

## RESEARCH AWARD 2008

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### The Uncinate nucleus in the human hypothalamus

The human brain is early in development structurally and functionally differentiating in a way that is different for females and males (Swaab, 2007). The first structural difference in the human hypothalamus was reported by our group in the sexually dimorphic nucleus of the preoptic area (SDN-POA) (Swaab and Fliers, 1985). Another clear sex difference was found by our group in the central nucleus of the bed nucleus of the stria terminalis (BSTc). Interestingly this sex difference was found to be reversed in transsexuals (Zhou et al., 1995; Kruijver et al., 2000). This shows that the human brain has structures that can be used as a marker to determine atypical foetal brain development.

We are currently studying, in the same brain material as used for the studies mentioned above, another potential marker for atypical foetal brain development: the Uncinate Nucleus that was recently defined by Koutcherov et al., (2007). This area of the brain is part of the Medial Preoptic Area of the hypothalamus, close to the SDN-POA. Koutcherov proposed that this nucleus is the same as the one Allen et al., (1989) called INAH3 and INAH4, based on thionin staining of human brain tissue. The problem was, however, that Allen et al. (1989) did not use a chemical markers for the INAH3 and 4, so that nobody knows what structures they measured exactly. Koutcherov et al., found several specific immunocytochemical markers for the Uncinate nucleus (2007), that have now also successfully been used by us, i.e. anti-Synaptophysin and anti-Neuropeptide-Y.

Our study of the last year shows that there is indeed a sex difference in the Uncinate nucleus. We want now to finish our study on the volume of this nucleus in 12 transsexual brains and 14 matched males and 12 females using

immunocytochemistry and computer assisted image-analysis in order to determine whether also the size of this structure agrees with the gender identity of the people involved, rather than their chromosomal sex or sex of their sex organs at birth. In addition, we include the hypothalami of people with abnormal hormone levels in order to see whether the size of the Uncinate nucleus is influenced by circulating hormone levels or rather permanently programmed in size during development.

Our hypothesis is that the Uncinate nucleus may be part of a network in the brain that is involved in gender identity. We expect that ultimately, when more structural markers have been determined that are reversed in their sex difference in transsexuals, a time window can be defined in which these alterations occurred during foetal development. This would be of great help in looking for the possible cause of the atypical brain development in transsexuals and in proposing preventive measures.

Alicia Garcia-Falgueras has spend one year on a fellowship of the Spanish *Ministerio de Educación Cultura y Deporte (MECD /Fulbright)* (Ministry of Education, Culture and Deport) in the group of Prof. Swaab. She needs 3 months extension of her fellowship (5,000 euros) in order to finish the statistics and cell density measurements and write the results down in a paper for a good international scientific journal.

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