

DEFINITION & SYNOPSIS OF THE ETIOLOGY OF ADULT GENDER IDENTITY DISORDER & TRANSSEXUALISM

1. Gender Identity Disorder is defined as an incongruence between the physical phenotype and the gender identity^[1], that is, the self identification as male or female. The experience of this incongruence is termed Gender Dysphoria. The most extreme form, in which individuals need to adapt their phenotype with hormones and surgery to make it congruent with their gender identity, is called transsexualism^[2]. Those individuals experiencing this condition are referred to as trans people, that is, trans men (female to male) and trans women (male to female).
2. Transsexualism can be considered to be a neuro-developmental condition of the brain.^[3] Several sexually dimorphic nuclei have been found in the hypothalamic area of the brain (Allen & Gorski, 1990; Swaab *et. al.*, 2001). Of particular interest is the sexually dimorphic limbic nucleus called the central subdivision of the bed nucleus of the stria terminalis (BSTc) which appears to become fully volumetrically sexually differentiated in the human brain by early adulthood. This nucleus has also been found to be sexually dimorphic in other mammalian and avian species (Miller *et. al.*, 1989; Grossmann *et. al.*, 2002). In human males the volume of this nucleus is almost twice as large as in females and its number of neurons is almost double ($P < 0.006$) (Zhou *et. al.*, 1995; Kruijver *et. al.*, 2000; Chung *et. al.*, 2002).
3. The Kruijver *et. al.* study, cited above, indicates that in the case of transsexualism this nucleus has a sex-reversed structure. This means that in the case of trans women ($n=7$), the size of this nucleus and its neuron count was found to be in the same range as that of the female controls ($n=13$) and, therefore, women in the general population. In the only available brain of a trans man, the volume and structure of this nucleus was found to be in the range of the male controls ($n=21$) and, therefore, men in the general population. It is hypothesised that this male-like BSTc will be present in other trans men as well. These findings were independent of sexual orientation and of the use of exogenous sex hormones. In the 42 human brains collected for this study, the BSTc was found to have a structure concordant with the psychological identification as male or female. It is inferred that the BSTc is an important part of a sexually dimorphic neural circuit, and that it is involved in the development of gender identity (Kruijver *et. al.*, 2000).
4. Sexual differentiation of the mammalian brain starts during fetal development and continues after birth (Kawata, 1995; Swaab *et. al.*, 2001). It is hypothesised that in humans, in common with all other mammals studied, hormones significantly influence this dimorphic development although, at present, the exact mechanism is incompletely understood. It is also postulated that these hormonal effects occur at several critical periods of development of the sexual differentiation of the brain during which gender identity is established, initially during the fetal period, then around the time of birth; and also post-natally. Factors which may contribute to an altered hormone environment in the brain at the critical moments in its early development might include genetic influences (Landén, 1999; Coolidge *et. al.*, 2002) and/or medication, environmental influences (Diamond *et. al.*, 1996; Whitten *et. al.*, 2002), stress or trauma to the mother during pregnancy (Ward *et. al.*, 2002; Swaab *et. al.*, 2002).
5. Gender identity usually continues along lines which are consistent with the individual's phenotype, however, a very small number of children experience their gender identity as being incongruent with their phenotype. Adult outcomes in such cases are varied and cannot be predicted with certainty. It is

^[1] The term 'gender identity' is used, in the UK, to indicate the self-identification as male or female. However, terminology varies around the world, and the term 'sexual identity' is preferred by many in the US. (pace Professor Milton Diamond). See "Sex and Gender are different: Sexual Identity & Gender Identity are Different", (2000) *Clinical Psychology & Psychiatry*, Vol 7 (3):320-334.

^[2] The transsexual condition is also referred to in various ways (Diamond M, 2002) "What's In a Name? Some terms used in the discussion of Sex and Gender". *Transgender Tapestry*.

^[3] The UK government recognises that transsexualism is not a mental illness. See Lord Chancellor's Department (now renamed Department of Constitutional Affairs) – government policy concerning transsexual people.
www.lcd.gov.uk/constitution/transsex/policy.htm

only in a minority of these children that, regardless of phenotypical socialisation and nurture, this incongruence will persist into adulthood and manifest as transsexualism (Green, 1987; Ekins, 1997; Prosser, 1998; Di Ceglie, 2000; Ekins & King, 2001; Bates, 2002).

6. As stated, in trans people, a sex-reversed BSTc has been found. The findings of a specific sex-reversed brain organisation in trans people provides evidence consistent with the concept of a biological element in the etiology of transsexualism. The evidence for an innate biological predisposition is supported by other studies, one example of which, indicates a higher than average correlation with left-handedness (Green & Young, 2001). Where the predisposition for transsexualism exists, psycho-social and other factors may subsequently play a role in the outcome, however, there is no evidence that nurturing and socialisation in contradiction to the phenotype can cause transsexualism, nor that nurture which is entirely consistent with the phenotype can prevent it (Diamond, 1996). There is further clear evidence from the histories of conditions involving anomalies of genitalia, that gender identity may resolve independently of genital appearance, even when that appearance and the assigned identity are enhanced by medical and social interventions (Imperato-McGinley *et al.*, 1974; Imperato-McGinley *et al.*, 1979a; Imperato-McGinley *et al.*, 1979b; Rösler & Kohn, 1983; Meyer-Bahlburg *et al.*, 1996; Diamond, 1997; Diamond & Sigmundson, 1997; Kipnis & Diamond, 1998; Reiner, 1999; Reiner, 2000). It is not possible to identify one single cause for transsexualism: rather, its causality is highly complex and multifactorial. The condition requires a careful diagnostic process, based largely on self-assessment, facilitated by a specialist professional.
7. In conclusion, transsexualism is strongly associated with the neurodevelopment of the brain. (Zhou *et al.*, 1995; Kruijver *et al.*, 2000). The condition has not been found to be overcome by contrary socialisation, nor by psychological or psychiatric treatments alone (Green, 1999). Individuals may benefit from an approach that includes a programme of hormones and corrective surgery to achieve realignment of the phenotype with the gender identity, accompanied by well-integrated psychosocial interventions to support the individual and to assist in the adaptation to the appropriate social role (Green and Fleming, 2000). Treatments may vary, and should be commensurate with each individual's particular needs and circumstances.

Signatories {original authors are asterisked}

Dr Henk Asscheman, MD, PhD. (The Netherlands)*
 Professor Michael Besser, DSC, MD, FRCP, SmedSci. (UK)
 Dr Susan Carr, MPhil. MFFFP. DDRCOG. (UK)
 Professor dr Peggy Cohen-Kettenis PhD. (The Netherlands)
 Dr Pamela Connolly PhD. (USA)
 Professor dr Petra De Sutter, PhD. (Belgium)
 Professor Milton Diamond, PhD. (Chair) (USA)*
 Dr Domenico Di Ceglie, FRCPsych., DIP. PSICHIAT. (Italy) (Child Section) (UK)*
 Professor Louis Gooren, MD, PhD. (The Netherlands)
 Professor Richard Green, MD, JD, FRCPsych. (UK)
 Dr Lynne Jones, MP, PhD. (UK)
 Dr Frank Kruijver, MD. (The Netherlands)*
 Dr Joyce Martin, MRCGP, MB, ChB, D.Obst.RCOG. (UK)*
 Dr Zoe-Jane Playdon, BA(Hons), PGCE, MA, MEd, PhD, DBA, FRSA. (UK)*
 Mr David Ralph, MBBS, BSc, FRCS, MS. (UK)
 Mrs Terry Reed, JP, BA(Hons), MCSP, SRP, Grad Dip Phys. (UK)*
 Dr Russell Reid, MB, ChB, FRCPsych. (UK)*
 Professor William Reiner, MD. (USA)
 Mr M. Royle, MBBS, FRCS (Urol) (UK)
 Professor Dick Swaab, MD, PhD. (The Netherlands)
 Mr Timothy Terry, BSc, MB, BS, LRCP, FRCS (Urol), MS (UK)
 Mr Philip Thomas MBBS, FRCS (Urol). (UK)
 Professor James Walker, MD, FRCP, FRCOG. (UK)
 Dr Philip Wilson, DPhil MRCP MRCPC FRCGP. (UK)
 Dr Kevan Wylie, MB, MmedSc, MD, FRCPsych, DSM. (UK)

References:

1. Allen LS & Gorski RA. (1990) Sex Difference in the bed nucleus of the stria terminalis of the human brain, Journal of Comparative Neurology **302**:697-706.
2. Bates DJ. (2002) Locating the transsexual narrative in the gendered landscape. The University of Waikato; New Zealand. 437 pages
3. Chung WCJ, De Vries GJ, Swaab D. (2002) Sex differentiation of the bed nucleus of the stria terminalis in Humans may extend into adulthood, Journal of Neuroscience , **22**(3):1027-1033.
4. Coolidge, FL, Theda LL, & Young SE (2002) The heritability of gender identity disorder in a child and adolescent sample. Behavior Genetics **32**:251-257.
5. Diamond, M (1996) Self-testing among transsexuals: a check on sexual identity. Journal of Psychology & Human Sexuality **8**(3): 61-82.
6. Diamond M, (1997) Sexual identity and sexual orientation in children with traumatized or ambiguous genitalia. Journal of Sex Research **34** (2 May): 199-222.
7. Diamond MT & Sigmundson HK, (1997), Sex reassignment at birth. Long term review and clinical implications. Archives of Pediatrics and Adolescent Medicine **151**: 298-304.
8. Di Ceglie D, (2000) Gender identity disorder in young people, Advances in Psychiatric Treatment, **6**:458-466.
9. Ekins R, (1997); Male Femaling. London, New York, Routledge, 185 pages.
10. Ekins R & King D, (2001) Telling body transgendered stories in Unseen Genders: Beyond the Binaries, editors: F Haynes & T McKenna. Peter Lang, New York.
11. Green R & Fleming DT, (2000); Transsexual Surgery Follow-up: Status in the 1990s, Annual Review of Sex Research, editor J Bancroft, **1**:163-174.
12. Green, R (1987) The "Sissy Boy Syndrome" and the Development of Homosexuality. New Haven CT, Yale Univ.
13. Green, R (1999) Cited in Bellinger v Bellinger, Ct of Appeal, para 32 July 17th (Judgement,2001)TLR 22-11-2000
14. Green R, & Young R, (2001) Hand Preference, Sexual Preference, and Transsexualism. Archives of Sexual Behavior **30**:565-574.
15. Grossmann, R, Jurkevich A, Kohler A. (2002) Sex dimorphism in the avian arginine vasotocin system with special emphasis to the bed nucleus of the stria terminalis. Comp Biochem Physiol A Mol Integr Physiol **131**(4):833-7.
16. Imperato- McGinley J, Guerrero L, Gautier T, and Peterson RE. (1974). Steroid 5 α -Reductase Deficiency in man: An inherited form of male pseudohermaphroditism. Science **27**, 1213-1215.
17. Imperato-McGinley, J. Peterson RE, Gautier T, Sturia E. (1979a) Male pseudohermaphroditism secondary to 5 α -reductase deficiency-a model for the role of androgens in both the development of the male phenotype and the evolution of a male gender identity. Journal of Steroid Biochemistry, **11**(1B):637-645.
18. Imperato-McGinley J, Peterson RE, Stoller R, and Goodwin WE. (1979b). Male pseudo-hermaphroditism secondary to 17 β -Hydroxysteroid Dehydrogenase Deficiency: Gender role change with puberty. Journal of Clinical Endocrinology and Metabolism **49**, 391-395.
19. Kawata M (1995) Roles of steroid hormones and their receptors in structural organization in the nervous system. Neuroscience Research **24**:1-46.
20. Kipnis K and Diamond M. (1998) Pediatric ethics and the surgical assignment of sex. Journal of Clinical Ethics **9**(4):398-410.
21. Kruijver FPM, Zhou J-N, Pool CW, Hofman MA, Gooren LJG, Swaab DF. (2000) Male to female transsexuals have female neuron numbers in a limbic nucleus. Journal of Clinical Endocrinology and Metabolism **85**(5):2034-2041.
22. Landén M (1999). Transsexualism, epidemiology, phenomenology, ætiology, regret after surgery, and public attitudes. PhD Göteborg University.
23. Mayer-Bahlburg HFL, Gruen RS, New MI, Bell JJ, Morishima A, Shimshi M, Bueno Y, Vagus I, Baker SW. (1996) Gender change from female to male in classical congenital adrenal hyperplasia. Hormones and Behavior **40**:319-332.
24. Miller MA, Vician L, Clifton DK, Dorsa D. (1989) Sex differences in vasopressin neurons in the bed nucleus of the stria terminalis by in situ hybridization. Peptides **10**(3):615-9.
25. Prosser J. (1998) Second skins: The body narratives of transsexuality. New York, Columbia University Press. 270 pages.
26. Reiner WG, Associate Professor, Division of Pediatric Urology, Johns Hopkins Medical Institutions, featured speaker at NYU Child Study Center Grand Rounds Summary September 29, (2000) The Genesis of Gender Identity in the Male: Prenatal Androgen Effects on Gender Identity and Gender Role.
27. Reiner, WG. (1999). Assignment of sex in neonates with ambiguous genitalia. Current Opinions in Pediatrics **11**(4):363-365.
28. Rösler A & Kohn G. (1983) Male pseudohermaphroditism due to 17 β -hydroxysteroid dehydrogenase deficiency: studies on the natural history of the defect and the effect of androgens on the gender role. Journal of Steroid Biochemistry **19**(1):663-674.
29. Swaab DF, Chung WCJ, Kruijver FPM, Hofman MA, Ishunina TA. (2001) Structural and functional differences in the human hypothalamus. Hormones and Behavior **40**:93-98.
30. Swaab DF, Chung WCJ, Kruijver FPM, Hofman MA, Hestiantoro A. (2003) Sex differences in the human

- hypothalamus in the different stages of human life. Neurobiology of aging Suppl 1:S1-16; discussion S17-9.
31. Ward OB, Ward IL, Denning JH, French JA, Hendricks SE. (2002) Postparturitional testosterone surge in male offspring of rats stressed and/or fed ethanol during late pregnancy. Hormones and Behavior **41**:229-235.
 32. Whitten PL, Patisaul HB, Young LJ. (2002) Neurobehavioral actions of coumestrol and related isoflavonoids in rodents. Neurotoxicology and Teratology **24**:47-54.
 33. Zhou J-N, Hofman MA, Gooren LJG, Swaab DF. (1995) A sex difference in the human brain and its relation to transsexuality. Nature **378**:68-70.

Funded by Gender Identity Research & Education Society, the King's Fund & the BCC Trans Group
The King's Fund bears no responsibility for the text

