

Sexual differentiation of the human brain

Swaab DF

Netherlands Institute for Brain Research, Amsterdam

Functional sex differences in cognition, reproduction, gender and sexual orientation and in the incidence of neurological and psychiatric diseases are presumed to be based on structural and functional differences in brain structures. Factors influencing gender, i.e., the feeling to be male or female, are prenatal hormones and compounds that change the levels of these hormones, such as anticonvulsants. While an influence of genetic factors must be present, an influence of postnatal social factors has not been established. Genetic factors and prenatal hormone levels are major factors in the determination of sexual orientation, i.e. heterosexuality, bisexuality or homosexuality. There is no convincing evidence for postnatal social factors involved in the determination of gender or sexual orientation. Stress and nicotine during pregnancy also have an influence on sexual orientation. In rodents masculinization of the brain in development is due to oestrogens that are formed by aromatization of testosterone. In sexual differentiation of the human brain direct effects of testosterone seem to be of primary importance. The period of overt structural sexual differentiation of the human hypothalamus occurs between approximately four years of age and adulthood, thus much later than is generally presumed, although the late sexual differentiation may of course be based upon processes that have already been programmed in mid-pregnancy or during the neonatal period. The reported structural differences in a number of structures in the human hypothalamus and adjacent structures depend strongly on age. In addition, functional sex differences that depend on the levels of circulating hormones in adulthood and extensive sex differences in estrogen and androgen receptors have been observed in several hypothalamic and other brain structures. In fact there seem to be few, if any, brain structures that are not sensitive to sex hormones in all stages of life.

Swaab, D.F. *The Human Hypothalamus. Basic and Clinical Aspects. Part I. Nuclei of the Hypothalamus* (2003). *Part II: Neuropathology of the Hypothalamus and Adjacent Brain Structure* (2004). *Handbook of Clinical Neurology*, Vol 79 and 80, Elsevier, Amsterdam.

D.F. Swaab, Netherlands Institute for Brain Research, Meibergdreef 33, 1105 AZ Amsterdam, The Netherlands, t 020-5665500, e-mail d.swaab@nih.knaw.nl

Hersenstichting lecture
session 23