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Letters to the Editor

Hardy Weinberg Equilibrium in Genetic PE Research Remains Critical to Avoid Misinterpretation

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Dear Sir:

With interest we have read the article of Ozbek *et al*. [1] regarding a possible association of the 5-HTTLPR gene polymorphism and lifelong premature ejaculation (PE) in Turkish men. However, by performing a reanalysis of their data in Table 1, we found major insufficiencies that seriously diminish the validity of their conclusion that there is a higher prevalence of SS genotype in men with lifelong PE. Apart from the fact that in Table 1, the total number of patients and controls should be 69 instead of 70, our reanalysis of their patient data showed that the observed number of genotypes in their patients is not in Hardy Weinberg equilibrium, as the authors have erroneously suggested. This becomes evident by calculating the fraction of observed genotypes in their patients (SS 0.53, SL 0.30, and LL 0.15), the fraction of expected genotypes (SS 0.47, SL 0.42, and LL 0.09), and the expected numbers of genotypes according to Hardy Weinberg. By using the required χ^2 –test within the genotype groups, we found a significant difference ($P < 0.05$) between the observed genotype numbers and the numbers that would be expected according to Hardy Weinberg equilibrium. Although the authors stated that the χ^2–test was used, they omitted to mention the important fact that the *P*-value of the χ^2–test was significantly different, which implicates with a probability of 95% that their population of men with lifelong PE does not fulfill Hardy Weinberg equilibrium. As Hardy Weinberg equilibrium is pivotal for this kind of laboratory DNA testing, it is most likely that either patient selection bias and/or inadequate laboratory DNA testing have become disturbing confounders in their study. Consequently, it is rather inevitable that comparison of their patient group with a control group, by using a χ^2–test between groups, will yield a statistically significant difference in the prevalence of genotypes, as happened in their study. Therefore, the outcome of a higher prevalence of SS genotype in Turkish men with lifelong PE could well be ascribed to methodological and/or laboratory bias and can't be generalized to the field of lifelong PE in general. In addition, contradictory to the claim by the authors, the study of Ozbek *et al* [1] is not the first report on 5-HTT genetics in premature ejaculation. In 1943, Bernhard Schapiro was the first who observed a high prevalence of PE in family members of men with lifelong PE. His historical paper, was followed by the hypothesis of Waldinger *et al* [2] in 1998 that both the intravaginal ejaculation latency time (IELT) and lifelong PE are genetically determined. In addition, in 1998 the group of Waldinger *et al* [3] reported a high prevalence of lifelong PE among first degree male relatives of Dutch men with lifelong PE and in 2007 Jern *et al.* [4] reported to have found indications that PE might be partly genetically determined in Finnish twins. For the sake of historical facts, it should also be noted that the real first DNA study showing an association between the IELT in men with lifelong PE and 5-HTTLPR polymorphism has been published by Janssen *et al* [5] in October 2008 (e-pub). In the latter study among 89 Dutch men with lifelong PE, in whom the IELT was measured with a stopwatch, it was shown that the prevalence of the LL, SL and SS genotypes was not statistically significantly different from male Caucasian Dutch controls [5]. This study also showed that men with lifelong PE, defined in terms of IELTs of less than 1 min, and with LL genotype ejaculated within a 100% shorter time ($P < 0.03$) than men with SL and SS genotypes [5]. In contrast of the current Turkish study, the observed and expected genotypes in the Dutch study of Janssen *et al*. [5] behaved according to Hardy Weinberg, meaning no statistically significant difference between the observed and expected genotypes for both patients ($P = 0.83$) and controls ($P = 0.59$).

References

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