Authors' response: is pupil diameter influenced by refractive error?

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Published in:
Optometry and Vision Science

DOI:
10.1097/OPX.0000000000000734

Publication date:
2015

Document Version
Peer reviewed version

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We appreciate the interest Guillon et al's have shown in our paper [1]. While we agree that the findings of a single study with a relatively small sample size cannot reach a definitive conclusion regarding the relationship between refractive error and pupil diameter, we disagree that our methodology is inadequate. We would contend that our study provides an important contribution to the literature as it is the first to investigate the relationship between pupil diameter and refractive error in young, age-matched emmetropic, myopic, and hyperopic subjects and to examine systematically how refractive correction, target luminance, and accommodative effort modulate this relationship.

We thank the authors for bringing additional articles investigating the relationship between pupil diameter and refractive error to our attention [2-5]. These articles were not omitted as a result of an incomplete literature search, as suggested by Guillon et al.; they were omitted from our citations because the methodology in these studies meant that they were not comparable to our study and therefore their inclusion would have been inappropriate. We also feel that it is unsatisfactory to cite conference abstracts in peer reviewed papers as the source data is not easily verifiable [5]. The data from all of the omitted studies [2-5] were collected under mesopic illumination conditions which, although relevant in the context of refractive surgery, are not comparable to our study in which we deliberately examined pupil diameter over a wide photopic illumination range. This is due to the fact that the influence of the accommodation response, which was central to our study, would not have been accurate in mesopic conditions and would have likely fallen to tonic resting levels.

While we appreciate the constructive criticism of Guillon et al. on our sample size and data analysis, we do not agree that our conclusions are erroneous. It is certainly true that if no significant difference is found between two or more means, this could be due to inadequate statistical power, however, this could also arise where there is no significant difference. Power is not only determined by sample size but also by experimental design and the statistical analysis used. In the re-analysis presented by Guillon et al., power was calculated assuming pairs of means were being compared using simple t-tests. In our study, we analysed our data using a Repeated Measures ANOVA, which uses pooled mean square errors to estimate both the treatment and repeated measure effects and interactions. These errors have large degrees of freedom (which can be seen in our results), demonstrating that the analysis has considerably more power to detect significant differences than that calculated by Guillon et al. For our statistical and experimental design, a power of 99% for detecting medium effect sizes was obtained (GPower), reducing to 41% for small effect sizes. This would imply that our experimental design has sufficient power to detect clinically significant differences in pupil diameter. This raises an important point: what is the minimum change in pupil diameter that is biologically meaningful in this context? If very small changes in pupil diameter are clinically insignificant then is there any need to recruit a significantly larger sample in order to demonstrate whether such a difference exists? Theoretically, studies with very large sample sizes could have so much power that clinically meaningless differences can be detected leading to exaggerated conclusions with little clinical relevance.

Furthermore, Bonferroni post-hoc tests were used in our analysis, which are highly conservative, and should therefore prevent type 1 errors, although the probability of a type 2 error will increase [6]. In order to check that no effects had been missed due to the conservatism of the Bonferroni post-hoc test, or the increased probability of a type 2 error, the data were re-analysed using a less conservative post-hoc test (Tukey HSD). Despite the use of a less conservative test, no significant differences in pupil size between the refractive groups was found.

In conclusion, we believe that our study has more power than Guillon et al. calculate because of the specific design and statistical analysis employed. The statistical power is adequate to detect medium differences in pupil diameter which correspond with clinical significance.

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