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Hormone-Dependent Brain Development and Behaviour

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Abstract

Hormone and neurotransmitter levels being homotypical for the own genetic sex result in homotypical ontogenesis or eugenesis. Such levels being heterotypical for the own genetic sex – i.e. more or less homotypical for the opposite sex – give rise to heterotypical ontogenesis or paragenesis. Paragenesis can be subdivided into sano-genetic paragenesis without severe complications and need of therapy (bi- and homosexuality) and pathogenetic paragenesis with severe complications and need of therapy (somatic pseudohermaphroditism and transsexualism). Hormone and neurotransmitter levels being abnormal or atypical for both sexes result in atypical ontogenesis or dysgenesis. Dysgenesis can be unified with pathogenetic paragenesis to teratogenesis. Hence, teratogenesis is the development of malformations (teratomorphogenesis) or malfunctions (teratophysio- or teratopsychogenesis). Due to this subdivision of ontogenesis, teratogenesis is always a process of pathogenesis, which should be prevented by optimizing the psychosocial and natural environment and/or correcting abnormal levels of hormones and neurotransmitters, especially during brain development. In contrast, the development of bi- or homosexuality is a process of sanogenesis. Hence, bi- and homosexuality can and should no longer be considered as diseases, but generally recognized, tolerated and accepted as natural sexual variants.

Zusammenfassung

Hormon- und Neurotransmitterspiegel sind homotypisch für das eigene genetische Geschlecht und steuern eine homotypische Ontogenese oder Eugenese. Wenn solche Spiegel heterotypisch für das

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eigene genetische Geschlecht sind, das heißt dann mehr oder weniger homotypisch für das entgegengesetzte Geschlecht, sind sie die Ursache für eine heterotypische Ontogenese oder Paragenese. Paragenetische Entwicklungen kann man in sanogenetische Paragenese ohne schwere Komplikationen und ohne Notwendigkeit von Therapie (Bi- und Homosexualität) und pathogenetischer Paragenese einteilen, bei der schwere Komplikationen und die Notwendigkeit von Therapie (somatischer Pseudohermaphroditismus und Transsexualismus) vorliegen. Wenn anormale oder atypische Hormon- und Neurotransmitterspiegel vorliegen, dann führt dies bei beiden Geschlechtern zu einer atypischen Ontogenese oder Dysgenese. Dysgenese kann mit pathogenetischer Paragenese zu Teratogenese zusammengefaßt werden. Dann ist also Teratogenese die Entwicklung von Fehlformen (Teratomorphogenese) oder Fehlfunktionen (Teratophysio- oder Teratopsychogenese). Entsprechend dieser Charakterisierung der Ontogenese ist eine Teratogenese immer ein Prozeß von Pathogenese, der dadurch vermieden werden sollte, daß die psychosoziale und natürliche Umgebung so optimal wie möglich gestaltet wird und, je nach Gegebenheit, anormale Hormon- und Neurotransmitterspiegel, besonders während der Hirnentwicklung, korrigiert werden. Demgegenüber ist die Entwicklung zur Bi- oder Homosexualität ein Prozeß der Sanogenese. Von daher können und sollen Bi- und Homosexualität nicht länger als Krankheiten betrachtet werden, sondern allgemein als natürliche sexuelle Varianten eingeschätzt, toleriert und akzeptiert werden.

Magnus Hirschfeld is world-wide recognized as outstanding pioneer and initiator of sex research (Hoenig, 1977; Whitam, 1980). As Jewish sexologist and champion of sexual minorities he was often exposed to unjustified attacks.

As early as 1897 he organized the „Wissenschaftlich-Humanitäre Komitee" (Scientific Humanitarian Committee) with the aim of decriminalization of sexual variations. Since 1899 he published the „Jahrbücher für sexuelle Zwischenstufen" (Annals of Sexual Intermediacy). In 1908 he founded the „Zeitschrift für Sexualwissenschaft" (Journal for Sex Research) and 1913 together with Bloch, Eulenburg and Körber the „Medizinische Gesellschaft für Sexualwissenschaft" (Medical Society for Sexual Science) and later on together with Ellis and Forel the World League for Sex Reform. In 1918 Hirschfeld founded the first Institute for Sexology in Berlin and gathered data of about 8000 homosexuals and 2000 transvestites and transsexuals, respectively. The term transsexualism was also introduced by Hirschfeld.

Hirschfeld was the first to postulate – in contrast to Freud – that genuine homosexuality occurs spontaneously and independently of postnatal psychosocial factors. This postulate was later strongly confirmed by psychologists and sociologists in a Kinsey-Institute-Report (Bell et al., 1980). Hirschfeld described behavioural differences between homosexuals and heterosexuals occurring in

childhood and observed that many homosexuals display homosexual tendencies as early as before puberty. Furthermore, he developed the „Sexuelle Zwischenstufentheorie" (Theory of Sexual Intermediacies). He emphasized the importance of Endocrinology for elucidation of the aetiogenesis of sexual variations and deviations. In 1912, he postulated endocrine substances which are produced in tests as "Andrin" and in ovaries as "Gynaecin" and are able to stimulate the sexual drive. Later on several researchers received the Nobel Prize for the isolation, characterization and synthesis of such substances. In addition, Magnus Hirschfeld postulated that a bisexual „Anlage" (lay-out) of the brain is responsible for different developments of the direction in sexual drive. Genetic and endocrine factors were presumed to be the reason for such variations. Genuine homosexuality was considered to be a inborn, natural, sexual variation.

On the one hand, Magnus Hirschfeld described an increased familial frequency of homosexuality as well as a high concordance in identical and discordance in nonidentical twins. This thesis of a genetic component in the aetiogenesis of homosexuality was then strongly supported by his friend Kallmann (1953) in the USA. On the other hand, Hirschfeld stimulated Eugen Steinach in Vienna to implant tests and ovaries in castrated animals of the opposite sexes and to study their effects on sexual behaviour. Steinach recognized that sex-specific mating and gender role behaviour are influenced, indeed, by endocrine factors of the gonads. Following prepubertal castration plus implantation of the opposite gonads he achieved a certain masculinization of psychosexual behaviour in females and feminization in males. Most of all, Steinach (1912) reported that these effects were the stronger the earlier gonadectomy and transplantation of the opposite gonads were carried out before puberty. Some years ago Hirschfeld had convinced his friend Iwan Bloch, who was the founder of interdisciplinary sexology, that genuine homosexuality should be recognized as an inborn phenomenon and separated from pseudohomosexuality, i.e., occasional homosexual activities. Subsequently, Bloch postulated at the beginning of this century a chemical factor to exist in the fetus that may affect sexual orientation in later life. In 1936, Vera Dantchakoff succeeded, indeed, in demonstrating that prenatal administration of the male sex hormone testosterone in female guinea pigs resulted in masculinization of their postpubertal sexual behaviour.

Since 1925 my teacher and predecessor Walter Hohlweg had worked with Eugen Steinach in Vienna and since 1928 in the laboratories of the Schering AG in Berlin. There he described the positive oestrogen feedback, i.e., the increased release of luteinizing hormone (LH) from the pituitary in female animals following oestrogen administration. Furthermore, he discovered the so-called "sex centre" in the brain which is affected by sex hormones and responsible for the secretion of gonadotrophins in the hypophysis. This discovery of the "hypothalamo-hypophysial-gonadal system" was later regarded as a decisive event for the foundation of Neuroendocrinology (Dörner and Hinz, 1988).

Some years before the discovery of the gonadotrophic hormones of the pituitary had been achieved by the outstanding Jewish scientists Selmar Aschheim and Bernhard Zondek in the hormone laboratory of the Department for Gynaecology and Obstetrics in the Charité, Berlin. Walter Hohlweg, who was called in

1945 to the Charité as successor of Aschheim, founded from this laboratory in 1952 our Institute of Experimental Endocrinoloy. In 1953, I received the M.D. of Humboldt University for a thesis written in this Institute and became successor of Hohlweg in 1962.

Since this period the following findings on "Sexual Endocrinology" were obtained by our group in extensive animal experiments and clinical studies. (Dörner, 1976; 1980; 1988a, b, c; Dörner et al., 1986).

1. Different regions of the brain are responsible for male and female sexual behaviour.
2. Variations of sex-specific sex hormone levels, when occurring during critical periods of brain development, lead to permanent structural and/or biochemical changes of these brain regions, which are associated with lifelong variations of sexual orientation (bi- or homosexuality). In this case, the development of male and female bi- or homosexuality is favoured by a deficiency of male sex hormones (androgens) in males and their excess in females, respectively. Thus, experimental models of male and female homosexuality were developed in rats. Castration performed shortly after birth in males followed by tests implantation or androgen administration in adulthood led to predominantly heterotypical sexual behaviour, i.e., to male homosexuality. On the other hand, androgen treatment that was started in females before birth gave rise to female homosexuality in later life. A clear-cut positive oestrogen feedback on LH secretion was only evokable in heterosexual female and homosexual male animals.
3. A positive feedback was also evokable in homosexual men following a singel oestrogen injection, in contrast to heterosexual men. This finding suggested that homosexual men possess, at least in part, a predomonantly female-differentiated brain. These data were than strongly confirmed by other authors (Gladue et al., 1984).
4. Stressful situations in prenatal life as well as specific genetic alterations were recognized as possible causes of androgen deficiency in males and androgen excess in females. Such alterations are responsible for variations of sexual brain differentiation. Thus, in homosexual women a slight, heterozygous form of 21-hydroxylase deficiency was diagnosed, which can lead to increased production of adrenal androgens and hence to more or less heterotypical brain development. Various heterozygous genetic alterations display a high prevalence in all populations and are generally not considered as a disease. Therefore, in my opinion, there is also no reason for the WHO to keep homosexuality in the international classification of diseases.
5. The effects of sex hormones on brain development are mediated, at least in part, by neurotransmitters. Moreover, neurotransmitters were recognized to be gene- and environment-dependent organizers of the brain. Therefore, the effects of genes, sex hormones and of the psychosocial environment on sexual differentiation, maturation and function of the brain do not represent alternative but complementary factors; the more so as all of them are mediated by neurotransmitters.

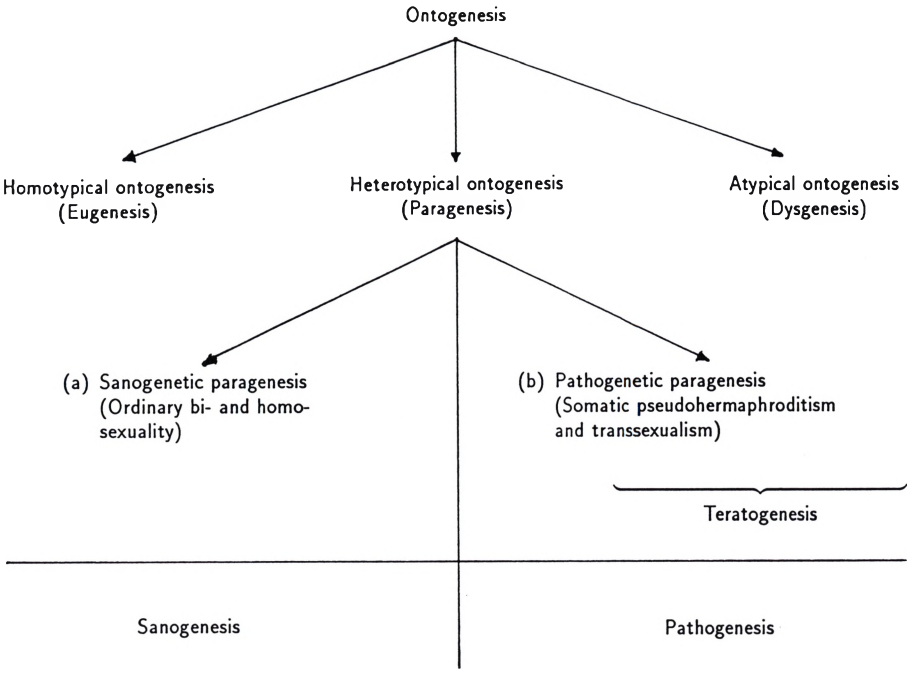

Fig. 1. Gene- and environment-dependent ontogenesis mediated by hormones and neurotransmitters

In the hormone- and neurotransmitter-dependent ontogenesis, we can distinguish between a homotypical, heterotypical and atypical ontogenesis (Fig. 1). In the case of homotypical ontogenesis or eugenesis a development occurs that is typical for the own genetic sex due to corresponding homotypical hormone and neurotransmitter levels. Hence, a homotypical somatic development and homotypical sexual behaviour, i.e., heterosexuality, is observed. In the case of heterotypical ontogenesis or paragenesis, on the other hand, a development occurs that is typical – at least in part – for the opposite genetic sex due to corresponding heterotypical hormone and neurotransmitter levels. Hence, in dependence of the beginning and the degree of such heterotypical hormone and/or neurotransmitter levels somatic pseudohermaphroditism or more or less heterotypical sexual behaviour, i.e. homo- or bisexuality, are found. Finally, in the case of atypical ontogenesis or dysgenesis, atypical structures and/or functions for both sexes, i.e., genuine malformations and/or malfunctions are developed. Such dysgenesis can be mediated by atypical, i.e., abnormal concentrations of hormones and/or neurotransmitters during critical differentiation and maturation periods, especially of the brain.

The heterotypical ontogenesis or paragenesis can be divided into paragenesis without severe complications and need of therapy. Simple or ordinary homosexuality per se is a heterotypical ontogenesis without severe complications and without need of therapy, whereas somatic pseudohermaphroditism or trans-

sexualism are heterotypical develoments with severe complications and need of therapy.

Structural paragenesis (somatic pseudohermaphroditism) as well as functional paragenesis with severe complications (transsexualism) can be united with dysgenesis to teratogenesis. Hence, teratogenesis is the development of malformations (teratomorphogenesis) or malfunctions (teratophysio- or teratopsychogenesis). Due to this subdivision of ontogenesis, teratogenesis is always a process of pathogenesis, which should be prevented as far as possible. In contrast, heterotypical ontogenesis without complications and need of therapy – i.e., the development of ordinary bi- or homosexuality – is no process of pathogenesis, but of sanogenesis.

Our extensive experimental and clinical studies of the past two decades suggest that genuine bi- and homosexuality are natural, biopsychosocial, gene- and/or environment-dependend sanogenetic and not pathogenetic developmental processes of the brain which are mediated by hormones and/or neurotransmitters. They are caused by heterotypical concentrations of sex hormones and/or neurotransmitters during sexual brain differentiation, which is timed in the human predominantly in prenatal life. This perception promoted already – at least in part – the decriminilization and dediscrimination of bi- and homosexuality and renders also possible a scientifically based depathologization of these sexual variations. Therefore, simple or ordinary homosexuality should no longer be considered as a disease. The complete tolerance and acceptance of bi- and homosexuality as natural sexual variants should be recognized as soon as possible by the WHO, UNESCO and World Church Council as well. Thus, simple or ordinary homosexuality is also no indication for a curative or preventive therapy. If emotions of homosexuals were partly violated in the past by a specific terminology used by our group, I would like to express my regret. This was never our intention and was mainly induced by malinterpretations through other authors. The main reason was the fact that in previous publications the total heterotypical ontogenesis – including ordinary bi- and homosexuality without complications – was united with atypical ontogenesis or dysgenesis to teratogenesis. Therefore this point was corrected in this paper (see Fig. 1).

Finally, I would like to expand the most important motto of Magnus Hirschfeld per scientiam ad justitiam"(per science to justice) to per scientiam ad justitiam et sanitatem"(per science to justice and health). This aim can be achieved for millions of human beings with ordinary bi- or homosexuality by a complete decriminilization, dediscrimination, depathologization and general social acceptance of such heterotypical sexual orientations. On the other hand, atypical behaviours for both sexes – such as developmental neuroses or even psychoses and mental disabilities – should be prevented as far as possible by optimizing the psychosocial and natural environment and/or by correcting abnormal levels of hormones and neurotransmitters during critical periods of brain development (Dörner, 1988b, c; 1989).

References

Bell, A. P., Weinberg, M. S. and Hammersmith, S. K. (1980). *Der Kinsey Institut Report über sexuelle Orientierung und Partnerwahl*, C. Bertelsmann, München

Dantchakoff, V. (1938). Rôle des hormones dans les manifestations des instincts sexuels. *Compt. rend. Acad. Sci. Paris* **206**, 945–947

Dörner, G. (1976). *Hormones and brain differentiation*. Elsevier, Amsterdam Oxford New York

Dörner, G. (1980). Sexual differentiation of the brain. *Vitamins and Hormones* **38**, 325–381

Dörner, G. (1988a). Neuroendocrine response to estrogen and brain differentiation in heterosexuals, homosexuals, and transsexuals. *Arch. Sex. Behav.* **17**, 57–75

Dörner, G. (1988b). Sexual endocrinology and terminology in sexology. *Exp. Clin. Endocrinol.* **91**, 129–134

Dörner, G. (1988c). Significance of hormone-dependent brain development and pre- and early postnatal psychophysiology for preventive medicine. Fedor-Freybergh, P. and Vogel, M. L. V. (eds.) *Prenatal and Perinatal Psychology and Medicine, Encounter with the Unborn*. The Parthenon Publishing Group, Lancs New Jersey, pp. 419–430

Dörner, G. and Hinz, G. (1988). Professor Dr. Walter Hohlweg zum 85. Geburtstag. *Zbl. Gynäkol.* **110**, 628–631

Dörner, G., McCann, S. M. and Martini, L. (1986). *Systemic hormones, neurotransmitters and brain development*. Karger, Basel

Gladue, B. A., Green, R. and Hellmann, R. E. (1984). Neuroendocrine response to estrogen and sexual orientation. *Science* **225**, 1496–1499

Hoenig, J. (1977). Dramatis peronae: selected biographical sketches of 19th century pioneers in sexology. In: Money, J. and Musaph, H. (eds.) *Handbook of sexology*. Excerpta Medica, Amsterdam London New York, pp. 21–43

Kallmann, F. J. (1953). *Heredity in health and mental disorders*. Norton, New York

Steinach, E. (1912). Willkürliche Umwandlung von Säugetier-Männchen in Tiere mit ausgeprägt weiblichen Geschlechtscharakteren und weiblicher Psyche. *Pflüger's Archiv ges. Physiol. des Menschen und der Tiere* **144**, 71–108

Whitam, F. L. (1980). Variant sexuality: Ellis, Freud, Hirschfeld, Kinsey. In: Forleo, R. and Pasini, W. (eds.) *Medical sexology*. Elsevier/North Holland Biomedical Press, Amsterdam New York Oxford, pp. 295–304