The Effect Of Reduced Pupil Size In Normal Young And Older Adults On Pattern Reversal Visual Evoked Potentials

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ABSTRACT

Visual evoked potential (VEP) responses are affected by ageing in otherwise healthy adults. Ageing also causes pupil miosis. However, the relationship between pupil size and VEP responses is unclear. In this study, we measured VEPs in young adults and compared the responses to those obtained in older adults, and those of young adults with reduced pupil size, achieved with prosthetic contact lenses, to mimic pupil miosis.
Methods: Pattern reversal VEP were recorded in 12 healthy subjects (20-60 years old) divided into three groups: (1) young adults (pupil size ≥5 mm), (2) young adults wearing prosthetic contact lens with 3mm pupil aperture, and (3) older adults with pupil size ≤3mm. P100 latencies and amplitudes were compared between these groups.
Result: Older adults showed significant reduction in P100 amplitude, but not P100 latency, compared to young adults. Reducing pupil size in young adults significantly reduced their P100 amplitude but not P100 latency. The difference in P100 amplitude and latency in young adults with reduced pupil size (3mm) was not significantly different to those of older adults whose pupil size was ≤3mm.
Conclusion: Reduced pupil size causes the retinal illumination to reduce and lead to reduction of P100 amplitudes in older adults. Our results indicate that reduced P100 amplitude in an otherwise healthy visual system is largely contributed by reduced pupil size. However, reduced retinal illumination does not appear to affect P100 latency in both young and older adults regardless of pupil size.

Keywords: Healthy ageing, visual evoked potential, pupil size, P100 amplitude, P100 latency

INTRODUCTION

The eye and certain visual functions decline with normal ageing, that is, in the absence of pathology or disease. During normal aging, retinal image quality decreases due to increased aberration (Artal, Guirao, Berrio, Piers, & Norrby, 2003). It is well established that there are also age associated declines in visual acuity (Weale, 1975), dark adaptation (McFarland, Domey, Warren, & Ward, 1960), and colour perception (Ohta & Kato, 1976). In addition, aging causes the cornea to lose its sensitivity (Millodot, 1977), the anterior chamber to become shallower (Haegerstrom-Portnoy & Morgan, 2007), senile miosis (Haegerstrom-Portnoy & Morgan, 2007; Winn, Whitaker, Elliott, & Phillips, 1994), presbyopia and selective absorption of light by the crystalline lens (Mellerio, 1987), together with sensorimotor and cognitive functions (Li & Lindenberger, 2002).

Cortical responses can be measured non-invasively using Visual evoked potential (VEP). VEP is an electroencephalographic (EEG) signal generated by visual stimuli and is recorded by placing an electrode associated with the skin over the scalp in the occipital area (Lam, 2005). Pattern reversal VEP, produced when the patient observes a checkerboard pattern that reverses in polarity at a specified frequency, is widely used clinically (Sharma, Joshi, Singh, & Kumar, 2015). VEP responses are known to be affected by age (Gupta & Gupta, 2016; Lek, Nguyen, McKendrick, & Vingrys, 2019; Mitchell, Howe, & Spencer, 1987; Porciatti, Burr, Morrone, & Fiorentini, 1992), gender (Gupta & Gupta, 2016; Sharma et al., 2015), visual acuity (Soares et al., 2016) and retinal illumination (Sokol, Moskowitz, & Towle, 1981).

VEP parameters, namely P100 latency and P100 amplitude, change with age (Sokol et al., 1981). These parameters are of interest as they reflect the integrity of the visual pathway, which may be altered even in the absence of any pathology. Pattern reversal VEP responses depend on the integrity of the visual pathway from retina to the primary visual cortex (Odom et al., 2010), other visual cortical areas (Di Russo et al., 2007) and feedback contributions from extrastriate cortical areas to the primary visual cortex (Salin & Bullier, 1995).

P100 latency approaches adult levels at about 20 years old and does not change significantly at the age of 20 to 59 years followed by an increase after the age of 59 (Allison, Wood, & Goff, 1983; Shaw & Cant, 1981). Similar findings on increase P100 latency are also reported in more recent studies (Gupta & Gupta, 2016; Lek et al., 2019). These changes could reflect a true effect of healthy ageing on VEP

responses, reflecting deterioration of the visual pathway. However, it could also be due to physiological changes that occur during healthy ageing, such as pupil miosis which would result in reduced retinal illumination thus alters VEP responses in older adults. Sokol et al. (1981) estimated that a change in pupillary diameter from 5 mm at age of 20 years to 3.5mm at age 80 years resulted in 0.3 log unit decrease in retinal illuminance.

In this study, we measured P100 amplitude and P100 latency in young (20-35 years old) and older adults (55 to 60 year olds), whose pupil sizes were ≥5mm and ≤3mm, respectively. The parameters were also measured in young adults wearing prosthetic contact lens with 3mm pupil diameter. This would have allowed the responses of these young adults to be compared with those of older adults while controlling the pupil size variable, enabling us to determine if changes in VEP responses were solely due to healthy ageing, or due to reduced pupil size i.e. reduced retinal illuminance.

MATERIALS AND METHODS

Participants were nine young adults aged between 20 to 35 years old and older adults aged between 55 to 60 years old. All participants had corrected visual acuity of logMAR 0.1 or better. Those with history of ocular and/or systemic diseases were excluded. All participants were informed of the objectives of the study and gave their informed consent before data collection was commenced.

VEP recording tool place at the Visual Electrophysiology Suite housed within the Optometry & Vision Science Programme, Universiti Kebangsaan Malaysia. A RETI-port/Scan 21 (Roland Instruments, Germany) was used in this study. Participant's preparation followed ISCEV standard for VEP protocols. Gold disc electrodes with diameter of 10 mm (Bradenburg, Germany) were used to record VEP. The distance between each participant's inion and nasion were measured and active electrode was placed at Oz (10% above the inion). Reference electrode was placed at Fz (30% above nasion). Ground electrode was placed at the temple. Prior to electrode placement, the skin and scalp were cleaned using NuPrep Skin Prepping Gel. Then, Ten-20 Conductive Paste was used to secure the electrode cup on the scalp to ensure stable electrical connections between the scalp and the electrodes. The electrode impedance was kept below 10 kΩ as per manufacturer's recommendation.

The stimuli used was a black and white checkerboard. VEP responses were recorded for two check sizes (60 arcmin and 15 arcmin). The checkerboard reversed in polarity at a rate of three reversals per second (frequency of 1.5 Hz). All stimuli were displayed on a 19" cathode ray tube monitor. VEP stimuli were presented to the participant's dominant eye while the other eye occluded with a soft black patch. Throughout the procedure, participants maintained their fixation on a red cross in the centre of the checkerboard pattern. For each experimental run, VEP recording were averaged from 100 pattern reversals for each stimulus size.

VEP were recorded in the young adult group with their natural pupils (pupil size ≥5 mm) first. Recording was repeated with the young adults with 3.00 mm pupil size achieved by wearing a Soflex prosthetic contact lens (base curve 8.60 mm, diameter 14.50 mm). VEP were recorded in older adult participants with their natural pupils (pupil size ≤ 3.00 mm). The Ethics Committee of Faculty of Health Sciences, Universiti Kebangsaan Malaysia approved the conduct of this research (UKM 1.21.3/244/NN-2018-067).

RESULTS

Table 1 compares latency and amplitude of the P100 parameter for young adult group (pupil size ≥5.00 mm) and older adult group (pupil size ≤3.00 mm). Independent t-test revealed that the difference in P100 latency between these groups was not significant for stimulus size 60 arcmin [$t_{(10)}$=-1.08, p=0.31] and 15 arcmin [$t_{(10)}$=-1.29, p=0.23]. However, the difference in P100 amplitude between these groups was statistically significant for stimulus size 60 arcmin [$t_{(10)}$=2.41, p=0.03] and 15 arcmin [$t_{(10)}$=2.75, p=0.02]. These differences could be either due to reduced pupil size or normal ageing.

Table 2 compares latency and amplitude of the P100 parameter for young adult group with natural pupil size (≥5.00 mm) and while wearing prosthetic contact lens with pupil size 3mm. To reiterate, VEP was always recorded with natural pupils first followed by recording with prosthetic contact lens. There was no significant effect of pupil size on P100 latency for stimulus size 60 arcmin [$t_{(5)}$=-1.93, p=0.11] and 15 arcmin [$t_{(5)}$=-1.94, p=0.11]. The reduction in P100 amplitude with smaller pupil size was statistically significant

for stimulus size 60 arcmin [$t_{(5)}$=2.85, p=0.04] and 15 arcmin [$t_{(5)}$=6.19, p=0.002]. These differences indicate that reduced P100 amplitude in an otherwise healthy visual system is largely contributed by reduced pupil size.

Table 1. P100 latency and amplitude in young adults (pupil size ≥5.0mm) and older adults (pupil size ≤3.00mm)

Stimulus size	Participant group	P100 latency (msec)	*p* value	P100 amplitude (microvolt)	*p* value
60 arcmin	Young adults pupil size ≥5.00 mm	103.90±3.40	0.31	16.00±6.35	0.03*
	Older adults pupil size ≤3.00 mm	105.73±2.42		9.12±2.93	
15 arcmin	Young adults pupil size ≥5.00 mm	110.67±4.60	0.23	20.48±6.03	0.02*
	Older adults pupil size ≤3.00 mm	115.33±7.58		11.47±5.30	

Table 2. P100 latency and amplitude in young adults with natural pupil (pupil size ≥5.0mm) and while wearing prosthetic contact lens (pupil size 3.00mm)

Stimulus size	Participant group	P100 latency (msec)	*p* value	P100 amplitude (microvolt)	*p* value
60 arcmin	Young adults pupil size ≥5.00 mm	103.90±3.40	0.11	16.00±6.35	0.04*
	Young adults pupil size 3.00 mm	107.63±2.98		12.42±4.90	
15 arcmin	Young adults pupil size ≥5.00 mm	110.67±4.60	0.11	20.48±6.03	0.002*
	Young adults pupil size 3.00 mm	116.92±3.75		14.35±4.94	

Table 3. P100 latency and amplitude in young adults while wearing prosthetic contact lens (pupil size 3.00mm) and in older adults (pupil size ≤3.00mm)

Stimulus size	Participant group	P100 latency (msec)	*p* value	P100 amplitude (microvolt)	*p* value
60 arcmin	Young adults pupil size 3.00 mm	107.63±2.98	0.25	12.42±4.90	0.19
	Older adults pupil size ≤3.00 mm	105.73±2.42		9.12±2.93	
15 arcmin	Young adults pupil size 3.00 mm	116.92±3.75	0.66	14.35±4.94	0.35
	Older adults pupil size ≤3.00 mm	115.33±7.58		11.47±5.30	

Table 3 compares P100 latency and parameter between young adults wearing prosthetic lens (pupil size 3.00mm) and older adults whose pupil size is ≤3.00mm. There was no significant difference in P100 latency for stimulus size 60 arcmin [$t_{(10)}$=1.21, p=0.24] and 15 arcmin [$t_{(10)}$=0.46, p=0.66]. There was also no significant difference in P100 amplitude for stimulus size 60 arcmin [$t_{(10)}$=1.42, p=0.19] and 15 arcmin [$t_{(10)}$=0.97, p=0.35].

DISCUSSION

In this study, we reported that in older participants with age-related pupil miosis, there is a significant reduction in P100 amplitude, but not P100 latency, compared to young adults. This is in contrast with the findings of earlier studies that did not find a significant change in P100 amplitude in older participants. For example, Gupta and Gupta (2016), with a larger sample size of 120 participants, reported a decrease in P100 amplitude that was not statistically significant. Mitchell et al. (1987) reported similar findings, although they actually defined P100 amplitude as the difference between P100 peak to N150 instead, which is dissimilar to the standards established by International Society for Clinical Electrophysiology for Vision (ISCEV) (Odom et al., 2010). It is well established that pattern reversal VEP responses are affected by healthy ageing (Tobimatsu, 1995). Indeed, these responses can also be highly variable between individual participants (Lek et al., 2019). (Lek et al., 2019) also reported no significant change in older adults for P100 amplitudes however they did not measure their participant's pupil size therefore the role of pupil size in influencing VEP responses remains unclear.

Gupta and Gupta (2016) and Mitchell et al. (1987) also reported a significant increase in P100 latency with increasing age, contrasting our findings. There are two possible reasons for such discrepancy. In these two studies, their participants age range are up to 80 years old, whereas the oldest participants in our study was 60 years old. Indeed, earlier studies have reported that the latency of P100 did not increase until the age of 60-65 years (Asselman, Chadwick, & Marsden, 1975; Hennerici, Wenzel, & Freund, 1977). In addition, at lower temporal frequencies (4–6 Hz), older adults demonstrate lower VEP magnitudes. With higher temporal frequency (above 8–10 Hz), VEP magnitudes tend to increase (Fiorentini, Porciatti, Morrone, & Burr, 1996; Porciatti et al., 1992). Our findings support the idea that the effects of age on VEP parameters are also stimulus dependent (Lek et al., 2019; Tobimatsu, 1995).

Our findings suggest that, the reduction in P100 amplitude for our older adults (age up to 60 years old) is not due to deterioration of the primary visual cortex but due to reduction in pupil size. Indeed, reduction in pupil size leads to reduced retinal illumination (Sokol et al., 1981) thus influencing P100 amplitude, as has been reported in earlier studies. We did not find significant change in P100 latency between younger and older adults, further supporting the idea that patterns of VEP responses were due to reduced pupil size i.e. reduced retinal illuminance, and not solely due to healthy ageing. However, in this study, participants were not strictly gender matched. In a future study, it is recommended that both age and gender factors could be investigated

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