**Media Release: European College of Neuropsychopharmacology (ECNP)**

*"For the science and treatment of disorders of the brain"*

## *Research shows testosterone changes brain structures in female-to-male transsexuals*

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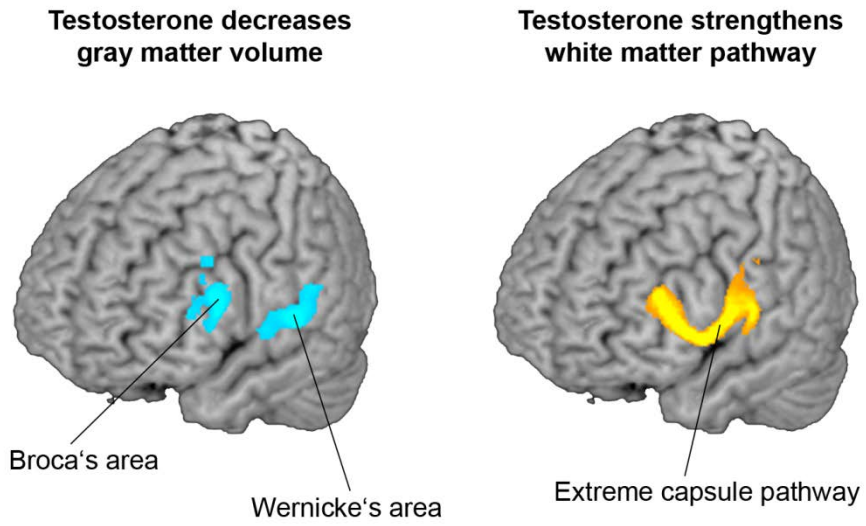
Brain imaging shows that testosterone therapy given as part of sex reassignment changes the brain structures and the pathway associated with speech and verbal fluency. This result supports research that women in general may deal with speech and interaction differently than men.

The sex hormone testosterone exerts a substantial influence on human behaviour and cognition. Previous studies have shown that testosterone has a particular influence on verbal fluency. But these investigations (which due to ethical reasons are mostly observational studies or one-off hormone administrations) have been limited in what they can show, as it has been impossible to follow the direct effect of the hormone on the brain structure.

Now a unique study has revealed the changes over time (longitudinal changes) in the brain of female-to-male transsexuals receiving continuous, high-dose hormone therapy as part of their sexual reassignment.

The results show that this therapy induces structural changes in areas of the brain involved in verbal fluency in female-to-male transsexuals. This may have wider implications, for example in the way that men and women handle speech and interaction.

The researchers, from Vienna and Amsterdam, worked with 18 female-to-male subjects (27.6 ±6.4 years), before and during testosterone treatment. The subjects underwent MRI brain scans before and after 4 weeks of the testosterone administration. The results showed that with testosterone treatment the volume of grey matter decreased in two specific regions of the brain, the Broca's and Wernicke's areas, which are mainly responsible for language processing. At the same time, the neuronal pathway (white matter) connecting these two regions via the extreme capsule got stronger.




According to researcher Dr Andreas Hahn (Vienna):

*'It has been known for some time that higher testosterone is linked to smaller vocabulary in children and that verbal fluency skills decrease in female-to-male transsexuals after testosterone treatment. This fits in well with our finding of decreased grey matter volume. However, the strengthening of the white matter in these areas was a surprise. We think that when it comes to certain language skills, the loss of grey matter outweighs the strengthened white matter connection'.*

Researcher Prof. Rupert Lanzenberger (Vienna, Austria) continued:

*'What we see is a real quantitative difference in brain structure after prolonged exposure to testosterone. This would have been impossible to understand without looking at a transsexual population. In more general terms, these findings may suggest that the genuine difference between the brains of women and men is substantially attributable to the effects of circulating sex hormones. Moreover, the hormonal influence on human brain structure goes beyond early developmental phases and is still present in adulthood'.*

Commenting for the ECNP Communications Committee, Dr Kamilla Miskowiak, said:

'*It is well-known that language development differs between girls and boys and that this is related to gender-related differences in brain maturation. However, this intriguing neuroimaging study of transsexuals before and after their female-to-male gender reassignment suggests that even adult men and women differ in brain structure within regions involved in language and speech. In particular, female-to-male gender reassignment resulted in local brain matter decrease within language processing regions, which may explain why verbal abilities are often stronger in women*.'

ENDS

**Notes for Editors**

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ABSTRACT

P.1.e.015 **Neuronal plasticity of language-related brain-regions induced by long-term testosterone-treatment-**A. Hahn[1]*, G. Kranz[1], R. Sladky[2], U. Kaufmann[3], S. Ganger[1],-A. Hummer[2], R. Seiger[1], M. Spies[1], T. Vanicek[1], D. Winkler[1],-S. Kasper[1], C. Windischberger[2], D. Swaab[4], R. Lanzenberger[1-1]*Medical University of Vienna, Department of Psychiatry and-Psychotherapy, Vienna, Austria; [2]Medical University of Vienna,-MR Center of Excellence – Center for Medical Physics and-Biomedical Engineering, Vienna, Austria; [3]Medical University-of Vienna, Department of Obstetrics and Gynecology, Vienna,-Austria; [4]Institute of the Royal Netherlands Academy of Arts and-Sciences, Netherlands Institute for Neuroscience, Amsterdam, The-Netherlands-*

**Introduction:** The sex steroid hormone testosterone exhibits a-substantial influence on behavior and cognition via the modulation-of underlying brain structures and function. Testosterone plays a-particular role in language function, showing associations with vocabulary-and sexually dimorphic gray matter regions [1]. However,-the majority of studies are limited to cross-sectional investigations-or single hormone applications due to ethical reasons. Here,-we assessed the influence of continuous high-dose testosterone-treatment on brain structure and function in female-to-male (FtM)-transsexuals before and after start of hormone therapy.-

**Methods:** Eighteen FtM subjects (27.3±6.4 years) underwent-3 and 7 Tesla magnetic resonance imaging (MRI) before and-after four weeks of testosterone treatment (1000 mg/12 weeks-intramuscular or 50 g/day transdermal). Blood samples were taken-at each MRI session to identify associations between bioavailable-testosterone (Tbio) and imaging parameters. First, gray matter-volume was assessed by segmentation of T1-weighted structural-images (MPRAGE, 1.1×1×1 mm) using voxel-based morphometry.-Second, white matter fiber tracts were reconstructed from-diffusion weighted images (1.64mm isotropic, 30 directions, bvalue=-800s/mm[2]) with probabilistic tractography. Diffusivity metrics-were then averaged along the entire tracts. Third, functional-connectivity was computed from resting-state functional MRI (7T-Tesla EPI, 1.5x1.5x3 mm). Preprocessing of functional connectivity-data included band-pass filtering and removal of motion-parameters, white matter and ventricular signal but not the global-signal. Significant clusters from the gray matter analysis were-used as seed regions for tractography and functional connectivity.-Regression analysis was carried out to evaluate relationships-between changes in Tbio and changes in imaging parameters-between the two MRI scans.-

**Results:**We observed negative associations between differences-in Tbio and differences in gray matter volume within the left-inferior frontal gyrus (Broca's area, r = −0.88) and the left superior-temporal gyrus (Wernicke's areas, r = −0.87, both p<0.05 whole-brain FWE-corrected). Accordingly, changes in Tbio predicted-changes in mean diffusivity of the extreme capsule pathway (rho=--0.63, p<0.005) but not the arcuate fasciculus. Finally, functional-connectivity between the above identified gray matter regions-increased with increasing levels of Tbio (rho=0.55, p<0.01).-None of these results changed when correcting for baseline Tbio,-baseline imaging parameters or age.-

**Conclusions:** In line with previous observations of neuronal-plasticity [1], decreases in gray matter volume of Broca's and-Wernicke's areas may be related to attenuated language performance-in men [2]. On the other hand, reductions in white matter-mean diffusivity have been demonstrated to reflect increases in-myelin formation [3]. This indicates a strengthening of the corresponding-fiber tract, which is involved in semantic processing and-language comprehension [4]. The enhanced structural connection-is further supported by the increased functional connectivity-between Broca's and Wernicke's areas. Taken together, it seems-that testosterone exhibits differential effects on neuronal plasticity-in language-specific regions of the adult human brain. Although-increases in structural and functional connectivity may compensate-deteriorations in gray matter volume, the latter effect appears-to be more important for cognitive function, since language performance-is decreased in men [2] and androgen-treated FtM [5].-

**References-**[1] Lombardo, M.V., et al., 2012. Fetal testosterone influences sexually-dimorphic gray matter in the human brain. J Neurosci 32(2): 674–680.-[2] Wolf, O.T., et al., 2000. Testosterone and cognition in elderly men: a-single testosterone injection blocks the practice effect in verbal fluency,-but has no effect on spatial or verbal memory. Biol Psychiatry 47(7):-650–654.-[3] Blumenfeld-Katzir, T., et al., 2011. Diffusion MRI of structural brain-plasticity induced by a learning and memory task. PloS One 6(6):-e20678.-[4] Saur, D., et al., 2008. Ventral and dorsal pathways for language. PNAS-105(46): 18035–18040.-[5] Van Goozen, S.H., et al., 1995. Gender differences in behaviour:-activating effects of cross-sex hormones. Psychoneuroendocrinology-20(4): 343–363.-**Disclosure statement:** This research was supported by a grant of the-Austrian Science Fund (FWF P23021) to R. Lanzenberger. The entire-manuscript was under review at the time of abstract submission.-