

Technical comment

The categorisation of male and female laboratory animals in terms of “gender”

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Received 4 December 2002; accepted 10 December 2002

In reports of scientific investigations the terms “sex” and “gender” are frequently used interchangeably in spite of longstanding acceptance that each refers to different qualities of an individual’s sexuality [20]. While sex is generally acknowledged as determined by biological characteristics that, in most cases, reasonably clearly define an individual as “female” or “male” in terms of their chromosomes, hormones, genitals and secondary sexual characteristics, gender is a human social construction pertaining to qualities of “masculinity” or “femininity”. Gender accordingly refers to the way in which an individual is defined and seen in terms of the psychological, social and cultural factors that determine it [10] i.e. gender attribution. It also reflects the extent to which individuals define themselves as masculine or feminine i.e. gender identity.

Although there is almost complete consistency between sex and gender in how most individual humans are classified, notable exceptions do occur. For example, because of genital ambiguities, mismatches between biological sex and gender development may occasionally occur as a result of inappropriate gender assignment at birth [11]. Likewise, transsexualism can be viewed as a conflict between gender identity and gender assignment independent of biological sexual characteristics [10]. Therefore, in biomedical/behavioural research where the biological substrates of genetically determined sex are important, reference to the gender of participants has little meaning. This applies particularly to research involving laboratory animals. Given that the concept of gender is a construction relating to the social attribution of and personal identification with human qualities of femininity and masculinity, it is absurdly anthropomorphic to classify animals in this way. And yet in recent years there has been a significant increase in the number of research reports which refer to the gender (rather than sex) of experimental animals.

Past research which illustrated the development of opposite sexed behaviour following castration in young male animals [8] or prenatal exposure to testosterone in females [7] might be viewed as examples of the development of feminine and masculine characteristics, respectively, since the subjects retained their original biological sexuality. However, such apparently “gender-related” behaviour was still primarily due to biologically determined sexual differentiation of the developing brain [6,13] rather than to the type of socio-cultural influence that gives rise to gender in humans. It would therefore be inappropriate to make reference to gender even when describing developmentally modified animals.

A survey of articles published since 1999 in a variety of journals revealed so many examples of references to gender in rats, mice and other nonhuman animals that it would be impossible to cite them all in this brief note. Some idea of the prevalence of the practice can be gained from the titles of a very small selection of reports published during the period surveyed that describe investigations of some interest to neuroscientists [1–5,7,12,15–17,19,22]. However, it should be emphasised that the practice characterises all areas of biomedical research e.g. [14,18,20,21]. The general situation is not helped by on-line literature search resources that use sex and gender interchangeably amongst their index terms, such as MEDLINE (PubMed) produced by the National Center for Biotechnology Information.

The prevalence of interchangeable references to sex and gender in laboratory animals was well exemplified in a special issue of *Pharmacology, Biochemistry and Behavior* entitled “Special issue: Gender differences in brain and behavior”. The laudable intent of this issue was to encourage the greater use of female animals in biomedical research [23] “to highlight for the research community both the importance of gender differences in the ability to generalize findings, and to emphasize the value of such differences as an informative window into brain function” (p. 653). Unfortunately, the decision to accept the terms sex and gender as

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interchangeable [9] merely reinforced the inappropriateness of the latter when applied to animals. Of the 24 articles involved, references were made to the gender of the subjects (mainly rats) in 13, gender and sex appeared interchangeably throughout in 1, and while in the remaining 10, sex was used exclusively in the text, in one of these, “gender differences” was included in the list of descriptive terms.

Clearly, any investigation involving both male and female subjects that impacts on brain function would be concerned with possible interactions between sex-related biological characteristics and the experimental treatment(s). In such contexts the issue of gender is therefore largely irrelevant for humans and totally irrelevant for animals. It is hoped that authors will in future carefully consider the appropriateness of classifying their subjects in terms of this concept. In view of its meaningless and anthropomorphic nature when applied to nonhumans, the practice of referring to male and female animals in terms of gender should no longer be tolerated.

References

- [1] T. Cicero, B. Nock, E. Meyer, Gender-linked differences in the expression of physical dependence in the rat, *Pharmacol. Biochem. Behav.* 72 (2002) 691.
- [2] D. Crippens, M.L. White, M.A. George, J.N. Jaworski, L.J. Brunner, F.E. Lancaster, R.A. Gonzales, Gender differences in blood levels, but not brain level, of ethanol in rats, *Alcohol Clin. Exp. Res.* 23 (1999) 414–420.
- [3] R. Czerniak, Gender-based differences in pharmacokinetics in laboratory animal models, *Int. J. Toxicol.* 20 (2001) 161–163.
- [4] O. Dale, L. Thommesen, B. Mortensen, B. Hagen, Gender aspects of liver slice incubations with *N,N,N*-triethylene-thiophosphamide (Thio-TEPA) in rats and mice, *Pharmacol. Toxicol.* 84 (1999) 122–124.
- [5] K.E. Dymond, J.E. Fewell, Gender influences the core temperature response to a simulated open field in adult guinea pigs, *Physiol. Behav.* 65 (1999) 889–892.
- [6] R.A. Gorski, J.H. Gordon, J.E. Shryne, A.M. Southam, Evidence for a morphological sex difference within the medial preoptic area of the rat brain, *Brain Res.* 143 (1978) 333–346.
- [7] R.W. Goy, W.E. Bridson, W.C. Young, Period of maximal susceptibility of the prenatal female guinea pig to masculinizing actions of testosterone propionate, *J. Comp. Physiol. Psychol.* 57 (1964) 166–174.
- [8] K.L. Grady, C.H. Phoenix, W.C. Young, Role of the developing rat testis in differentiation of the neural tissues mediating mating behavior, *J. Comp. Physiol. Psychol.* 59 (1965) 176–182.
- [9] S.J. Kelly, N.L. Ostrowski, M.A. Wilson, Gender differences in brain and behavior: hormonal and neural bases, *Pharmacol. Biochem. Behav.* 64 (1999) 655–664.
- [10] S.J. Kessler, W. McKenna, *Gender: An Ethnomethodological Approach*, Wiley, New York, 1978.
- [11] J. Money, A. Ehrhardt, *Man and Woman, Boy and Girl*, Johns Hopkins University Press, Baltimore, MD, 1972.
- [12] O. Mrabet, Z. Es-Salah, A. Telhiq, A. Aubert, S. Liège, K. Choulli, P.J. Neveu, Influence of gender and behavioural lateralisation on two exploratory models of anxiety in C3H mice, *Behav. Proc.* 52 (2000) 35–42.
- [13] G. Raisman, P.M. Field, Sexual dimorphism in the neuropil of the preoptic area of the rat and the dependence on neonatal androgen, *Brain Res.* 54 (1973) 1–29.
- [14] J.F. Reckelhoff, H. Zhang, K. Srivastava, Gender differences in development of hypertension in spontaneously hypertensive rats: role of the rennin-angiotensin system, *Hypertension* 35 (2000) 490–493.
- [15] R.L. Roof, E.D. Hall, Estrogen-related gender difference in survival rate and cortical blood flow after impact-acceleration head injury in rats, *J. Neurotrauma* 17 (2000) 1155–1169.
- [16] R.L. Roof, D.G. Stein, Gender differences in Morris water maze performance depend on task parameters, *Physiol. Behav.* 68 (1999) 81–86.
- [17] C.W. Schindler, J.G. Bross, E.B. Thorndike, Gender differences in the behavioural effects of methamphetamine, *Eur. J. Pharmacol.* 442 (2002) 231–235.
- [18] F. Schmidt, Y. Yoshimura, R.X. Ni, S. Kneesel, C.E. Constantinou, Influence of gender on the diurnal variation of urine production and micturition characteristics of the rat, *Neuroural. Urodyn.* 20 (2001).
- [19] F.E. Sieber, P. Hurn, N.J. Alkayed, R.J. Traystman, Gender-based differences in Na^+ – K^+ adenosine triphosphatase activity occur in the microcirculation of the diabetic brain, *Anesthesiology* 94 (2001) 372–375.
- [20] R.K. Unger, Towards a redefinition of sex and gender, *Am. Psychologist* 34 (1979) 1085–1094.
- [21] B.C. van der Eerden, N.P. van Til, A.O. Brinkmann, C.W. Lowik, J.M. Wit, M. Karperien, Gender differences in expression of androgen receptor in tibial growth plate and metaphyseal bone in the rat, *Bone* 30 (2002) 891–896.
- [22] M.A. Vicente-Torres, P. Gil-Loyzaga, Age- and gender-related changes in the cochlear sympathetic system of the rat, *Neurosci. Lett.* 319 (2002) 177–179.
- [23] M.A. Wilson, S.J. Kelly, S.E. File, Editorial, *Pharmacol. Biochem. Behav.* 64 (1999) 653.