*Letters to the Editor***Pupil Motility in Long-term Diabetes**

Dear Sir,

Dr. A. B. Hreidarsson, in a recent article [4], reported that the pupil response, studied by use of infrared TV-pupillography and an "open loop" stimulatory technique, was the same in a group of long-term juvenile diabetics and a control group of nondiabetics. The evidence is persuasive. However, in describing other characteristics of his subjects, he states that "the degree of neuropathy", which ranged from nil to severe, was "judged by vibratory perception threshold and pupil size".

Are vibratory perception threshold and pupil size both measures of the same thing, diabetic neuropathy? In fact, the data in the author's article suggest they are not.

The relationship between pupil size and duration of diabetes, calculated from the author's Table 1, is inverse, as might be expected ($r = -0.43$): greater disease duration was associated with smaller pupil size. However, the relationship between disease duration and vibratory perception threshold is not even in the "expected" direction; if anything, shorter duration of disease tended to be linked to higher vibratory thresholds ($r = -0.37$).

Age, in these diabetics, was unrelated to pupil size ($r = 0.08$) but was well correlated with vibratory perception threshold ($r = 0.67$), even if one controls for the effect of disease duration ($r = 0.64$) [5]. But the relation between pupil size and disease duration, noted above, was little affected by age, yielding a first-order partial correlation [5] of $r = -0.42$.

Finally, the specific linear correlation between pupil size and vibratory perception threshold is, at best, modest ($r = -0.18$): variability in one measure of "neuropathy" accounts for only 3% of the variability in the other measure of "neuropathy".

Examination of data for male and female diabetics in Dr. Hreidarsson's sample leads to further questions. Mean ages were very similar (36 years for

males and 34 years for females); and duration of disease, which was 17 years for males and 23 years for females, was comparable. Similarly, mean pupil size of males, 27.9 mm^2 , was virtually the same as that of females, 26.8 mm^2 . On the other hand, vibratory perception threshold for males, whose mean was 20.7, was considerably higher than that for females, 12.8 (arbitrary units).

Pearson correlation coefficients based on small samples are likely to be lacking in stability [5]; nonetheless, examination of the correlation matrix relating age, duration, vibratory threshold, and pupil size, calculated from the data of Table 1 for males and for females, suggests some intriguing differences. Disease duration and pupil size were negatively correlated in females ($r = -0.59$) but not in males ($r = 0.24$). However, in males there was the "expected" relationship between smaller pupil size and higher vibratory perception threshold ($r = -0.51$); but in females the relationship was much weaker ($r = -0.12$). The correlation between age and vibratory threshold was stronger in males, $r = 0.73$, explaining two times as much variance as the same relationship, $r = 0.50$, in females.

For males, nearly three-quarters of the variance in vibratory threshold can be explained by considering the combined effect of age and pupil size ($R^2 = 0.74$); whereas for females, much less can be predicted from this combination ($R^2 = 0.28$) [5].

For several reasons, including the nature of the sample, which is clearly a selected one or "sample of convenience" [2], the various correlation coefficients above should be viewed merely as descriptive measures of association or in terms of variance explained. Tests of "significance" would be axiomatically meaningless [1, 2] in this situation.

The author suggests, reasonably, I think, in view of his findings concerning responsivity of the pupil in his sample of diabetics, that autonomic neuropathy,

not intrinsic "stiffness" of the iris tissues, must account for observed abnormalities in diabetics. Dr. Hreidarsson particularly suspects impairment of the sympathetic, not the parasympathetic, innervation to the pupil in diabetics. This again is a reasonable surmise. But I wonder whether further examination of the issue considering sex as a factor might be rewarding. Gibbons et al. found that recovery from forefoot amputation in diabetics was better for males than for females [3]. Perhaps sympathetic autonomic neuropathy is a particular concomitant of diabetes in females. As regards pupil size, at least, Professor Hreidarsson's data, showing a correlation of -0.59 between pupil size and duration of diabetes in females, but one of 0.24 in males, support this idea.

In any case, with apologies to Gertrude Stein, I think we must be careful to avoid the presupposition that in diabetics, neuropathy is neuropathy is neuropathy! Dr. Hreidarsson has presented data to suggest that pupil size and vibratory perception threshold are not measuring the same thing; and if they are both indicators of types of diabetic

neuropathy, these types appear to have different patterns of association and are only vaguely related to one another.

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References

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