- The EEG is thought to be primarily generated by cortical pyramidal neurons in the cerebral cortex that are oriented perpendicularly to the brain's surface. The neural activity detectable by the EEG is the summation of the excitatory and inhibitory postsynaptic potentials of relatively large groups of neurons firing synchronously (Britton et al, 2016)
- When activated with a certain degree of synchrony, pyramidal neurons of the cortex generate coherent electric/magnetic fields. these neurons are similar to "current dipoles" (Da Silva, 2010).
- These fields can be recorded by means of electrodes from the scalp.
- Each electrode records the electrical activity (radial) at a site *(active electrode)* relative to a distant site *(indifferent electrode)*, such as the ear lobe.

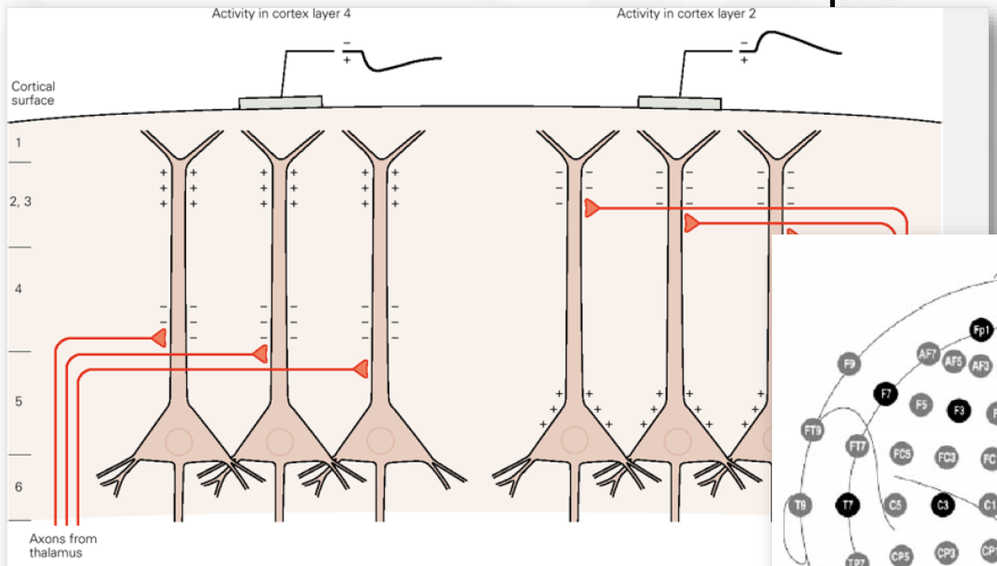


Figure 46-3 The polarity of the surface EEG depends on the location of the synaptic activity within the cortex. A thalam
(**left**) causes a downward deflection at the surface EEG electrode because the EEG electrode is nearer to the source. In contrast, e
contralateral hemisphere in layer 2 (**right**) causes an upward deflection because it is nearer to the sink.

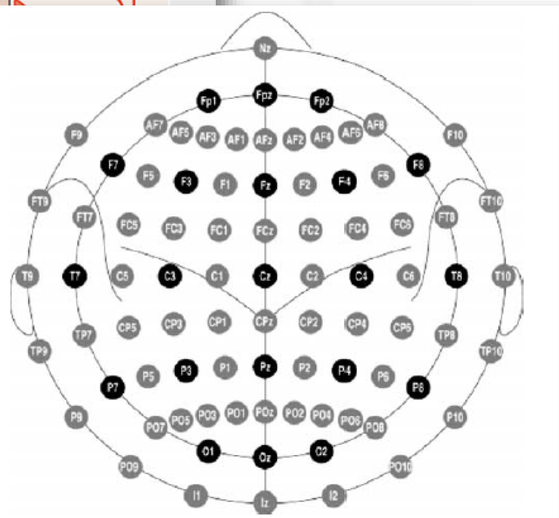
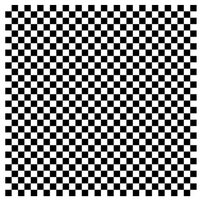


Figure 3.3. Electrode positions and labels in the International 10–20 System. Black circles denote electrode positions and labels from the 10–20 system; gray circles denote additional electrode positions and labels introduced with the 10–10 system. Reprinted from Clinical Neurophysiology, Vol. 112, Oostenveld, R. & Praamstra, P., The five percent electrode system for high-resolution EEG and ERP measurements, pp. 713–719, Copyright (2001), with permission from International Federation of Clinical Neurophysiology.

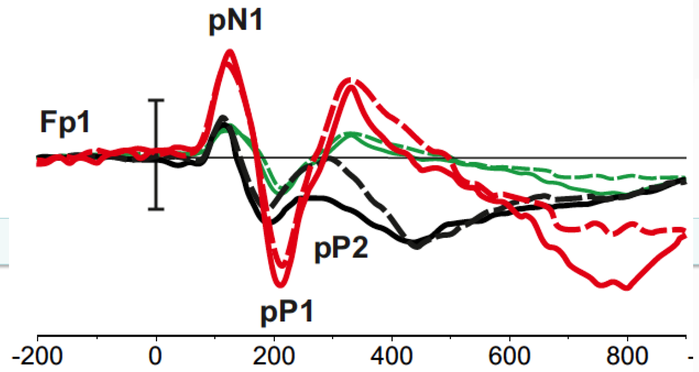
Electrophysiological measurements: ERP - VEP

Event-related potentials (ERP) are specifically time-locked to events and reflect brain activity from synchronously active populations of neurons that occurs in preparation for or in response to discrete events, be they internal or external to the subject. (Fabiani et al , 2007 in Cacioppo et al Handbook of Psychophysiology)

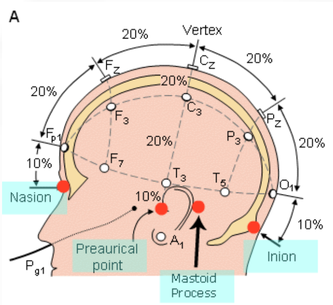


Stimulus onset

Electrodes on the scalp



at definite locations over the scalp



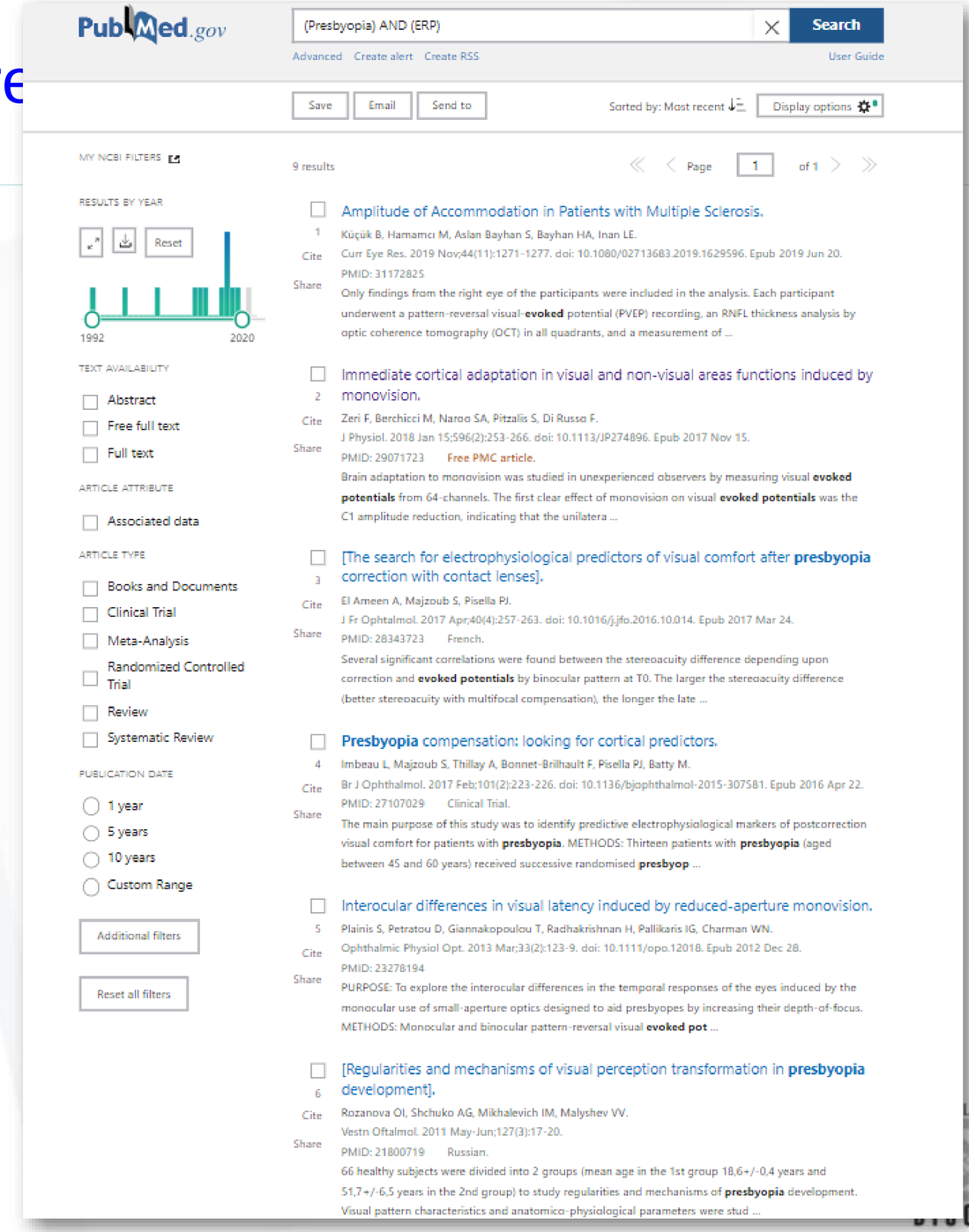
timeline

early (50-250 ms) components

late (300-600 ms) components

Electrophysiological measure

PubMed search was carried out for the keywords:
“Presbyopia” AND “ERP”
“Presbyopia” AND “VEP”
“Presbyopia” AND “EEG”



Electrophysiological measurements: ERP - VEP

Clinical science

Presbyopia compensation: looking for cortical predictors

Léa Imbeau,[1] Sadi Majzoub,[1] Alix Thillay,[2] Frederique Bonnet-Brilhault,[2] Pierre-Jean Pisella,[1] Magali Batty[2]

Imbeau L, *et al*. *Br J Ophthalmol* 2016;**0**:1–4. doi:10.1136/bjophthalmol-2015-307581

Is there a cortical predictor for successful adaptation to MCLs or Monovision?

Binocular summation effect results in a slightly shorter and larger binocular PI00 than monocular.

Either Monovision and MCLs impair binocular vision (i.e stereoacuity).

Their hypothesis is that the relative loss of stereoacuity resulting from monovision or MCLs might be better tolerated by patients in whom the binocular enhancement is slightly less.

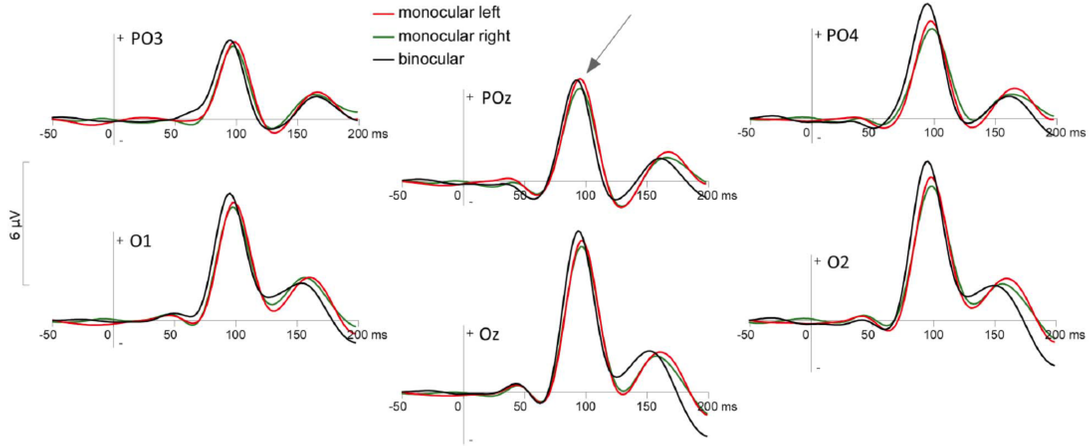


Figure 1 Grand averaged ERPs to pattern-reversing checkerboard stimuli at T0 from six electrodes (Oz, POz, O1, O2, PO3, PO4) recorded binocularly (purple lines) and monocularly (right in green lines and left in red lines). The arrow indicates the component P100 measured.

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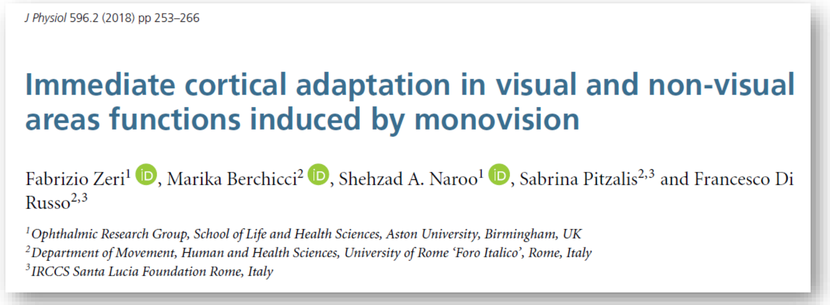
Brain Adaptation to MCLs: the BAM study

This study was partly supported by an investigator lead unrestricted grant from Alcon Italia Spa. The funding organization had no role in the design or conduct of this research.

Aim

To evaluate the brain correlates of initial adaptation to multifocal CLs through high-density visual evoked potential (VEP) measures in visual and non-visual brain areas.



J Physiol 596.2 (2018) pp 253–266

Immediate cortical adaptation in visual and non-visual areas functions induced by monovision

Fabrizio Zeri[1], Marika Berchicci[2], Shehzad A. Naroo[1], Sabrina Pitzalis[2,3] and Francesco Di Russo[2,3]

[1]*Ophthalmic Research Group, School of Life and Health Sciences, Aston University, Birmingham, UK*
[2]*Department of Movement, Human and Health Sciences, University of Rome 'Foro Italico', Rome, Italy*
[3]*IRCCS Santa Lucia Foundation Rome, Italy*

Subjects

Inclusion Criteria:

- Age 45-55 years.
- Not previously fitted with MCLs.
- Refractive error in the range -8.00 D and +4.00 D, with astigmatism up to 0.75 DC and an anisometropia lower than 2.00 D between the two eyes.
- Near addition required at 40 cm between +1.00 and +1.75 DS.
- Monocular BCVA at distance equal to or greater than 0.10 logMAR (20/25) in both eyes with a difference between the two eyes lower than 0.1 logMAR.
- Stereoscopic acuity of at least 160 arcsec.
- Having good binocular vision (no strabismus) and anomalies in ocular motility.
- Absence of any known ocular pathologies

- 15 healthy presbyopic people
- 6 males
- mean age 51.8 ± 2.6 years

Brain Adaptation to MCLs: the BAM study

Study Design: Prospective Single-masked Randomised Crossover

Far Distance

Monofocal CLs	MCLs Low Add	MCLs Medium Add
MSE at distance	MSE at distance distance (and add +0.25 binocularly) and low addition power	MSE at distance distance (and add +0.25 binocularly) and medium addition power

Near Distance

Monofocal CLs	MCLs Low Add	MCLs Medium Add
MSE at distance plus add for near	MSE at distance distance (and add +0.25 binocularly) and low addition power	MSE at distance distance (and add +0.25 binocularly) and medium addition power

Daily disposable CLs:
Dailies Total 1® Spherical / Multifocal (Low and Medium Add)
Delefilcon A, 33%H_2O core, ≥80% H_2O surface%, BOZR: 8.5 mm, TD:14.1 mm.

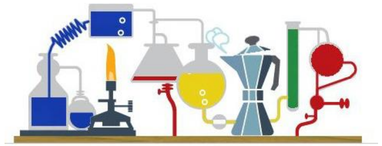
Brain Adaptation to MCLs: the BAM study

Stimuli

0.5 logMAR Sloan letters (SF 9.6 cpd)
high contrast (94%)

Two distances: 0.40 and 4 m.

Presented foveally for 250 ms with an ISI ranging from 1 to 2 s



Apparatus

-32-channel BrainAmp™ amplifiers (BrainProducts GmbH., Munich, Germany)

-64-channel electroencephalographic (EEG) active-cap

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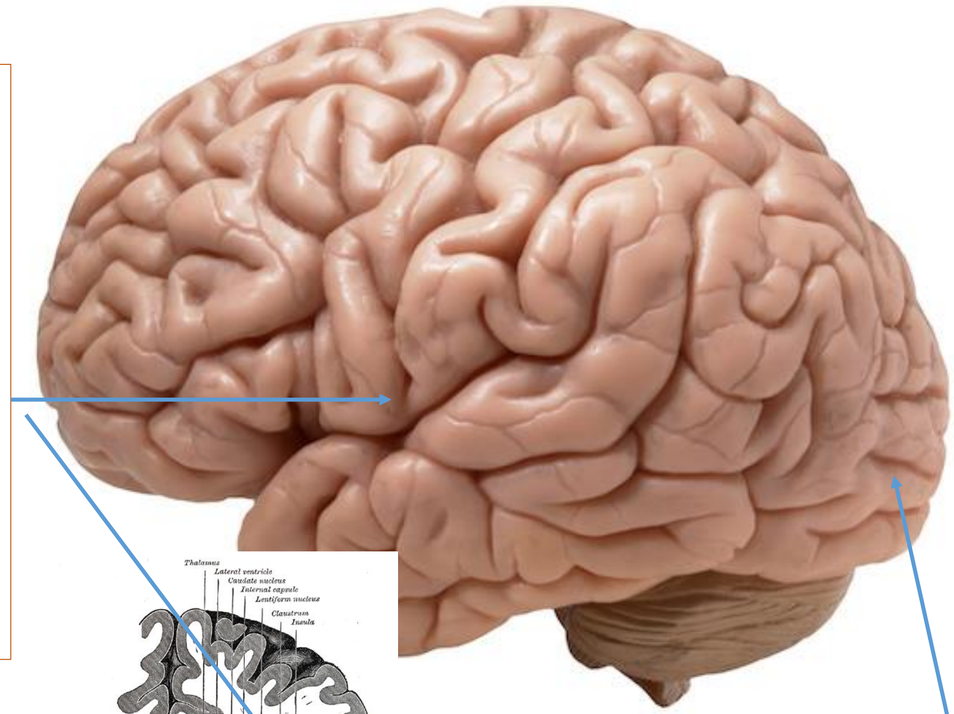
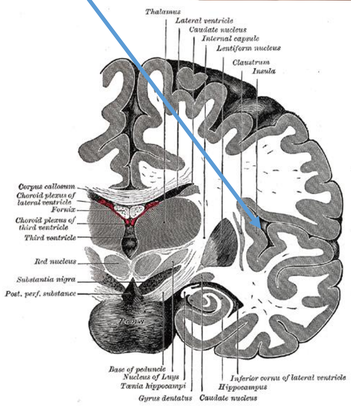
Dependent variables

Amplitude and Latency of Prefrontal Components
(anterior insula)

- **pN1**
- **pP1**
- **pP2**





Amplitude and Latency of early components

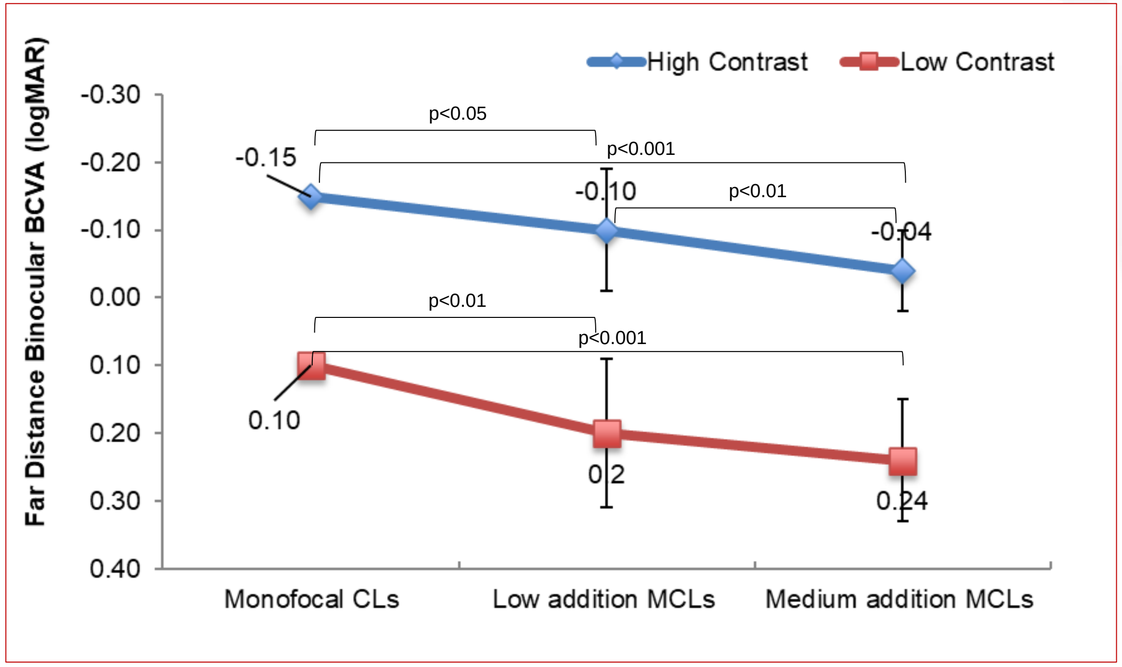
- **C1**
- **P1**
- **N1**

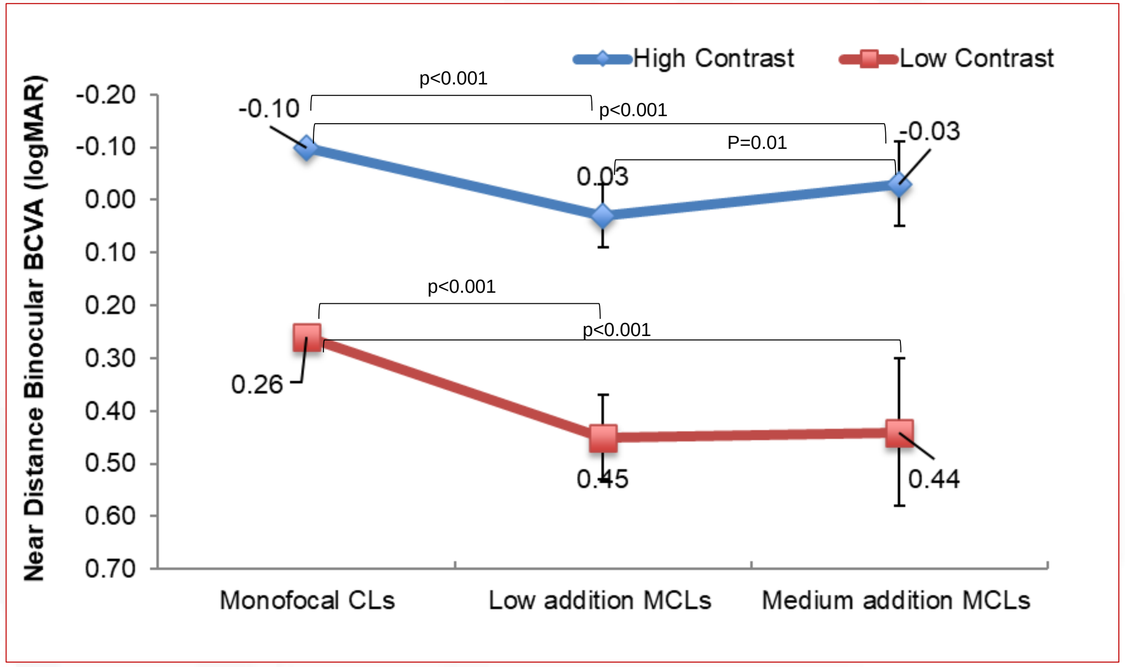
striate, extrastriate visual cortices

- **P2**

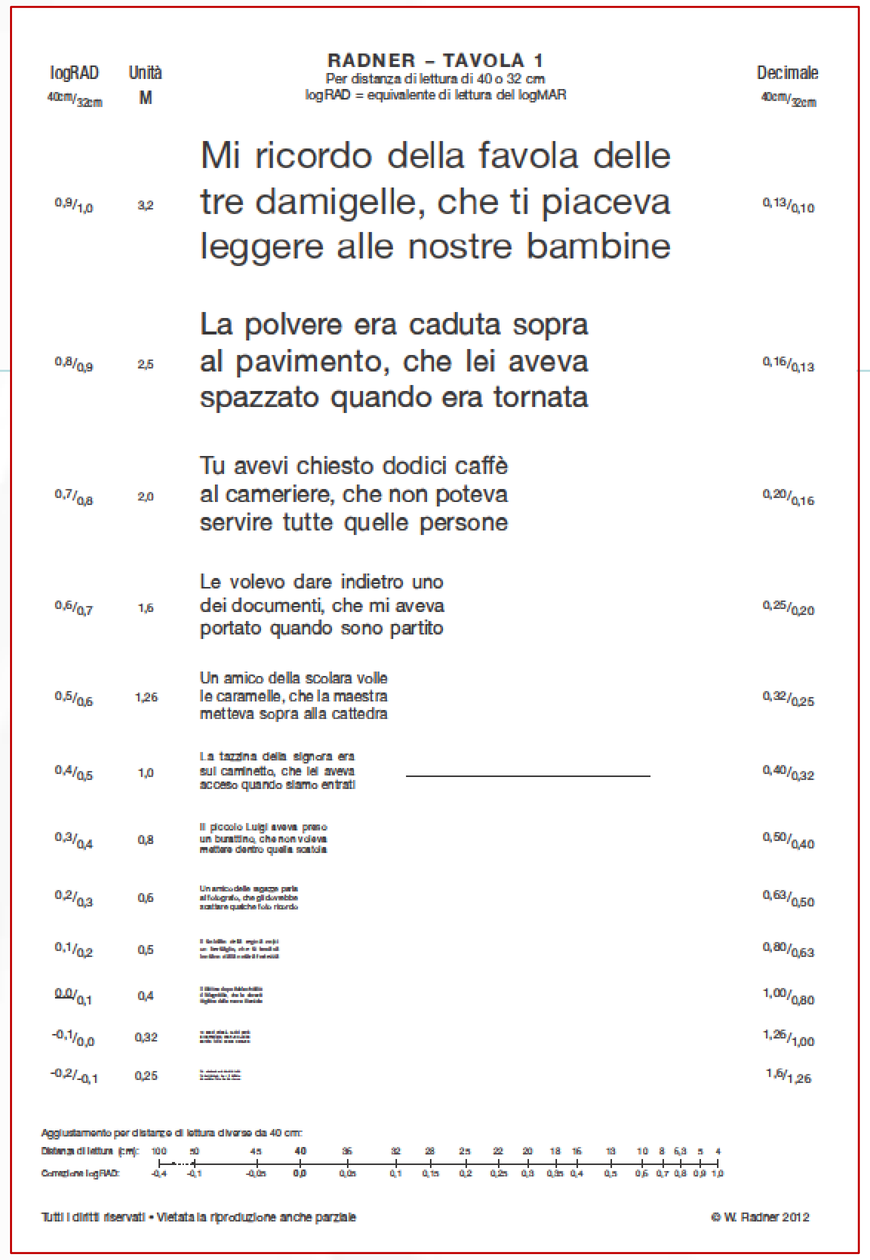
posterior parietal cortex

Results: visual assessment





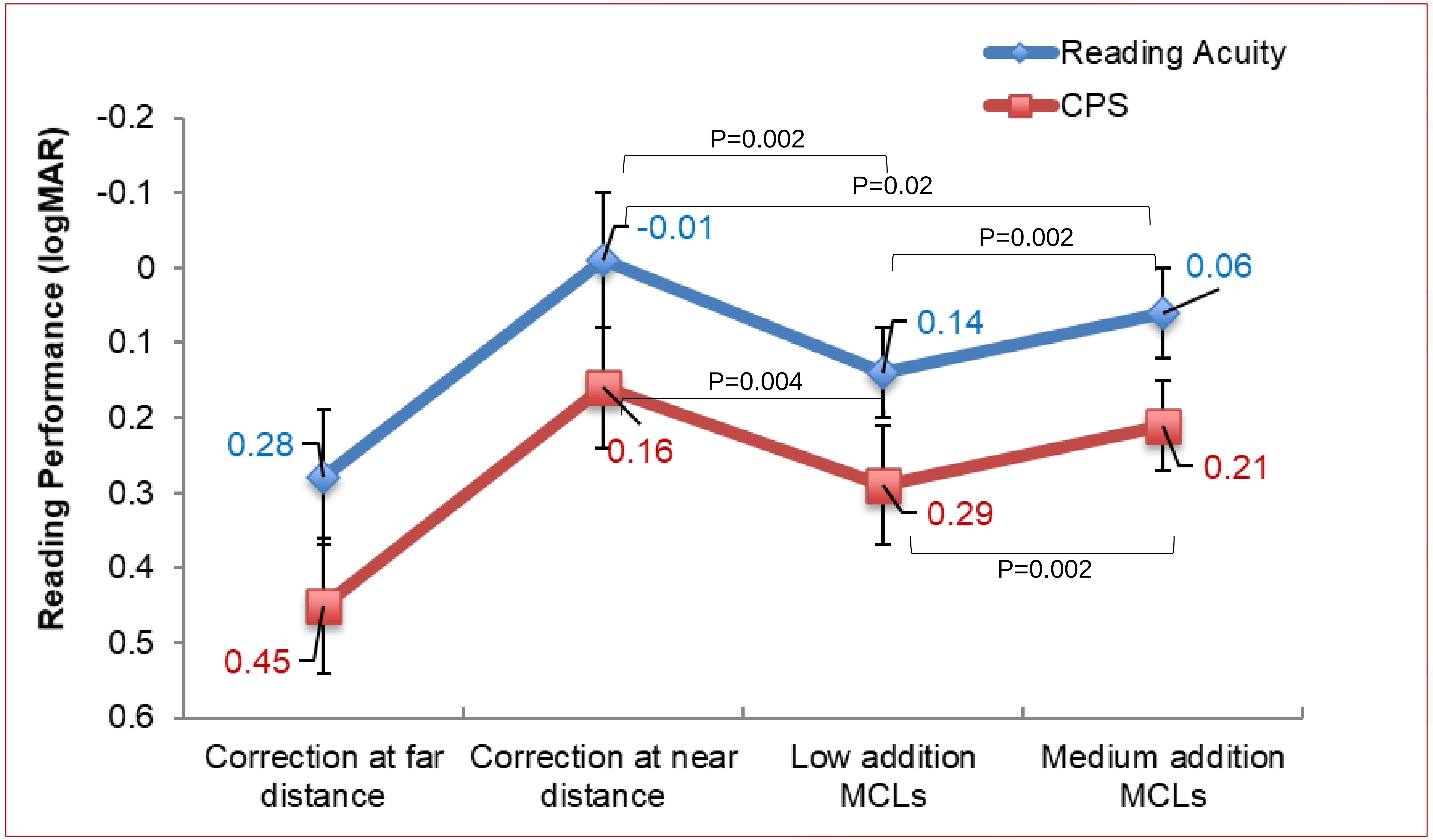
Results: visual assessment



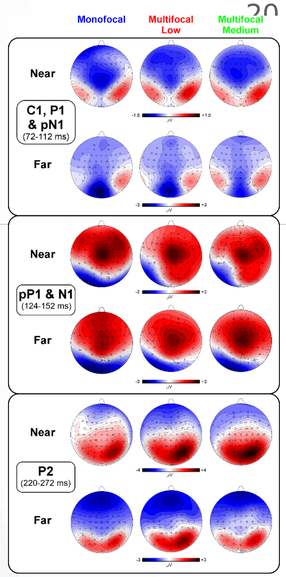
RADNER – TAVOLA 1
Per distanza di lettura di 40 o 32 cm
logRAD = equivalente di lettura del logMAR

logRAD 40cm/32cm	Unità M		Decimale 40cm/32cm
0,9/1,0	3,2	Mi ricordo della favola delle tre damigelle, che ti piaceva leggere alle nostre bambine	0,13/0,10
0,8/0,9	2,5	La polvere era caduta sopra al pavimento, che lei aveva spazzato quando era tornata	0,16/0,13
0,7/0,8	2,0	Tu avevi chiesto dodici caffè al cameriere, che non poteva servire tutte quelle persone	0,20/0,16
0,6/0,7	1,6	Le volevo dare indietro uno dei documenti, che mi aveva portato quando sono partito	0,25/0,20
0,5/0,6	1,26	Un amico della scolara volle le caramelle, che la maestra metteva sopra alla cattedra	0,32/0,25
0,4/0,5	1,0	La tazzina della signora era sul caminetto, che lei aveva acceso quando siamo entrati	0,40/0,32
0,3/0,4	0,8		0,50/0,40
0,2/0,3	0,6		0,63/0,50
0,1/0,2	0,5		0,80/0,63
0,0/0,1	0,4		1,00/0,80
-0,1/0,0	0,32		1,26/1,00
-0,2/-0,1	0,25		1,6/1,26

Tutti i diritti riservati • Vietata la riproduzione anche parziale © W. Radner 2012



Results: VEP components



Grand-averaged VEP waveforms for the three corrections (overlapped and displayed on electrodes pools)

Compensatory Activities

pP1 no changes
(anterior Insula, awareness of the sensory-motor integration)

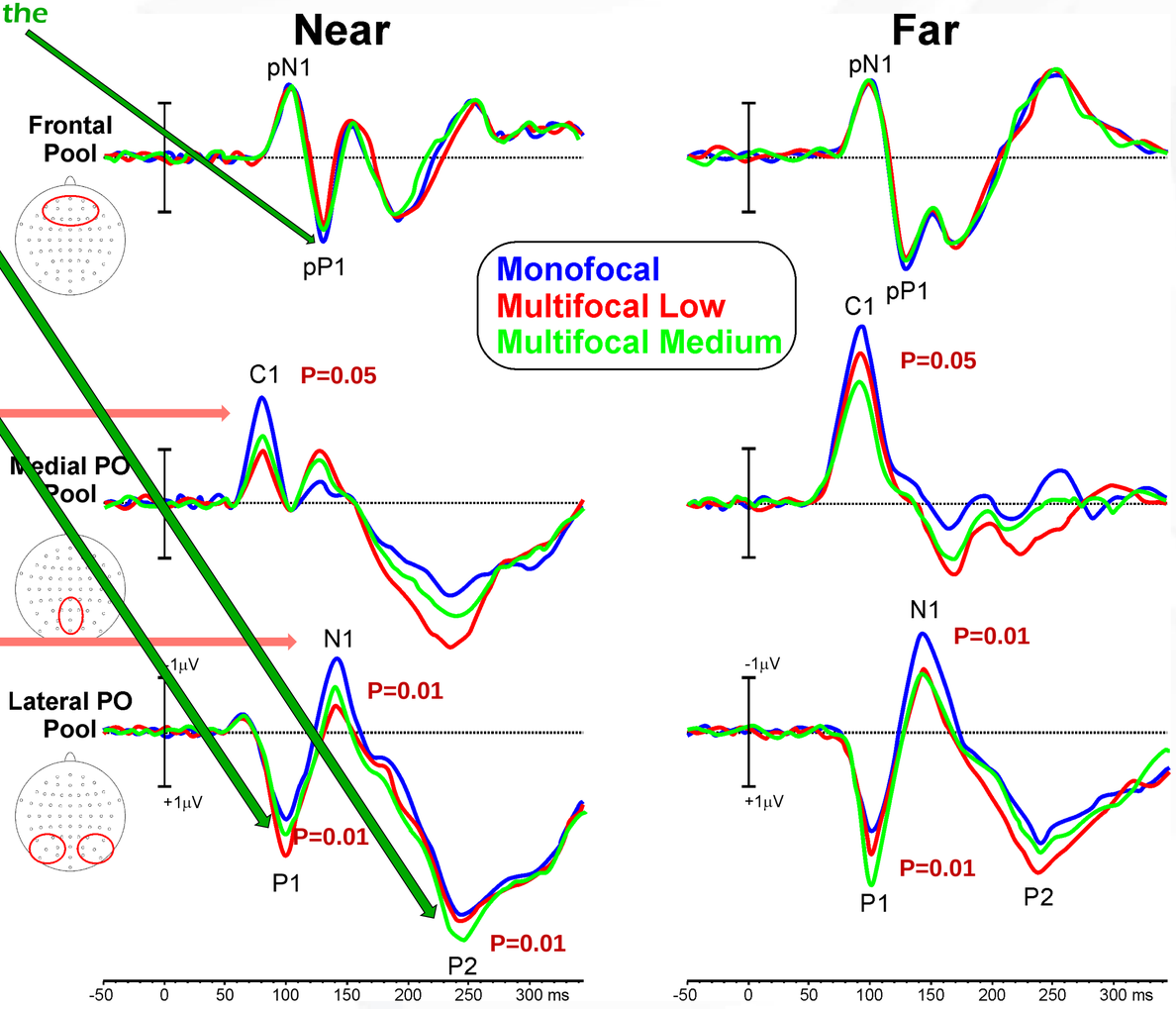
P2 amplitude increasing
re-entrant feedback activity from associative parietal areas to the visual cortex

P1 amplitude increasing
(V3A, attentional compensatory activity)

Inibition of the feed-forward activity

C1 amplitude reduction
(afferent volley in V1)

N1 amplitude reduction
(extrastriate visual areas, encoding stimulus)



Results: Monovision

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Immediate cortical adaptation in visual and non-visual areas functions induced by monovision

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[2]Department of Movement, Human and Health Sciences, University of Rome 'Foro Italico', Rome, Italy
[3]IRCCS Santa Lucia Foundation Rome, Italy

Grand-averaged waveforms

pP1 increasing is correlated with VA at distance in non-dominant eye and it is higher at far distance

Inibition of the feed-forward activity

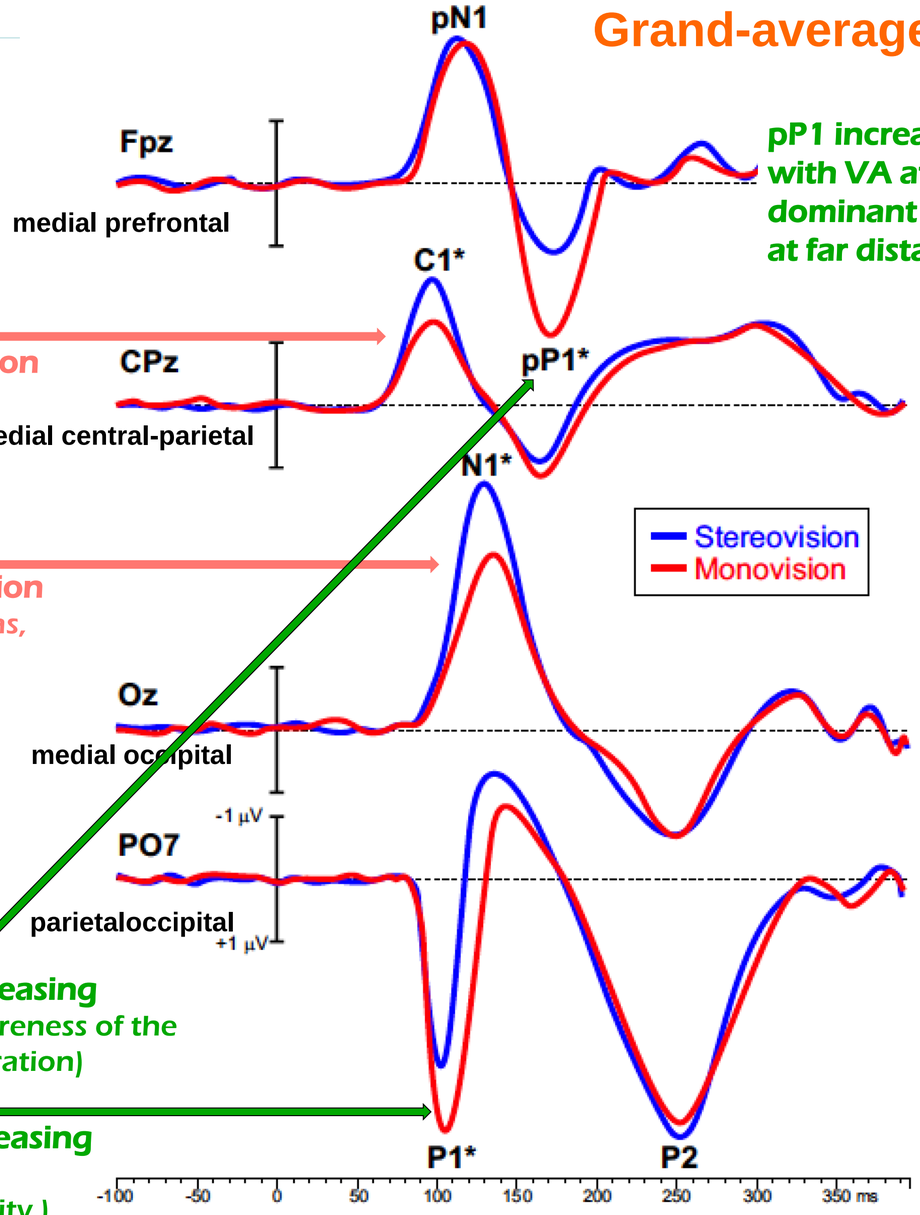
C1 amplitude reduction
(afferent volley in V1)

N1 amplitude reduction
(extrastriate visual areas, encoding stimulus)

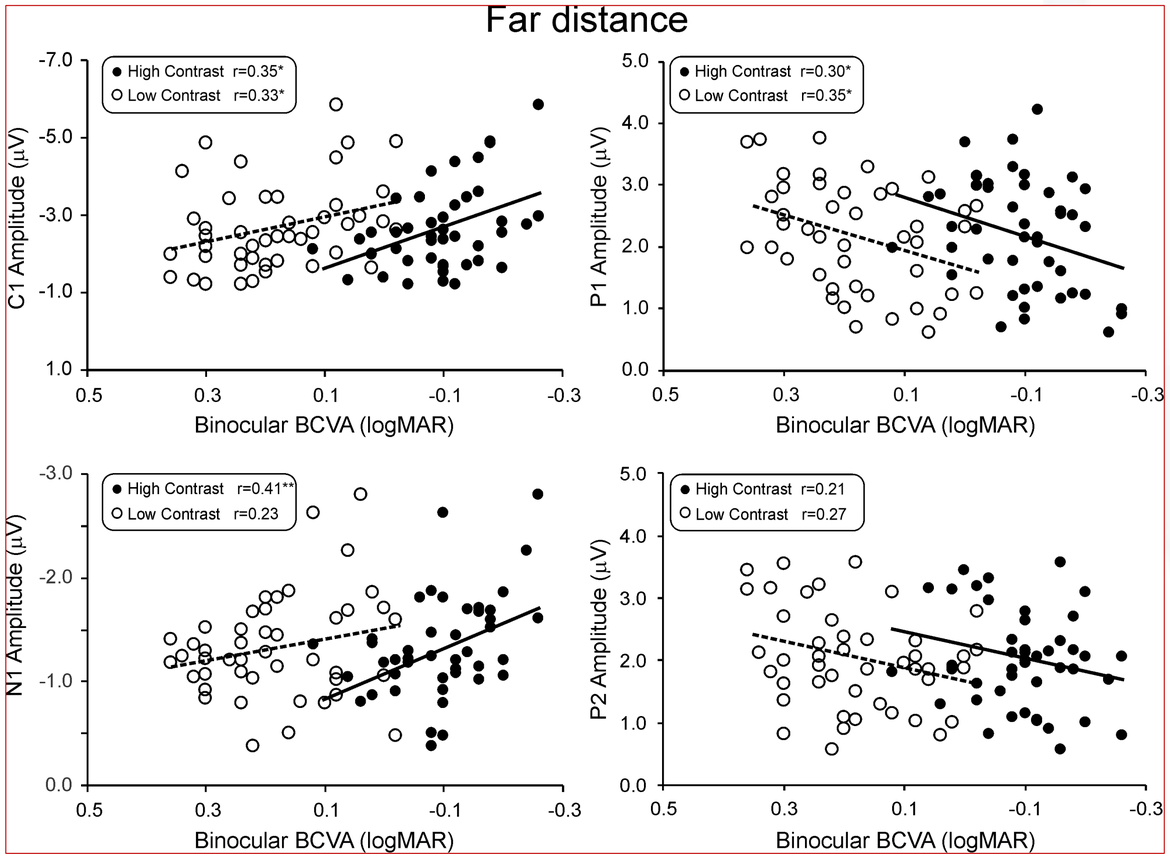
Compensatory Activities

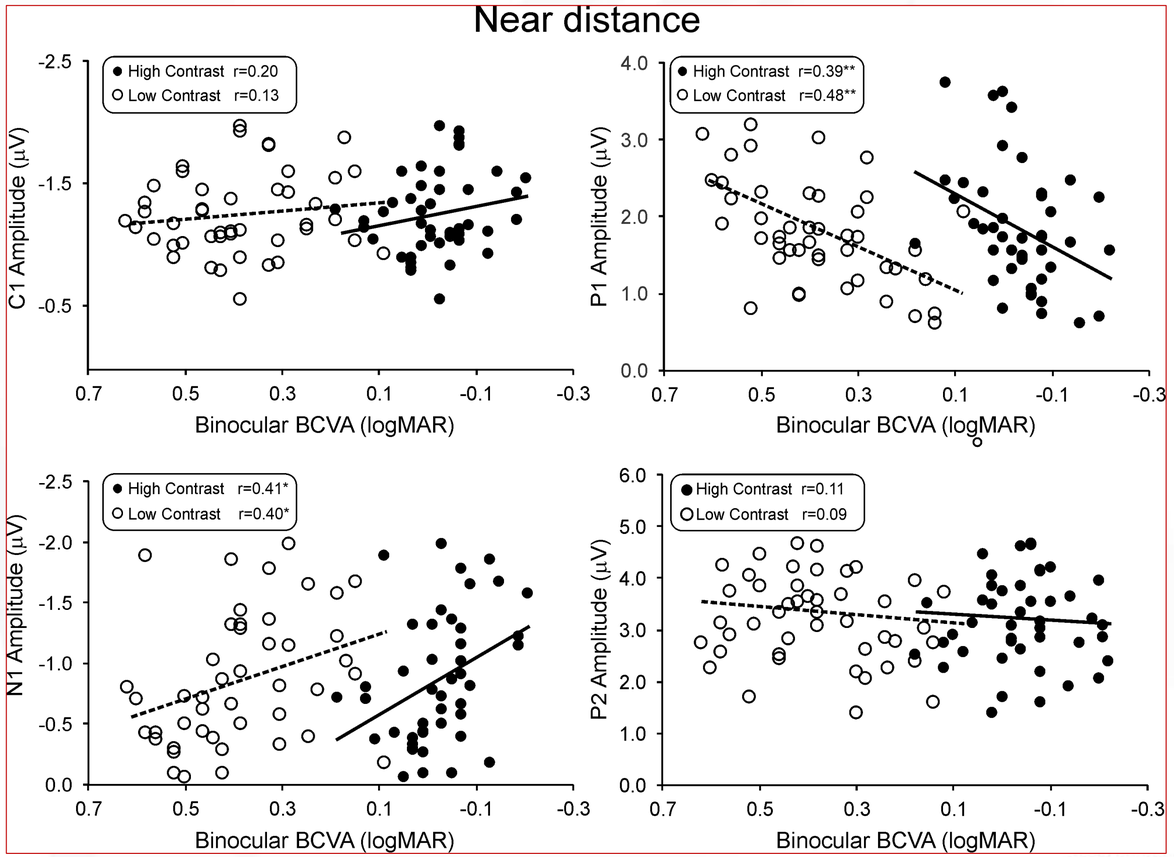
pP1 amplitude increasing
(anterior Insula, awareness of the sensory-motor integration)

P1 amplitude increasing
(V3A, attentional compensatory activity)



Results: correlation between VEP components and BCVA





so what?

Conclusions

- Compared to monofocal optics, MCLs induced:
  -**Visual signal reduction in primary visual cortex**: Reduction of feed-forward activity (decrease of C1 and N1 components amplitude)
  -**Compensatory activity in the extrastriate visual areas** : enhancement of P1 that could compensate the reduction of feed-forward activity in the primary visual cortex

- Considering the adaptation variability that characterizes this type of correction, future studies may verify the possible association of P1 amplitude changes with successful adaption to MCLs by looking for different ERP patterns in adapted and non-adapted patients

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