

Presbyopia compensation: looking for cortical predictors

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ABSTRACT

Background/aims New surgical techniques have recently been developed in order to compensate for visual impairment and to improve visual comfort for patients with presbyopia. However, the results are still variable, depending on the correction modality used and/or the patient. The main purpose of this study was to identify predictive electrophysiological markers of postcorrection visual comfort for patients with presbyopia.

Methods Thirteen patients with presbyopia (aged between 45 and 60 years) received successive randomised presbyopia compensation with contact lenses supplying monovision (one eye corrected for distance, the other for near vision) and simultaneous vision (progressive lenses). The period for each type of correction lasted for 3 weeks, with a 2-week break without any presbyopia compensation between the two test phases. Examinations were performed at entry (T0) and after each correction modality (Tmono and Tsimult). They included testing for near and distance visual acuity, stereoacuity, binocular contrast sensitivity and electrophysiological recordings (monocular and binocular visual evoked potentials).

Results Follow-up showed no significant differences between the two compensation modalities for either clinical or electrophysiological criteria. However, a significant correlation was found between the difference in TNO score (monovision–simultaneous vision) and the P100 latency evoked by the binocular pattern at T0, suggesting that late P100 latency could be associated with a lesser degree of decrease in stereoacuity with monovision.

Conclusions While our findings do not permit decisions regarding the superiority of one type of compensation over another, these preliminary results support using the P100 latency evoked by binocular patterns as a predictor of postcompensation stereoacuity.

Trial registration number NCT02444130, Pre-results.

INTRODUCTION

With the huge improvements in surgical techniques, the number of patients with presbyopia who do not want to wear glasses or contact lenses and who consider the solution of refractive surgery has increased considerably, and presbyopia correction has become the new refractive surgery challenge.

Different strategies of presbyopia compensation are available such as monovision and simultaneous vision. Previous studies have attempted to compare these two methods and have reported contradicting results and no clear difference in visual acuity (VA).^{1–4} However, the patients' ease and satisfaction may differ,^{5–7} with complaints about halos in

simultaneous vision⁸ and a decrease in stereopsis with monovision.⁹ While the success reported with monovision is quite high (between 70% and 80%),^{9–10} the reduction in stereoacuity that has been reliably reported^{9–11–12} affects performance in complex spatial-motor tasks, resulting in real and considerable difficulties in everyday life. One of the first studies in monovision correction reported that depth perception decreased with increasing anisometropia up to +2D.¹³ This relationship was then confirmed, revealing that loss of stereoacuity worsens with increasing monocular add powers.^{14–15} However, a loss of stereoacuity has also been reported with multifocal lenses,^{16–17} and problems with glare and halos has also been reported by patients with monovision.⁹

While ocular surgeons agree that the choice of the intervention must be made according to each patient's specific features and needs, no clear indices have been identified to determine which compensation works for whom. While the decrease in stereopsis is the most important reason why monovision does not always satisfy the demands of patients with presbyopia, the link between the initial tendency to rely on binocular vision and the real functional loss of stereopsis with monovision has never been investigated.

Electrophysiological correlates of binocular vision were identified >30 years ago. The differences between visual evoked potentials (VEPs) to pattern stimuli recorded during monocular stimulation and those recorded during binocular stimulation have been widely used to test visual functions in children and adults. The well-known binocular summation effect results in a slightly shorter and larger binocular P100 than monocular.^{18–20} Moreover, the binocular summation effect does not occur when binocular vision is absent, it has therefore been proposed as a marker of binocularity.

The main purpose of this study was to identify electrophysiological markers that could be predictive of ease and satisfaction after presbyopia compensation. We believe that the individual assessment of binocular vision, including binocular VEPs, could offer objective assistance when deciding between the different strategies in order to ensure individual personalised treatment. The underlying physiological hypothesis is that the relative loss of stereoacuity resulting from monovision might be better tolerated by patients in whom the binocular enhancement is slightly less. This study, therefore, compared monovision and simultaneous vision by investigating both clinical aspects and electrophysiological responses.



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METHODS

Seventeen young (45–60 years of age) presbyopic subjects were tested in this event related potentials (ERP) study. All participants were recruited from the ophthalmologic centre of the University Hospital of Tours where they were seeking correction of presbyopia via surgery. The exclusion criteria comprised neurological disorders, ocular diseases such as cataract, absence of binocular vision (assessed with TNO plates) and prior experience with monovision or multifocal contact lenses. For technical reasons (mostly manipulation of contact lenses) only 13 participants (mean age = 52 ± 4.3 years; 10 females) were entered in the analysis. Four of them were myopic (31%), six hyperopic (46%), two astigmatic (15%) and one emmetropic (8%). All subjects were appropriately corrected, their initial binocular VA being $\geq 20/20$. All participants gave informed written consent. The study was performed in accordance with the ethical standards laid down in the Declaration of Helsinki and was approved by the Ethics Committee of Tours Hospital, France.

For each participant, presbyopia was compensated for with contact lenses (CooperVision Biofinity) by monovision for 3 weeks (anisometropia ranged from 1 to 1.5 D) and simultaneous vision (further 3 weeks) with a 2-week break without presbyopia compensation placed between the two randomised phases of the test. Addition in monovision conditions ranged from 1.00 to 1.75 D (average addition = 1.50 D). Additions in multifocal conditions ranged from 1.00 to 2.00 D (with an average addition of 1.77 D). For monovision conditions, the dominant eye (determined with the hole-in-the card test) was fitted with the distance lens and the non-dominant eye with the near lens. For simultaneous vision conditions, we used the Coopervision nomogram with D lens for the dominant eye and N lens for the non-dominant eye. Proclear toric multifocal lenses were used for patients with astigmatism.²

All subjects were tested three times: that is, before any compensation (T0), after 3 weeks with monovision (Tmono) and after 3 weeks with simultaneous vision (Tsimult). Each testing session was exactly the same, including visual examinations and VEPs to pattern-reversing checkerboard stimuli:

- ▶ The vision examination consisted of testing for monocular and binocular VA at far and near distances (Monoyer and Parinaud scales, respectively), quantitative measurement of stereopsis (with TNO plates), oculomotor evaluation and contrast sensitivity measurement (six frequencies tested between 0.6 and 14.2 cycles per degree with photopic conditions set at 90 cd/m² using MonPack3@Metrovision).
- ▶ During each test session, VEPs to pattern-reversing checkerboard stimuli were recorded binocularly and monocularly in random order. Subjects were seated in a comfortable armchair at an observation distance of 130 cm from a monitor. A black and white checkerboard pattern with a reversal rate of 1/s and a visual angle of 15° was delivered (check size 1°). Electroencephalographic data were recorded using a 64 channels Biosemi ActiveTwo system (BioSemi, The Netherlands). The signal was recorded at a sample frequency of 512 Hz and filtered at 0–104 Hz. Data were referenced offline to the common average potential and a 0.3 Hz digital high pass filter was applied.²¹ Additional electrodes were applied below the right eye, allowing automatic correction for horizontal and vertical eye movements (independent component analysis), and movement artefacts were discarded manually. The ELAN software package was used for analysis. A minimum of 200 trials was then averaged over a 700 ms analysis period, including a 100 ms prestimulus baseline, and were filtered digitally (low pass at 30 Hz). Maximum amplitudes and peak

latencies of the P100 were measured at the electrode sites of interest (Oz, POz, O1, O2, PO3, PO4) for each subject within a 40 ms time window around the peak of the grand average waveform.

For each session, P100 characteristics (amplitude and latency) were submitted to repeated measures analysis of variance (ANOVA) according to stimulation condition (three levels: binocular, monocular left, monocular right), hemisphere (three levels: central, left, right), electrode site (two levels: occipital vs parieto-occipital) as within-subject factors. All results were corrected for multiple comparisons using the Greenhouse–Geisser test. Significant interactions were followed by Bonferroni post hoc comparisons to determine where the differences lay. An α level of 0.05 was used for all statistical tests.

A Friedmann test was used to assess the clinical effects of compensation (T0, Tmono, Tsimult) on VA and TNO score. Follow-up of VEP was submitted to ANOVA repeated measures according to compensation method (three levels: T0, Tmono, Tsimult), hemisphere (three levels: central, left, right) and electrode site (two levels: occipital vs parieto-occipital). Finally, Spearman correlations were then computed between clinical and electrophysiological data.

RESULTS

Mean VA at entry was 12.9/10 (± 2.78) P1,5, the mean stereoacuity was 76 s arc (± 56.9). The mean contrast sensitivities for low, mean and high frequencies were, respectively, 19.8 dB (± 2.7), 23.7 dB (± 1.7) and 17.1 dB (± 5.5) in photopic conditions.

The waveforms elicited by monocular and binocular stimulation at T0 are shown in figure 1. A main effect of the stimulation condition was found on P100 latency at T0 ($F(2,13) = 10.40$, $p < 0.002$, $\eta_p^2 = 0.46$, power = 0.98). Post hoc comparisons revealed that P100 latency evoked by binocular stimulation was significantly earlier than when evoked by right or left monocular stimulation ($p = 0.001$ and $p = 0.002$, respectively), confirming the binocular summation effect (figure 2). A main effect of hemisphere was also found on P100 latency ($F(2,13) = 7.54$; $p = 0.007$, $\eta_p^2 = 0.38$, power = 0.92) and amplitude ($F(2,13) = 15.39$, $p < 0.001$, $\eta_p^2 = 0.56$, power = 1), revealing an earlier and larger P100 at central occipital sites than at lateral sites ($p < 0.003$; $p < 0.001$).

When assessing the effects of compensation, the analysis revealed a reduction in VA at far distance after compensation (VA at T0 = $12.9/10 \pm 2.8$ vs VA at Tmono = $10.5/10 \pm 1.66$ and VA at Tsimult = $10.8/10 \pm 1.01$) and a difference in stereopsis scores (TNO at T0 = 76 ± 57 s arc vs TNO at Tmono = 327 ± 178 s arc and TNO at Tsimult = 171 ± 109 s arc). However, none of these differences reached significance when comparing monovision and simultaneous vision. Moreover, no significant difference was found between the two compensation modalities with regard to contrast sensitivity (whatever the frequency used) or near VA. Neither did the characteristics of the binocular P100 change according to the compensation strategy.

Correlations were computed to investigate whether any patient characteristics at T0 could be predictive of preference between the two compensation strategies. A significant correlation was found between the initial binocular P100 latency and the difference in stereoacuity (Tmono–Tsimult): the earlier the P100 latency to the binocular reversal pattern at T0, the greater the loss of stereoacuity with monovision (vs simultaneous vision) ($R = -0.58$; $p < 0.05$). Figure 3 illustrates the P100 evoked by the binocular pattern at T0, for two subgroups of subjects according to their differences in stereoacuity between monovision and simultaneous vision.

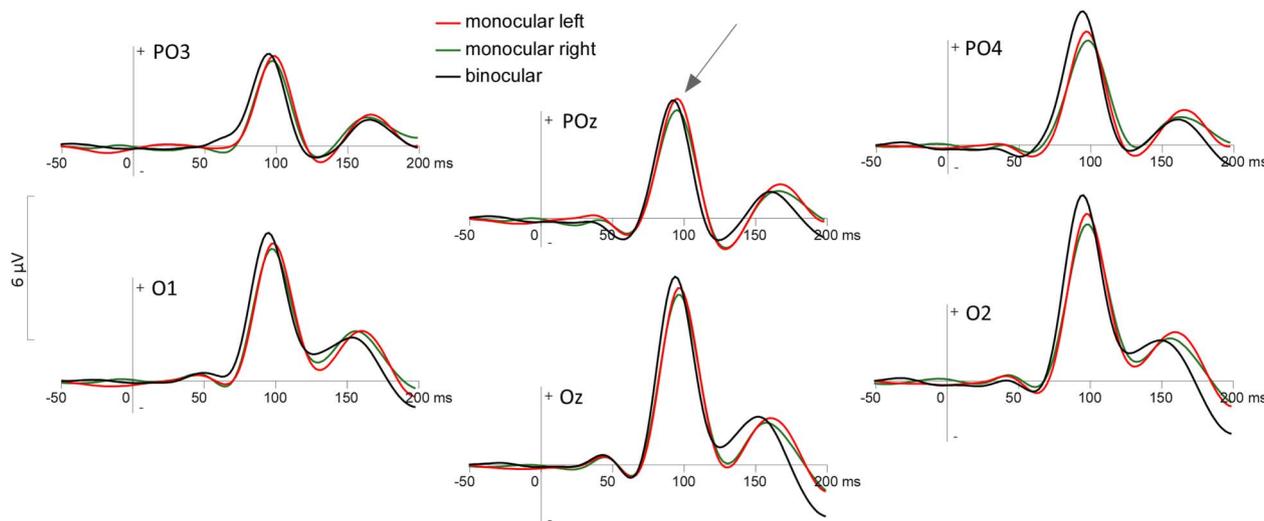


Figure 1 Grand averaged ERPs to pattern-reversing checkerboard stimuli at T0 from six electrodes (Oz, POz, O1, O2, PO3, PO4) recorded binocularly (purple lines) and monocularly (right in green lines and left in red lines). The arrow indicates the component P100 measured.

DISCUSSION

In the face of the dilemma ocular surgeons meet when they have to decide between the different compensation methods available, it has become urgent to define objective criteria that could help in making this choice. There has, therefore, been an increase in studies comparing presbyopia compensation strategies. Unfortunately, just as the results reported in the literature are very contradictory, our study failed to reveal significant clinical differences between monovision and simultaneous vision.

While far VA did not differ between monovision and simultaneous vision, it decreased significantly after compensation for presbyopia. Most of the studies that investigated refractive surgery (monovision or simultaneous vision) involved patients with cataract,^{2,3} who by definition had lower initial VA than the subjects included in the present study, for whom the VA improved after surgery due to cataract removal. However, studies investigating outcomes with multifocal and/or monovision contact lenses reported consistent loss of VA for both lens types.^{10,12,22} In agreement with these previous studies, the slight loss of VA between baseline and the correction offered by both contact lenses was clinically small and of little importance to the patients who maintained adequate vision (better than 20/20).

On average, our results revealed a 251 s arc loss of stereoacuity between T0 and monovision, which constitutes the most important complaint from patients. However, neither this loss between T0 and Tmono nor the difference between Tmono and Tsimult (156 s arc) reached significance in the present study. In the study by Richdale *et al*,¹² the loss of stereoacuity from baseline to monovision was less (56 s arc) than ours and also not significant. However, they reported a significant difference between monovision and simultaneous vision (79 s arc) in agreement with most previous studies.^{7,9,22–24} While the small sample size of our study ($n=13$ vs 38 in Richdale's study) could partly explain this absence of significant difference, the very high SD could also be a cause (TNO at T0= 76 ± 57 s arc vs TNO at Tmono= 327 ± 178 s arc and TNO at Tsimult= 171 ± 109 s arc). Although this heterogeneity might explain why the statistical analysis did not reach significance, it is also the main reason for wishing to adapt the correction method for each subject according to individual characteristics. However, the loss of stereoacuity measured with the TNO test could have been enhanced by measuring the impact of such loss in everyday activities.

While all previous studies comparing presbyopia compensation strategies have been based on subjective data such as

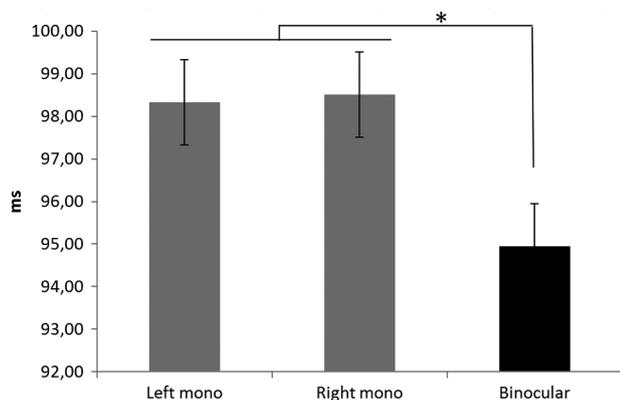


Figure 2 Mean latencies (ms) of the P100 component at entry recorded in left and right monocular condition (grey) and in binocular condition (black). The significant earlier P100 latency evoked by binocular stimulation confirms the binocular summation effect.

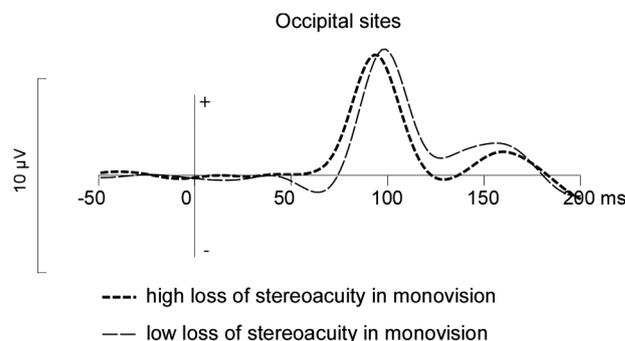


Figure 3 Visual evoked potentials (VEPs) to pattern-reversing checkerboard stimuli recorded binocularly at T0, averaged from the six occipital electrodes. Subjects were divided in two groups according to their differences in stereoacuity between monovision and simultaneous vision (Tmono–Tsimult). The VEP averaged from the six subjects having the greatest loss of stereoacuity with monovision (compared with simultaneous vision) revealed a shorter P100 latency at T0.

self-appreciated ease and/or on VA assessments, our study is unique in that an electrophysiological marker was investigated. In accordance with the retinotopic organisation of the visual cortex, P100 was earlier and larger when recorded on midline occipital electrodes than on lateral occipital sites. As expected, the latency of the monocular P100 was longer than that of the binocular P100 (binocular summation effect). During normal development, the binocular summation effect has been reported to parallel the acquisition of binocular function.¹⁸ This gain in P100 latency persists in adults with normal visual function, while it is not found when binocular vision is absent,²⁰ suggesting that the binocular P100 might be a good marker of stereopsis.

As monovision challenges visual pathways and binocular vision, our initial hypothesis was that monovision would be better tolerated in subjects whose stereovision is lower at baseline, that is, subjects having a later (and possibly smaller) binocular P100 than in monocular conditions (and conversely, multifocal compensation would be preferred by subjects with an earlier (and larger) P100). This hypothesis was confirmed because the subjects for whom the loss of stereoacuity in monovision was the greatest presented the earliest binocular P100 at entry.

Many studies have examined and compared the advantages and disadvantages of monovision and simultaneous vision, mostly with contradictory results. This variability of results could at least partly be explained by the heterogeneity of the protocol designs used. While some studies compared two groups of patients, each study testing only one presbyopia correction, other studies chose a cross-over test. Another important difference is the interval chosen for outcome measurements, classically ranging from 1 week to 3 months. While our study compared the two lens types in the same group of patients, we chose a 3-week interval for assessment of outcome measures in order to avoid too long a period with a correction type that did not suit the patient and might cause inconvenience. We suspect that this short period might not have been sufficient for neuro-adaptation, and therefore, that our data might not offer insight into the final status of stereoacuity. In a recent study comparable to ours, with a larger sample of subjects and a 2-week interval, subjects were asked to complete subjective rating surveys four times over the 2 weeks.⁷ The results revealed a significant decrease in the ratings over this time, suggesting progressive adaptation of the subjects to the correction. These findings confirm the importance of taking into account the adaptation period when comparing data from different studies and the need to monitor the outcomes longitudinally and not at one point in time.

CONCLUSION

Because of the high SD in stereoacuity and the limited sample of patients with presbyopia was tested, we consider that our findings are preliminary and need to be confirmed with a larger sample. Although the optical concepts of intraocular lenses and contact lenses are different, we believe that the results after contact lens wearing can be extrapolated to intraocular lenses, particularly in cases of unsuccessful adaptation to monovision. Finally, due to the significant correlation between the binocular P100 latency to a checkerboard pattern and the stereoacuity after presbyopia compensation, we suggest the systematic use of visual ERP recordings (non-invasive, easy and quick to include in routine assessments) in the presurgery examination of patients with presbyopia who do not want to wear glasses or

cannot use contact lenses in order to guide the selection of correction method.

Contributors LI, SM, AT, FB-B, P-JP, MB have provided substantial contributions to the conception or design of the work, the acquisition, analysis and interpretation of data for the work. All the authors were involved in drafting the work, revising it critically for important intellectual content. All the authors have given their final approval of the version to be published, and their agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Competing interests None declared.

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